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## **Cortisone can increase risk of acute pancreatitis**

### **Patients treated with cortisone should be advised to refrain from alcohol and smoking**

A new study from Karolinska Institutet in Sweden shows that cortisone – a hormone used in certain medicines – increases the risk of acute pancreatitis. The results are published in the scientific journal JAMA Internal Medicine. According to the researchers, they suggest that patients treated with cortisone in some forms should be informed of the risks and advised to refrain from alcohol and smoking.

Acute pancreatitis is the most common disease of the pancreas and is caused by a sudden inflammation of the pancreas. Most patients recover without complications. However in 15 to 20 per cent of patients the disease develops to a life-threatening condition. The most common causes of the disease are gallstones and high alcohol consumption, but in a quarter of patients the causes are unknown.

Previous studies based on individual cases have indicated a link between acute pancreatitis and some medicines, such as preparations containing cortisone. Endogenous cortisone derives from an adrenal hormone and is related to stress and the regulation of the circadian rhythm. The most common form in humans is cortisol (or hydrocortisone). Synthetic cortisone is used to treat a number of medical conditions, such as asthma and autoimmune diseases (e.g. rheumatic diseases).

The present study is the first systematic study to demonstrate the relationship between medical cortisone and acute pancreatitis. Six thousand patients diagnosed with acute pancreatitis between 2006 and 2008 were compared with 61,000 healthy controls. The results show that people treated with cortisone in tablet form ran a 70 per cent higher risk of developing acute pancreatitis. This connection was observed after three days' medication, substantiating the evidence that the causal factor was the cortisone rather than the treated disease per se.

"However, there was no observable increase in risk for people who used aerosol cortisone, such as asthma inhalers," says the study's principal author Dr Omid Sadr-Azodi. "But people who start a course of cortisone are recommended to refrain from drinking and smoking, which are risk factors for acute pancreatitis."

*Publication: 'Oral glucocorticoid use is associated with an increased risk of acute pancreatitis – a population-based nested case-control study', Omid Sadr-Azodi, Fredrik Mattsson, Tomas Sjöberg Bexelius, Mats Lindblad, Jesper Lagergren & Rickard Ljung, JAMA Internal Medicine, online 25 februari 2013. Embargoed until 25th February 2013 at 4 pm US ET / 2200 CET / 2100 UK time.*

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## **Antioxidant improves donated liver survival rate to more than 90 percent**

### **Researchers from Italy have found that the antioxidant, N-acetylcysteine (NAC), when injected prior to harvesting of the liver, significantly improves graft survival following transplantation.**

Results published in the February issue of Liver Transplantation, a journal of the American Association for the Study of Liver Diseases (AASLD), suggest that the NAC effect on early graft function and survival is higher when suboptimal organs are used.

A 2010 World Health Organization (WHO) report estimates that 22,000 liver transplants were performed worldwide, with nearly 18,500 from deceased donors. According to the Organ Procurement and Transplantation Network (OPTN) close to 16,000 U.S. patients are currently on the waiting list for a liver. Nearly 18,500 deceased donor transplants were performed between January and October 2012 in the U.S. OPTN reports that roughly 7,000 livers were recovered from deceased donors during the same time period.

"Liver transplantation is the standard treatment for end-stage liver disease," explains lead author Dr. Francesco D'Amico from Padova University in Italy. "Antioxidants such as NAC could potentially reduce damage to deceased donor livers, improving graft function." Studies have shown that ischemia-reperfusion injury (IFI) - damage to the liver tissue when blood supply returns to the liver after lack of oxygen (ischemia) - often occurs during storage and preservation of donated livers, and impacts early graft function post-transplantation.

For the present study researchers assigned 140 organs to adult candidates with liver disease undergoing their first transplant. An NAC infusion of 30 mg/kg was administered to one hour prior to liver procurement and another infusion of 300 mg (150mg/kg liver weight) through the portal vein before cross-clamping. There were 69 transplant candidates who received an NAC infused organ and 71 patients who had a standard transplant without NAC.

Results indicate that graft survival rates at 3 and 12 months were 93% and 90%, respectively, for patients receiving NAC infused livers; rates were 82% and 70% in the control group. Post-transplant complication rates were 23% for the NAC group and 51% in the control group. Analysis of the 61 patients receiving suboptimal livers the incidence of organ dysfunction was lower in the NAC group compared to controls at 15% and 32%, respectively.

Dr. D'Amico concludes, "Our study was the first randomized trial to investigate the use of NAC antioxidant infusion during the liver procurement procedure. We propose that NAC be used during organ harvesting to improve liver transplantation outcomes, particularly with the increased use of suboptimal organs. NAC has a good safety profile and the very low cost per patient, make this protocol highly cost-effective in consideration of grafts survival, length of hospital stays and post operative complications. Moreover we are performing further analyses to determine beneficial effects on the other organ procured with NAC protocol."

In a related editorial published this month in *Liver Transplantation* the authors from the University of California, San Francisco (UCSF) and OneLegacy (Organ Procurement Organization, Los Angeles) highlight the importance and rarity of deceased organ donor research, such as the study by D'Amico et al., despite the fact that randomized clinical trials are essential to evidence-based medicine. Dr. Claus Niemann from the Department of Anesthesia and the Department of Surgery, Division of Transplantation at UCSF said, "Well-controlled deceased donor research is crucial to uncovering superior clinical practices that improve organ utilization and transplant outcomes. However, researchers are currently operating in a regulatory and legal vacuum since no review and oversight policies are established."

*Full citations: "Use of N-Acetylcysteine During Liver Procurement: A Prospective Randomized Controlled Study." Francesco D'Amico, Alessandro Vitale, Anna Chiara Frigo, Donatella Piovan, Alessandra Bertacco, Domenico Bassi, Rafael Ramirez Morales, Pasquale Bonsignore, Enrico Gringeri, Michele Valmasoni, Greta Garbo, Enrico Lodo, Francesco Enrico D'Amico, Michele Scopelliti, Amedeo Carraro, Martina Gambato, Alberto Brolese, Giacomo Zanus, Daniele Neri and Prof. Umberto Cillo. Liver Transplantation; (DOI: 10.1002/lt.23527) Print Issue Date: February, 2013.*

*Editorial: "Deceased Organ Donor Research: The Last Research Frontier?" Thomas Mone, John Heldens and Claus U. Niemann. Liver Transplantation; (DOI: 10.1002/lt.23579) Print Issue Date: February, 2013.*

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**OHSU scientists first to grow liver stem cells in culture, demonstrate therapeutic benefit**  
***New mouse research published in Nature raises hope that human liver stem cells can be grown, transplanted in a similar way***

PORTLAND, Ore. - For decades scientists around the world have attempted to regenerate primary liver cells known as hepatocytes because of their numerous biomedical applications, including hepatitis research, drug metabolism and toxicity studies, as well as transplantation for cirrhosis and other chronic liver conditions. But no lab in the world has been successful in identifying and growing liver stem cells in culture -- using any available technique -- until now.

In the journal *Nature*, physician-scientists in the Papé Family Pediatric Research Institute at Oregon Health & Science University Doernbecher Children's Hospital, Portland, Ore., along with investigators at the Hubrecht Institute for Developmental Biology and Stem Cell Research, Utrecht, Netherlands, describe a new method through which they were able to infinitely expand liver stem cells from a mouse in a dish.

"This study raises the hope that the human equivalent of these mouse liver stem cells can be grown in a similar way and efficiently converted into functional liver cells," said Markus Grompe, M.D., study co-author, director of the Papé Family Pediatric Research Institute at OHSU Doernbecher Children's Hospital; and professor of pediatrics, and molecular and medical genetics in the OHSU School of Medicine.

In a previous *Nature* study, investigators at the Hubrecht Institute, led by Hans Clever, M.D, Ph.D., were the first to identify stem cells in the small intestine and colon by observing the expression of the adult stem cell marker *Lgr5* and growth in response to a growth factor called *Wnt*. They also hypothesized that the unique expression pattern of *Lgr5* could mark stem cells in other adult tissues, including the liver, an organ for which stem cell identification remained elusive.

In the current *Nature* study, Grompe and colleagues in the Papé Family Pediatric Research Institute at OHSU Doernbecher used a modified version of the Clever method and discovered that *Wnt*-induced *Lgr5* expression not only marks stem cell production in the liver, but it also defines a class of stem cells that become active when the liver is damaged.

The scientists were able to grow these liver stem cells exponentially in a dish -- an accomplishment never before achieved -- and then transplant them in a specially designed mouse model of liver disease, where they continued to grow and show a modest therapeutic effect.

"We were able to massively expand the liver cells and subsequently convert them to hepatocytes at a modest percentage. Going forward, we will enlist other growth factors and conditions to improve that percentage. Liver stem cell therapy for chronic liver disease in humans is coming," said Grompe.

*The study, "In vitro expansion of single Lgr5+ liver stem cells induced by Wnt-driven regeneration," was funded by National Institutes of Health Grant ROI DK05192.*

*Investigators who contributed to this research include: Grompe, Craig Dorrell, Annelise Haft, Papé Family Pediatric Research Institute, OHSU Doernbecher Children's Hospital; Clever, Meritxell Huch, Sylvia Boj, Johan van Es, Vivian Li, Mare van de*

Wetering, Toshiro Sato, Karien Hamer, Nobuo Sasaki, Robert Vries, Hubrecht Institute for Developmental Biology and Stem Cell Research; and Milton Finegold, Texas Children's Hospital Houston.

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## **Study finds maize in diets of people in coastal Peru dates to 5,000 years ago**

### ***The very earliest emergence of civilization in South America was indeed based on agriculture as in the other great civilizations***

For decades, archaeologists have struggled with understanding the emergence of a distinct South American civilization during the Late Archaic period (3000-1800 B.C.) in Peru. One of the persistent questions has been the role of agriculture and particularly corn (maize) in the evolution of complex, centralized societies. Up until now, the prevailing theory was that marine resources, not agriculture and corn, provided the economic engine behind the development of civilization in the Andean region of Peru. Now, breakthrough research led by Field Museum curator Dr. Jonathan Haas is providing new resolution to the issue by looking at microscopic evidence found in soil, on stone tools, and in coprolites from ancient sites and dated with over 200 Carbon-14 dates.

After years of study, Haas and his colleagues have concluded that during the Late Archaic, maize (*Zea mays*, or corn) was indeed a primary component in the diet of people living in the Norte Chico region of Peru, an area of remarkable cultural florescence in 3rd millennium B.C. Their research is the subject of a paper that appears in the online Early Edition issue of Proceedings of the National Academy of Sciences (PNAS) the week of February 25, 2013. "This new body of evidence demonstrates quite clearly that the very earliest emergence of civilization in South America was indeed based on agriculture as in the other great civilizations of Mesopotamia, Egypt, India, and China," said Haas.

Haas and his team focused on sites in the desert valleys of Pativilca and Fortaleza north of Lima where broad botanical evidence pointed to the extensive production, processing and consumption of maize between 3000 and 1800 B.C. They studied a total of 13 sites. The two most extensively studied sites were Caballete, about six miles inland from the Pacific Ocean and consisting of six large platform mounds arranged in a "U" shape, and the site of, about 14 miles inland and consisting one very large mound and several much smaller mounds on either side.

The scientists targeted several areas at the sites including residences, trash pits, ceremonial rooms, and campsites. A total of 212 radiocarbon dates were obtained in the course of all the excavations.

Macroscopic remains of maize (kernels, leaves, stalks, and cobs) were rare.

However, the team looked deeper and found an abundance of microscopic evidence of maize in various forms in the excavations. One of the clearest markers was the abundance of maize pollen in the prehistoric soil samples. While maize is grown in the area today, they were able to rule out modern day contamination because modern maize pollen grains are larger and turn dark red when stain is applied. Also, modern soil samples consistently contain pollen from the Australian Pine (Casuarinaceae *Casuarina*), a plant which is an invasive species from Australia never found in prehistoric samples.

A majority of the soil samples analyzed came from trash pits associated with residential architecture. Other samples were taken from places such as room floors and construction debris. Of the 126 soil samples (not counting stone tools and coprolites) analyzed, 61 contained *Z. mays* pollen. (In fact, *Z. mays* was the second most common pollen found in the total of all samples, behind only pollen from cattails which have wind-pollinated flowers.) This is consistent with the percentage of maize pollen found in pollen analyses from sites in other parts of the world where maize is a major crop and constitutes the primary source of calories in the diet. Haas and his colleagues also analyzed residues on stone tools used for cutting, scraping, pounding, and grinding. The tools were examined for evidence of plant residues, particularly starch grains and phytoliths (plant silica bodies). Of the 14 stone tools analyzed, 11 had maize starch grains on the working surfaces and two had maize phytoliths.

Coprolites (preserved fecal material) provide the best direct evidence of prehistoric diet. Among 62 coprolites analyzed of all types – 34 human, 16 domesticated dog, and others from various animals – 43 (or 69 percent) contained maize starch grains, phytoliths, or other remains. Of the 34 human coprolites, 23 (or 68 percent) contained evidence of maize. (The second most common grain in humans came from sweet potatoes.)

Coprolites also showed that fish, mostly anchovies, did provide the primary protein in the diet, but not the calories.

The researchers concluded that the prevalence of maize in multiple contexts and in multiple sites indicates this domesticated food crop was grown widely in the area and constituted a major portion of the local diet, and it was not used just on ceremonial occasions. The research ultimately confirms the importance of agriculture in providing a strong economic base for the rise of complex, centralized societies in the emergence of the world's civilizations.

*All of the botanical work conducted on this project was carried out at the new Laboratorio de Palinología y Paleobotánica at the Universidad Peruana Cayetano Heredia, under the direction of Luis Huamán. Analysis of the botanical remains was a collaboration among Huaman, David Goldstein, National Park Service, Karl Reinhard, University of Nebraska, Cindy Vergel, Universidad Peruana Cayetano Heredia. The Project was co-directed by Haas and Winifred Creamer, Northern Illinois University, with funding from the National Science Foundation.*

[http://www.eurekalert.org/pub\\_releases/2013-02/uons-phc022513.php](http://www.eurekalert.org/pub_releases/2013-02/uons-phc022513.php)

### **Protecting health care workers**

#### ***Special face masks prevent bacterial infections as well as clinical respiratory ones: Surprise finding***

Health care workers who consistently wear special fitted face masks while on duty are much less likely to get clinical respiratory and bacterial infections, according to new research led by University of New South Wales (UNSW) academics.

The results, published in *The American Journal of Critical Care Medicine*, are particularly significant with the threat of possible pandemics and severe flu seasons, such as the current outbreak in the United States.

"When there are no drugs and vaccines available, sometimes for months at a time, then all you have is masks," says the paper's first author, Professor Raina MacIntyre, an infectious diseases expert at UNSW Medicine.

"Our health care workers, particularly those who work in emergency and respiratory departments, are at the front line of risk, and these special masks, or respirators, can protect them," she says. "They need to be wearing these regularly when they work in high risk settings or during a pandemic, not just when they think they are at risk."

The high filtration fitted face masks (known as N95 in the US, or P2 in Australia) are more expensive, and not as readily available as regular surgical face masks. Health care workers in Western countries do not regularly use any face masks, except when in theatre.

The study was conducted in China where face masks are commonplace in all health settings. Close to 1700 doctors and nurses in 19 Beijing hospitals were recruited for the study. Staff in respiratory and emergency departments, who are more likely to come across these sorts of infections, took part.

In a surprise finding, those who continuously used the N95 face masks had a protective effect not only against clinical respiratory infections, but bacterial ones too.

"Outbreaks in hospitals tend to be viral. No-one has thought of bacterial diseases as being responsible for outbreaks," Professor MacIntyre says. "In addition, bacterial co-infections commonly occur during influenza outbreaks. We suspect that if you have one infection it predisposes you to the other. There is a complex synergy between bacteria and viruses in the respiratory tract."

Those who wore the N95 mask consistently were more than twice as likely to be protected from infection, compared with those who wore a surgical mask all the time.

But the result is only significant for those who wear the masks continuously.

"This is a particularly important point," says Professor MacIntyre, the head of the School of Public Health and Community Medicine. "Many health professionals only put on a mask when they feel that they are at risk, such as if influenza has been diagnosed in their patient. But patients are often asymptomatic, and health workers may not identify all situations of risk, especially in a busy ward with high patient flow."

Professor MacIntyre has called for more awareness among health professionals and policy makers about the benefits of continuous use of N95 masks.

"You can't change a culture overnight. Practice and policy changes over time as scientific evidence changes," she says. "We need to get our health care workers used to wearing these masks, so that we are ready for any pandemic. This research is relevant for occupational health and safety policy for health workers."

Currently N95 masks are only recommended for use only in a targeted, intermittent way for some infections.

*Professor MacIntyre and UNSW's Holly Seale, Zhanhai Gao, Bayzidur Rahman, Anthony Newall and Anita Heywood worked with lead author Dominic Dwyer from Westmead Hospital and the University of Sydney, and a team at the Beijing Center for Disease Prevention and Control headed by Dr Wang Quanyi.*

*The work was funded by the National Health and Medical Research Council.*

<http://econ.st/WIKCz9>

### **A tantalising prospect**

#### ***Exotic but useful metals such as tantalum and titanium are about to become cheap and plentiful***

ALUMINIUM was once more costly than gold. Napoleon III, emperor of France, reserved cutlery made from it for his most favoured guests, and the Washington monument, in America's capital, was capped with it not because the builders were cheapskates but because they wanted to show off. How times change. And in aluminium's case they changed because, in the late 1880s, Charles Hall and Paul Héroult worked out how to separate the stuff from its oxide using electricity rather than chemical reducing agents. Now, the founders of

Metalysis, a small British firm, hope to do much the same with tantalum, titanium and a host of other *recherché* and expensive metallic elements including neodymium, tungsten and vanadium.

The effect could be profound. Tantalum is an ingredient of the best electronic capacitors. At the moment it is so expensive (\$500-2,000 a kilogram) that it is worth using only in things where size and weight matter a lot, such as mobile phones. Drop that price and it could be deployed more widely. Neodymium is used in the magnets of motors in electric cars. Vanadium and tungsten give strength to steel, but at great expense. And the strength, lightness, high melting point and ability to resist corrosion of titanium make it an ideal material for building aircraft parts, supercars and medical implants - but it can cost 50 times as much as steel. Guppy Dhariwal, Metalysis's boss, thinks however that the company can make titanium powder (the product of its new process) for less than a tenth of such powder's current price.

At the moment, titanium is usually produced by the Kroll process, which William Kroll, a metallurgist from Luxembourg, developed in the 1940s. The Kroll process starts with titanium oxide, which is derived from ores like rutile and is cheaply available (artists use it as a brilliant-white pigment). First, the oxide is reacted with chlorine, to get rid of the oxygen. The resulting chloride is then reacted with liquid magnesium or sodium, to get rid of the chlorine. This creates a porous material, titanium sponge, which is crushed and melted in a vacuum furnace to yield titanium ingots. Making tantalum is similarly onerous. The oxide (which comes from an ore called coltan) is converted to a fluoride using hydrofluoric acid, and the fluoride is then reduced with liquid sodium. Both processes are similar to the way aluminium was prepared before the days of Hall and Héroult.

Their insight was that electricity, which was starting to be generated in industrial quantities in the 1880s, could be used instead of chemicals to split the metal from the oxygen in aluminium oxide. And that is what Metalysis is doing in its new tantalum factory, and what it hopes to do for titanium and the rest.

The difference between its process and that of Hall and Héroult (and why electrolysis has not previously been used to make metals such as tantalum and titanium) is that the Hall-Héroult method requires both input oxide and output metal to be in liquid form. That demands heat. But aluminium has a fairly low melting point and its oxide can be dissolved in a substance called cryolite that also has a low melting point, so the amount of heat needed is manageable. Titanium and tantalum are not so obliging. The Metalysis trick is to do the electrolysis on powdered oxides directly, without melting them.

This was shown to be possible in 1997 when researchers at Cambridge University found that immersing small samples of certain oxides in baths of molten salt and passing a current through them transformed the material directly into metal. Metalysis was set up in 2001 to commercialise the idea and in 2005 the firm moved to Wath-upon-Deane, a village near Sheffield, in South Yorkshire, in order to tap the local engineering skills that once made the county (home of silver plate, stainless steel and the Bessemer converter) the California of metallurgy. These skills turned a technique that could produce a few grams of metal in a laboratory into a process that operates on an industrial scale.

### **The full Monty**

The process starts with powdered metal oxide, which serves as the cathode. The anode is made of carbon, and the molten salt (which has a temperature of 1,000°C) acts as an electrolyte, permitting current, in the form of oxygen ions, to pass from cathode to anode. There, the ions react to form carbon dioxide, while the cathode is gradually transformed from oxide to metal.

The company's first product is tantalum. Its factory is not much bigger than a house, but has enough capacity to supply 3-4% of the 2,500 tonnes of this metal that are used around the world each year. The resulting income, the firm hopes, will provide it with the grubstake it needs to move on to the big prize: titanium.

Even at its current price, some 140,000 tonnes of titanium are sold every year, for a total of around \$4 billion.

As the price falls, that tonnage is likely to rise, for cheap titanium has many potential uses, such as making car components that would be lighter than steel ones, thus saving fuel. This would require the powdered metal produced by Metalysis's process to be made into ingots or sheets of the sort currently used in factories. The powder itself, however, could be employed directly in what is known as additive manufacturing, which uses 3D printers to build up objects a layer at a time. Cheaper metal powders would make 3D printing much easier. This will require a far bigger factory, so Metalysis is on the lookout for a redundant aluminium smelter to convert. And if things go well with titanium, the other metals will gradually be introduced - possibly as mixtures, for Mr Dhariwal says the process will allow mixed oxides to be converted into alloys that were hitherto hard or impossible to make because of the different melting points of the components: titanium and tungsten, for example.

Modern economics have not been kind to South Yorkshire. A place that was once a centre of innovation has been sidelined by sunnier, sexier climes. But if Metalysis's technology does work at scale it may prove every

bit as important as Henry Bessemer's converter. That was the device which made steel the material of the industrial revolution, displacing wrought iron. The idea that steel itself might one day be displaced by titanium is a long shot, but it is no longer inconceivable.

<http://www.sciencedaily.com/releases/2013/02/130225112350.htm>

### **Cleaning Oil Spills With Paper Mill Sludge?**

*Eco-innovation is at its best when the waste of one industry becomes the raw material of another.*

This is precisely what the EU funded research project CAPS, is attempting to do with waste sludge from the paper industry. Its objective is to convert it into a highly absorbent material capable of cleaning up oil and chemical spills.

There are about 18 million tons of paper mill sludges produced in the EU, each year. Most of it is disposed of by burning it. This could soon change. Franc Černek, project leader at the Technological, Environmental and Logistic Centre in Koper, Slovenia came up with an innovative idea almost 17 years ago to reuse this by-product of the paper industry. "I knew about the high absorption rate of paper mill sludge for years," he said. "So I thought, why not use these characteristics and turn the waste into a useful product."

Petrol stations, car parks, laboratories and harbours could all soon use the new absorbent. Indeed, it is capable of absorbing any oil or fluid spilled on hard or water surfaces. As by-product from the paper industry, its main benefit is to be much cheaper to produce than any synthetic absorbent currently in use.

Know the first marine outdoor test has been successfully held in the harbour of Koper. In less than 3 minutes the absorbent surrounded by hydrophobic (water repellent) gauze absorbed about 1 litre of bio-diesel floating on the water surface. Another test was successfully conducted at a petrol station near Ljubljana, where accidentally spilled fuel was absorbed of the ground equally good than with the conventional absorbent. As a result, Finland and several South American countries have already expressed interest in starting their own production of the paper mill sludge absorbent.

<http://www.sciencedaily.com/releases/2013/02/130225153141.htm>

### **Virus Shows Promise as Prostate Cancer Treatment**

*A virus kills all kinds of prostate cancer cells, including hormone-resistant cells, but leaves normal cells unscathed*

A recombinant Newcastle disease virus kills all kinds of prostate cancer cells, including hormone-resistant cells, but leaves normal cells unscathed, according to a paper published online ahead of print in the Journal of Virology. A treatment for prostate cancer based on this virus would avoid the adverse side effects typically associated with hormonal treatment for prostate cancer, as well as those associated with cancer chemotherapies generally, says corresponding author Subbiah Elankumaran of Virginia Polytechnic Institute, Blacksburg. The modified virus is now ready to be tested in preclinical animal models, and possibly in phase I human clinical trials.

Newcastle disease virus kills chickens, but does not harm humans. It is an oncolytic virus that hones in on tumors, and has shown promising results in a number of human clinical trials for various forms of cancer. However, successful treatments have required multiple injections of large quantities of virus, because in such trials the virus probably failed to reach solid tumors in sufficient quantities, and spread poorly within the tumors. The researchers addressed this problem by modifying the virus's fusion protein. Fusion protein fuses the virus envelope to the cell membrane, enabling the virus to enter the host cell. These proteins are activated by being cleaved by any of a number of different cellular proteases. They modified the fusion protein in their construct such that it can be cleaved only by prostate specific antigen (which is a protease). That minimizes off-target losses, because these "retargeted" viruses interact only with prostate cancer cells, thus reducing the amount of virus needed for treatment.

Retargeted Newcastle disease virus has major potential advantages over other cancer therapies, says Elankumaran. First, its specificity for prostate cancer cells means it would not attack normal cells, thereby avoiding the various unpleasant side effects of conventional chemotherapies. In previous clinical trials, even with extremely large doses of naturally occurring strains, "only mild flu-like symptoms were seen in cancer patients," says Elankumaran. Second, it would provide a new treatment for hormone-refractory patients, without the side effects of testosterone suppression that result from hormonal treatments.

About one man in six will be diagnosed with prostate cancer, and one in 36 will die of this disease. Men whose prostate cancer becomes refractory to hormone treatment have a median survival of about 40 months if they have bone metastases, and 68 months if they do not have bone metastases.

R. Shobana, S. K. Samal, S. Elankumaran. Prostate Specific Antigen Retargeted Recombinant Newcastle Disease Virus for Prostate Cancer Virotherapy. *Journal of Virology*, 2013; DOI: 10.1128/JVI.02394-12

<http://www.bbc.co.uk/news/health-21572686>

## **Bad sleep 'dramatically' alters body**

*A run of poor sleep can have a potentially profound effect on the internal workings of the human body, say UK researchers.*

**By James Gallagher Health and science reporter, BBC News**

The activity of hundreds of genes was altered when people's sleep was cut to less than six hours a day for a week. Writing in the journal PNAS, the researchers said the results helped explain how poor sleep damaged health.

Heart disease, diabetes, obesity and poor brain function have all been linked to substandard sleep. What missing hours in bed actually does to alter health, however, is unknown. So researchers at the University of Surrey analysed the blood of 26 people after they had had plenty of sleep, up to 10 hours each night for a week, and compared the results with samples after a week of fewer than six hours a night. More than 700 genes were altered by the shift. Each contains the instructions for building a protein, so those that became more active produced more proteins - changing the chemistry of the body.

Meanwhile the natural body clock was disturbed - some genes naturally wax and wane in activity through the day, but this effect was dulled by sleep deprivation.

Prof Colin Smith, from the University of Surrey, told the BBC: "There was quite a dramatic change in activity in many different kinds of genes."

Areas such as the immune system and how the body responds to damage and stress were affected.

Prof Smith added: "Clearly sleep is critical to rebuilding the body and maintaining a functional state, all kinds of damage appear to occur - hinting at what may lead to ill health. "If we can't actually replenish and replace new cells, then that's going to lead to degenerative diseases." He said many people may be even more sleep deprived in their daily lives than those in the study - suggesting these changes may be common.

Dr Akhilesh Reddy, a specialist in the body clock at the University of Cambridge, said the study was "interesting". He said the key findings were the effects on inflammation and the immune system as it was possible to see a link between those effects and health problems such as diabetes.

The findings also tie into research attempting to do away with sleep, such as by finding a drug that could eliminate the effects of sleep deprivation.

Dr Reddy said: "We don't know what the switch is that causes all these changes, but theoretically if you could switch it on or off, you might be able to get away without sleep. "But my feeling is that sleep is fundamentally important to regenerating all cells."

<http://www.bbc.co.uk/news/science-environment-21538969>

## **Desert finds challenge horse taming ideas**

*Recent archaeological discoveries on the Arabian Peninsula have uncovered evidence of a previously unknown civilisation based in the now arid areas in the middle of the desert.*

**By Sylvia Smith BBC News**

The artefacts unearthed are providing proof of a civilisation that flourished thousands of years ago and have renewed scientific interest in man and the evolution of his relationship with animals.

The 300-odd stone objects so far found in the remote Al Magar area of Saudi Arabia include traces of stone tools, arrow heads, small scrapers and various animal statues including sheep, goats and ostriches.

But the object that has engendered the most intense interest from within the country and around the world is a large, stone carving of an "equid" - an animal belonging to the horse family.



*The Al Magar finds appear to show horse-like animals with the accessories of domestication*

According to Ali bin Ibrahim Al Ghabban, vice-president of the Saudi Commission for Tourism and Antiquities, DNA and carbon-14 (radiocarbon) tests are continuing. But initial evidence suggests that the artefacts date back 9,000 years. "These discoveries reflect the importance of the site as a centre of civilisation," he told BBC News.

"It could possibly be the birthplace of an advanced prehistoric civilisation that witnessed the domestication of animals, particularly the horse, for the first time during the Neolithic period."

The crucial find is that of a large sculptural fragment that appears to show the head, muzzle, shoulder and withers of an animal that bears a distinct resemblance to a horse. The piece is unique in terms of its size, weighing more than 135kg. Moreover, further discoveries on the same site of smaller, horse-like sculptures, also with bands across their shoulders, have opened the possibility that an advanced civilisation here may already have been using the accessories of domestication - tack - in order to control horses.

**Question time**

While archaeologists and other experts have held that horses were first tamed and exploited by man some 6,000 years ago in west Kazakhstan, experts are now starting to consider whether both location and date should be revised in light of these remarkable finds.

Whether yoking man and animal together in this way is supported by evidence is one of the many questions that face an international scientific team brought together to examine the finds. Selected from a wide background of specialisations, their unique expertise is expected to paint a picture of life in the area during pre-historic times. Michael Petraglia, professor of human evolution and prehistory at the University of Oxford has been working on the radiocarbon dating at Al Magar. He says that the site dates back even further than first thought and can reveal much about the fluctuations between wet and dry periods in the Arabian Peninsula. He adds that the horse fragment dating links with the peninsula going through a wet phase.

"This is a crucial piece of information about an area that is now hyper arid but in the past must have been a lush river valley," he explains. "It confirms that there were savannahs and grassland in the vicinity," he explains. Traces of other stone tools such as scrapers have been estimated as dating back more than 50,000 years. They were found at the site and suggest that Al Magar was a hospitable place for humans to settle in over thousands of years. In part this is due to its topography, or terrain.

Michael Petraglia says that in the past, the spot must have been a lush river valley: "There is a major valley across the area which once was a river running westward forming waterfalls and taking water to the low fertile lands west of Al-Magar," he explains. "Al Magar was situated on both banks of the river. Man lived in this area before the last desertification or before the drastic climatic changes ended with the hot dry conditions and development of deserts."

**Huge impact**

The name Al Magar means gathering or meeting place. Juris Zarins, who worked in the early days of archaeology in Saudi Arabia and found tethering stones dating back to the Neolithic period, claims that the site is within an archaeological hot bed.

"There has not been enough exploration carried out," he says. "Discoveries like this could change things." And indeed the finds have had a huge impact, sparking intense interest in Arabia's prehistory. Other finds made beyond the large and well-preserved Al Magar dovetail with current Arabian passions. Of particular interest are canine remains that resemble one of the oldest known domesticated dog breeds, the desert saluki, as well as traces of a dagger.

Abdullah Al Sharekh, an archaeologist at King Sa'ud University in Riyadh, and a pioneer of the Al Magar site, found statues within the precinct of a building. This, he says, may reveal vital clues about trade, migration and ritual. "The variety of the finds can tell us about social life and culture," he explains. "This will take time but all the evidence is here."

The discovery of the large horse sculpture fragment has naturally awakened regional interest. This in turn has compounded curiosity about other important Arabian finds.

"It is an amazing discovery that raises all sorts of questions about when man stopped tracking down wild horses and began taming and exploiting them for transport," Mr Al Ghabban says. "On this site there are very important symbols of authentic Arabian culture - equestrianism, falconry, the saluki hunting dog and wearing of the dagger."

More excavations are planned of yet other sites which have never been surveyed, and further studies are expected to unveil more important information on the Al Magar civilisation along with its impact on the history of Saudi Arabia.

[http://www.eurekalert.org/pub\\_releases/2013-02/uob-bfa022613.php](http://www.eurekalert.org/pub_releases/2013-02/uob-bfa022613.php)

**Blueprint for an artificial brain**

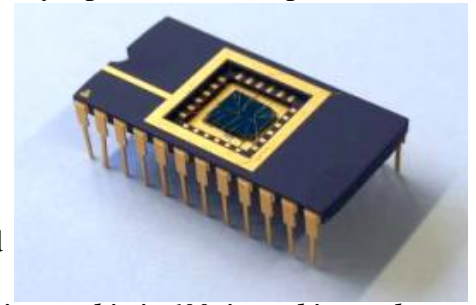
*Bielefeld physicist Andy Thomas takes nature as his model*

*This press release is available in [German](#).*

Scientists have long been dreaming about building a computer that would work like a brain. This is because a brain is far more energy-saving than a computer, it can learn by itself, and it doesn't need any programming. Privatdozent [senior lecturer] Dr. Andy Thomas from Bielefeld University's Faculty of Physics is experimenting with memristors – electronic microcomponents that imitate natural nerves. Thomas and his colleagues proved that they could do this a year ago. They constructed a memristor that is capable of learning. Andy Thomas is now using his memristors as key components in a blueprint for an artificial brain. He will be presenting his results at the beginning of March in the print edition of the prestigious Journal of Physics published by the Institute of Physics in London.



Memristors are made of fine nanolayers and can be used to connect electric circuits. For several years now, the memristor has been considered to be the electronic equivalent of the synapse. Synapses are, so to speak, the bridges across which nerve cells (neurons) contact each other. Their connections increase in strength the more often they are used. Usually, one nerve cell is connected to other nerve cells across thousands of synapses. Like synapses, memristors learn from earlier impulses. In their case, these are electrical impulses that (as yet) do not come from nerve cells but from the electric circuits to which they are connected. The amount of current a memristor allows to pass depends on how strong the current was that flowed through it in the past and how long it was exposed to it.



*A nanocomponent that is capable of learning: The Bielefeld memristor built into a chip is 600 times thinner than a human hair. Bielefeld University*

Andy Thomas explains that because of their similarity to synapses, memristors are particularly suitable for building an artificial brain – a new generation of computers. 'They allow us to construct extremely energy-efficient and robust processors that are able to learn by themselves.' Based on his own experiments and research findings from biology and physics, his article is the first to summarize which principles taken from nature need to be transferred to technological systems if such a neuromorphic (nerve like) computer is to function. Such principles are that memristors, just like synapses, have to 'note' earlier impulses, and that neurons react to an impulse only when it passes a certain threshold.

Thanks to these properties, synapses can be used to reconstruct the brain process responsible for learning, says Andy Thomas. He takes the classic psychological experiment with Pavlov's dog as an example. The experiment shows how you can link the natural reaction to a stimulus that elicits a reflex response with what is initially a neutral stimulus – this is how learning takes place. If the dog sees food, it reacts by salivating. If the dog hears a bell ring every time it sees food, this neutral stimulus will become linked to the stimulus eliciting a reflex response. As a result, the dog will also salivate when it hears only the bell ringing and no food is in sight. The reason for this is that the nerve cells in the brain that transport the stimulus eliciting a reflex response have strong synaptic links with the nerve cells that trigger the reaction.

If the neutral bell-ringing stimulus is introduced at the same time as the food stimulus, the dog will learn. The control mechanism in the brain now assumes that the nerve cells transporting the neutral stimulus (bell ringing) are also responsible for the reaction – the link between the actually 'neutral' nerve cell and the 'salivation' nerve cell also becomes stronger. This link can be trained by repeatedly bringing together the stimulus eliciting a reflex response and the neutral stimulus. 'You can also construct such a circuit with memristors – this is a first step towards a neuromorphic processor,' says Andy Thomas.

'This is all possible because a memristor can store information more precisely than the bits on which previous computer processors have been based,' says Thomas. Both a memristor and a bit work with electrical impulses. However, a bit does not allow any fine adjustment – it can only work with 'on' and 'off'. In contrast, a memristor can raise or lower its resistance continuously. 'This is how memristors deliver a basis for the gradual learning and forgetting of an artificial brain,' explains Thomas.

Andy Thomas, 'Memristor-based neural networks', *Journal of Physics D: Applied Physics*, <http://dx.doi.org/10.1088/0022-3727/46/9/093001>, released online on 5 February 2013, published in print on 6 March 2013.

<http://www.sciencedaily.com/releases/2013/02/130226081236.htm>

## **Bariatric Surgery Restores Pancreatic Function by Targeting Belly Fat**

*Gastric bypass surgery reverses diabetes by uniquely restoring pancreatic function in moderately obese patients with uncontrolled type 2 diabetes*

In a substudy of the STAMPEDE trial (Surgical Therapy And Medications Potentially Eradicate Diabetes Efficiently), Cleveland Clinic researchers have found that gastric bypass surgery reverses diabetes by uniquely restoring pancreatic function in moderately obese patients with uncontrolled type 2 diabetes.

The two-year substudy evaluated the effects of bariatric surgery and intensive medical therapy on blood sugar levels, body composition, and pancreatic beta-cell function. Striking metabolic changes were observed in patients who underwent bariatric surgery compared with intensive medical therapy, particularly in the gastric bypass treatment group.

"The substudy results extend the findings from our initial 12-month report that showed bariatric surgery can eliminate the need for diabetes medications in many obese patients with uncontrolled diabetes," said lead investigator Sangeeta Kashyap, M.D., an endocrinologist at Cleveland Clinic's Endocrinology & Metabolism Institute. "Furthermore, we observed that gastric bypass can resurrect a failing pancreas."

The cells of the pancreas that produce insulin, a hormone that helps the body store and use sugar, are called beta cells. Malfunctioning pancreatic beta cells can cause the pancreas to not release enough insulin; they can also produce insulin that the body does not recognize. When the body can't use insulin properly, it can't regulate the amount of glucose in its bloodstream.

"Gastric bypass surgery seems to uniquely restore pancreatic beta-cell function, presumably by targeting belly fat and modifying the hormones in the gastrointestinal tract," said Kashyap. "Gastric bypass remarkably targets belly fat where hormones that are toxic to the body develop."

Researchers observed that patients who underwent gastric bypass saw a greater reduction in belly fat compared to the patients who underwent sleeve gastrectomy. The substudy results indicate a correlation between a decrease in belly fat and the ability of the pancreas to start working again.

Diabetes Care just published the study results.

The prospective, randomized, controlled substudy followed 60 patients from the original STAMPEDE trial to determine the durability of the initial results and examine the metabolic changes observed with bariatric surgery. The patients were divided into three groups of 20: those who received intensive medical therapy of their diabetes, those who received intensive medical therapy plus gastric bypass surgery, and those who received intensive medical therapy plus sleeve gastrectomy. The researchers measured metabolic parameters at baseline, and at 12 and 24 months.

After two years, 41 percent of the patients who underwent gastric bypass saw their blood sugar levels back to normal. Only 10 percent of the patients who underwent sleeve gastrectomy and 6 percent who received intensive medical therapy achieved the same results.

At 12 and 24 months, patients who underwent gastric bypass achieved near normal blood sugar levels following a mixed meal test. These results were associated with a remarkable 5.8-fold increase in overall pancreatic cell function. Patients who received intensive medical therapy or underwent sleeve gastrectomy saw a 2-fold increase.

The substudy results show that gastric bypass surgery is a viable therapeutic option for the treatment of uncontrolled type 2 diabetes in moderately obese patients. The authors will continue to follow these patients for three years as further studies examining hormonal effects are warranted.

*S. R. Kashyap, D. L. Bhatt, K. Wolski, R. M. Watanabe, M. Abdul-Ghani, B. Abood, C. E. Pothier, S. Brethauer, S. Nissen, M. Gupta, J. P. Kirwan, P. R. Schauer. Metabolic Effects of Bariatric Surgery in Patients With Moderate Obesity and Type 2 Diabetes: Analysis of a randomized control trial comparing surgery with intensive medical treatment. Diabetes Care, 2013; DOI: 10.2337/dc12-1596*

<http://www.sciencedaily.com/releases/2013/02/130226113431.htm>

## **Blood Vessels 'Sniff' Gut Microbes to Regulate Blood Pressure**

*A specialized receptor in the nose is also in blood vessels throughout the body senses molecules created by intestinal microbes and responds by increasing blood pressure*

Researchers at The Johns Hopkins University and Yale University have discovered that a specialized receptor, normally found in the nose, is also in blood vessels throughout the body, sensing small molecules created by microbes that line mammalian intestines, and responding to these molecules by increasing blood pressure. The finding suggests that gut bacteria are an integral part of the body's complex system for maintaining a stable blood pressure.

A description of the research, conducted in mice and test tubes, appeared online Feb. 11 in the journal *Proceedings of the National Academy of Sciences*.

"The contribution that gut microbes apparently make to blood pressure regulation and human health is a surprise," says Jennifer Pluznick, Ph.D., assistant professor of physiology at the Johns Hopkins University School of Medicine. "There is still much to learn about this mechanism, but we now know some of the players and how they interact," she adds.

Pluznick says that several years ago, thanks to a "happy coincidence," she found -- in the kidney -- some of the same odor-sensing proteins that give the nose its powers. Focusing on one of those proteins, olfactory receptor 78 (Olf78), her team specifically located it in the major branches of the kidney's artery and in the smaller arterioles that lead into the kidney's filtering structures. Olf78 also turned up in the walls of small blood vessels throughout the body, she says, particularly in the heart, diaphragm, skeletal muscle and skin.

To figure out which molecules bind and activate Olf78, the scientists programmed cells to have Olf78 protein receptors on their surface. They also gave these same cells the ability to start a light-producing chemical reaction whenever Olf78 is activated. By adding different cocktails of molecules to the cells and measuring the

light the cells produced, they homed in on a single mixture that activated Olfr78. They then tested each component in that mix and found that only acetic acid (a.k.a. vinegar) bound Olfr78 and caused the reaction. Acetic acid and its alter ego, acetate, are part of a group of molecules known as short chain fatty acids (SCFAs). When the team tested other molecules in this group, they found that propionate, which is similar to acetate, also binds Olfr78. In the body of mammals, including humans, SCFAs are made when zillions of bacteria lining the gut digest starch and cellulose from plant-based foods. The SCFAs are absorbed by the intestines into the blood stream, where they can interact with Olfr78.

To pinpoint the effect of Olfr78, the scientists gave SCFAs to mice missing the Olfr78 gene and found that the rodents' blood pressure decreased, suggesting that SCFAs normally induce Olfr78 to elevate blood pressure. However, when they gave SCFAs to normal mice with intact Olfr78, they did not see the expected increase in blood pressure, but rather a decrease, though it was less pronounced than before.

To test the effect of reducing the SCFAs available to Olfr78, the team gave mice a three-week course of antibiotics to wipe out the gut microbes responsible for SCFA production. In this case, normal mice showed very little change in blood pressure, but mice without Olfr78 experienced an increase in blood pressure, suggesting that there were other factors involved in the Olfr78/SCFA/blood pressure relationship.

The mystery was solved, Pluznick says, when the team examined mice lacking Gpr41, a non-smell-related protein receptor located in blood vessel walls that also binds SCFAs. When SCFAs bind to Gpr41, blood pressure is decreased. The researchers eventually discovered that Olfr78 and Gpr41 both are activated by SCFAs, but with contradictory effects. The negative effect of Gpr41 is counterbalanced by the positive effect of Olfr78, but Gpr41's effect is stronger, so an increase in SCFAs produces an overall decrease in blood pressure.

"We don't have the full story yet," says Pluznick. "There are many players involved in the maintenance of stable levels of blood pressure, and these are just a few of them. We don't know why it would be beneficial for blood pressure to decrease after eating or why gut microbes would play a part in signaling that change. But our work opens the door for exploring the effects of antibiotic treatments, probiotics and other dietary changes on blood pressure levels in mice, and perhaps eventually people."

Other authors of the report include Ryan Protzko of the Johns Hopkins University School of Medicine; Jinah Han, La-Xiang Wan, Tong Wang, Anne Eichmann and Michael Caplan of the Yale University School of Medicine; Haykanush Gevorgyan, Arnold Sipos and Janos Peti-Peterdi of the University of Southern California; and others from the College de France, Columbia University, the Washington University School of Medicine and the University of Texas Southwestern Medical Center.

*J. L. Pluznick, R. J. Protzko, H. Gevorgyan, Z. Peterlin, A. Sipos, J. Han, I. Brunet, L.-X. Wan, F. Rey, T. Wang, S. J. Firestein, M. Yanagisawa, J. I. Gordon, A. Eichmann, J. Peti-Peterdi, M. J. Caplan. Olfactory receptor responding to gut microbiota-derived signals plays a role in renin secretion and blood pressure regulation. Proceedings of the National Academy of Sciences, 2013; DOI: 10.1073/pnas.1215927110*

<http://www.scientificamerican.com/article.cfm?id=doubts-emerge-cholesterol-level-target>

## **Doubts Emerge on the Value of Very Low Cholesterol Levels**

*Revised guidelines for heart health are set to move away from target-based approach*

By Heidi Ledford

Soon after Joseph Francis learned that his levels of 'bad' LDL cholesterol sat at twice the norm, he discovered the short-comings of cholesterol-lowering drugs - and of the clinical advice guiding their use. Francis, the director of clinical analysis and reporting at the Veterans Health Administration (VA) in Washington DC, started taking Lipitor (atorvastatin), a cholesterol-lowering statin and the best-selling drug in pharmaceutical history. His LDL plummeted, but still hovered just above a target mandated by clinical guidelines. Adding other medications had no effect, and upping the dose of Lipitor made his muscles hurt - a rare side effect of statins, which can cause muscle breakdown.

So Francis pulled back to moderate Lipitor doses and decided that he could live with his high cholesterol. Later, he learned that other patients were being aggressively treated by doctors chasing stringent LDL targets. But Francis found the science behind the target guidelines to be surprisingly ambiguous. "You couldn't necessarily say lowering LDL further was going to benefit the patient," he says.

The standard advice may soon change. For the first time in more than a decade, the US National Heart, Lung and Blood Institute is revising the clinical guidelines that shaped Francis's treatment (see 'How low can you go?'). Expected to be released later this year, the fourth set of guidelines, called ATP IV, has been drawn up by an expert panel of 15 cardiologists appointed by the institute. The guidelines will set the tone for clinical practice in the United States and beyond, and will profoundly influence pharmaceutical markets. They will also reflect the growing debate over cholesterol targets, which have never been directly tested in clinical trials.

Since 2002, when ATP III called on doctors to push LDL levels below set targets, the concept of low cholesterol has become synonymous with heart health. Patients brag about their cholesterol scores, physicians joke about adding statins to drinking water, and some hospitals reward doctors when patients hit cholesterol targets.

In 2011, US doctors wrote nearly 250 million prescriptions for cholesterol-lowering drugs, creating a US\$18.5-billion market, according to IMS Health, a health-care technology and information company based in Danbury, Connecticut. “The drug industry in particular is very much in favour of target-based measures,” says Joseph Drozda, a cardiologist and director of outcomes research at Mercy Health in Chesterfield, Missouri. “It drives the use of products.”

ATP III reflected a growing consensus among physicians that sharply lowering cholesterol would lessen the likelihood of heart attacks and strokes, says Richard Cooper, an epidemiologist at the Loyola University of Chicago Stritch School of Medicine in Illinois, who served on the committee that compiled the guidelines. The committee drew heavily on clinical data, but also took extrapolations from basic research and post hoc analyses of clinical trials. LDL targets were set to be “less than” specific values to send a message, Cooper says. “We didn’t want to explicitly say ‘the lower the better’ because there wasn’t evidence for that,” he says. “But everybody had the strong feeling that was the correct answer.”

By contrast, the ATP IV committee has pledged to hew strictly to the science and to focus on data from randomized clinical trials, says committee chairman Neil Stone, a cardiologist at Northwestern University School of Medicine in Chicago. If so, Krumholz argues, LDL targets will be cast aside because they have never been explicitly tested. Clinical trials have shown repeatedly that statins reduce the risk of heart attack and stroke, but lowering LDL with other medications does not work as well. The benefits of statins may reflect their other effects on the body, including fighting inflammation, another risk factor for heart disease.

Krumholz’s scepticism is rooted in experience. In 2008 and 2010, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) clinical trial challenged dogma when it reported that lowering blood pressure or blood sugar to prespecified targets did not reduce the risk of heart attack or stroke. In the case of blood sugar, the risks were worsened. The trial demonstrated the folly of assuming that risk factors must have a causal role in disease, says Robert Vogel, a cardiologist at the University of Colorado, Denver. “Short people have a higher risk of heart disease,” he says. “But wearing high heels does not lower your risk.”

Jay Cohn, a cardiologist at the University of Minnesota Medical School in Minneapolis, also worries that the focus on LDL levels offers up the wrong patients for statin therapy. Most of those who have a heart attack do not have high LDL, he notes. Cohn advocates treating patients with statins based on the state of health of their arteries, as revealed by noninvasive tests such as ultrasound. “If your arteries and heart are healthy, I don’t care what your LDL or blood pressure is,” he says.

“We can’t just assume that modifying the risk factor is modifying risk.”

Not all cardiologists want to abolish LDL targets. Indeed, Seth Martin, a fellow in cardiology at Johns Hopkins University School of Medicine in Baltimore, Maryland, believes that ATP IV should reduce LDL targets further. The simplicity of targets has helped to deliver an important public-health message, he says, and motivated many patients to get the statin therapy that he believes they need. “Just to throw that out the window doesn’t seem like the ideal scenario.”

Whatever the decision, the pharmaceutical industry will be watching closely, says Donny Wong, an analyst at Decision Resources, a market-research company based in Watertown, Massachusetts. Although most statins are off patent, the big pharmaceutical companies are racing to bring the next LDL-lowering drug to market. In particular, millions of dollars have been poured into drugs that inhibit a protein called PCSK9, an enzyme involved in cholesterol synthesis. This approach lowers LDL but has not yet been shown to reduce heart attacks or strokes.

Francis expects the new guidelines to relax the targets. He and his colleagues decided last autumn to change the VA’s own clinical standards, so that they no longer rely solely on an LDL target but instead encourage doctors to prescribe a moderate dose of statin when otherwise healthy patients have high LDL cholesterol. The ATP IV guidelines will take a similar approach, he speculates, noting that the VA consulted several outside experts who are also serving on the ATP committee.

Despite an increasingly vegetarian diet, Francis’s cholesterol has not budged. “Sometimes I want to call my physician and say, ‘Don’t worry about that target,’” he says. “It’s going to be changing very soon.”

<http://www.sciencedaily.com/releases/2013/02/130226194006.htm>

## Increased Risk of Sleep Disorder Narcolepsy in Children Who Received Swine Flu Vaccine

*A study finds an increased risk of narcolepsy in children and adolescents who received the A/H1N1 2009 influenza vaccine (Pandemrix) during the pandemic in England.*

The results are consistent with previous studies from Finland and Sweden and indicate that the association is not confined to Scandinavian populations. However, the authors stress that the risk may still be overestimated, and they call for longer term monitoring of the cohort of children and adolescents exposed to Pandemrix to evaluate the exact level of risk.

In 2009, pandemic influenza A (H1N1) virus spread rapidly, resulting in millions of cases and over 18,000 deaths in over 200 countries. In England the vaccine Pandemrix was introduced in October 2009. By March 2010, around one in four (24%) of healthy children aged under 5 and just over a third (37%) aged 2-15 in a risk group had been vaccinated.

In August 2010 concerns were raised in Finland and Sweden about a possible association between narcolepsy and Pandemrix. And in 2012 a study from Finland reported a 13-fold increased risk in children and young people aged 4-19. But a lack of reported cases in other countries led to speculation that any possible association might be restricted to these Scandinavian populations.

Narcolepsy is a chronic disorder of excessive daytime sleepiness, often accompanied by sudden muscle weakness triggered by strong emotion (known as cataplexy). To evaluate the risk after vaccination in England, a team of researchers reviewed case notes for 245 children and young people aged 4-18 from sleep centres and child neurology centres across England. Of these, 75 had narcolepsy (56 with cataplexy) with onset after 1 January 2008. Eleven had been vaccinated before onset of symptoms; seven within six months.

After adjusting for clinical conditions, vaccination at any time was associated with a 14-fold increased risk of narcolepsy, whereas vaccination within six months before onset was associated with a 16-fold increased risk. In absolute numbers, this means that one in 52,000 to 57,500 doses are associated with narcolepsy, say the authors.

They write: "The increased risk of narcolepsy after vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine indicates a causal association, consistent with findings from Finland. Because of variable delay in diagnosis, however, the risk might be overestimated by more rapid referral of vaccinated children."

While further use of this vaccine for prevention of seasonal flu seems unlikely, they say their findings "have implications for the future licensure and use of AS03 adjuvanted pandemic vaccines containing different subtypes such H5 or H9."

And they conclude: "Further studies to assess the risk, if any, associated with the other A/H1N1 2009 vaccines used in the pandemic, including those with and without adjuvants, are also needed to inform the use of such vaccines in the event of a future pandemic."

*E. Miller, N. Andrews, L. Stellitano, J. Stowe, A. M. Winstone, J. Shneerson, C. Verity. Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis. BMJ, 2013; 346 (feb26 2): f794 DOI: 10.1136/bmj.f794*

<http://phys.org/news/2013-02-resurrection-billion-year-old-antibiotic-resistance-proteins.html>

## Resurrection of 3-billion-year-old antibiotic-resistance proteins

*Laboratory "resurrection" of antibiotic-resistant proteins that existed 3 billion years ago may point the way to new antibiotics for the 21st century.*

Scientists are reporting "laboratory resurrections" of several 2-3-billion-year-old proteins that are ancient ancestors of the enzymes that enable today's antibiotic-resistant bacteria to shrug off huge doses of penicillins, cephalosporins and other modern drugs. The achievement, reported in the Journal of the American Chemical Society, opens the door to a scientific "replay" of the evolution of antibiotic resistance with an eye to finding new ways to cope with the problem.

Jose M. Sanchez-Ruiz, Eric A. Gaucher, Valeria A. Risso and colleagues explain that antibiotic resistance existed long before Alexander Fleming discovered the first antibiotic in 1928. Genes that contain instructions for making the proteins responsible for antibiotic resistance have been found in 30,000-year-old permafrost sediment and other ancient sites. Their research focused on the so-called beta-lactamases, enzymes responsible for resistance to the family of antibiotics that includes penicillin, which scientists believe originated billions of years ago.

They describe using laboratory and statistical techniques to reconstruct the sequences of beta-lactamase proteins dating to Precambrian times, 2-3 billion years ago. The team also synthesized the inferred ancestral

enzymes and conducted studies on their stability, structure and function. "The availability of laboratory resurrections of Precambrian beta-lactamases opens up new possibilities in the study of the emergence of antibiotic resistance," the report states. "For instance, it should now be possible to perform laboratory replays of the molecular tape of lactamase evolution and use such replays to probe the molecular determinants of the efficiency of lactamases to adapt to different types of antibiotics." The authors also note that the extreme stability and catalytic features displayed by the 2-3-billion-year-old lactamases suggest that resurrected Precambrian proteins have utility for the biotechnology industry.

*More information: Hyperstability and Substrate Promiscuity in Laboratory Resurrections of Precambrian Beta-Lactamases, Journal of the American Chemical Society. 2013, 135 (8), pp 2899–2902*

DOI: 10.1021/ja311630a

#### **Abstract**

*We report a sequence reconstruction analysis targeting several Precambrian nodes in the evolution of class-A  $\beta$ -lactamases and the preparation and experimental characterization of their encoded proteins. Despite extensive sequence differences with the modern enzymes (100 amino acid differences), the proteins resurrected in the laboratory properly fold into the canonical lactamase structure. The encoded proteins from 2–3 billion years (Gyr)-old  $\beta$ -lactamase sequences undergo cooperative two-state thermal denaturation and display very large denaturation temperature enhancements (35 °C) relative to modern  $\beta$ -lactamases. They degrade different antibiotics in vitro with catalytic efficiencies comparable to that of an average modern enzyme. This enhanced substrate promiscuity is not accompanied by significant changes in the active-site region as seen in static X-ray structures, suggesting a plausible role for dynamics in the evolution of function in these proteins. Laboratory resurrections of 2–3 Gyr-old  $\beta$ -lactamases also endowed modern microorganisms with significant levels of resistance toward a variety of antibiotics, opening up the possibility of performing laboratory replays of the molecular tape of lactamase evolution. Overall, these results support the notions that Precambrian life was thermophilic and that proteins can evolve from substrate-promiscuous generalists into specialists during the course of natural evolution. They also highlight the biotechnological potential of laboratory resurrection of Precambrian proteins, as both high stability and enhanced promiscuity (likely contributors to high evolvability) are advantageous features in protein scaffolds for molecular design and laboratory evolution.*

Provided by American Chemical Society

<http://www.sciencedaily.com/releases/2013/02/130227085838.htm>

## **Too Much Vitamin D During Pregnancy Can Cause Food Allergies, Research Suggests**

***Pregnant women should avoid taking vitamin D supplements, new research suggests.***

Substitution appears to raise the risk of children developing a food allergy after birth. This was the conclusion drawn from a new survey carried out by the Helmholtz Centre for Environmental Research and the Martin Luther University in Halle-Wittenberg in Germany which was published in the February issue of the medical journal *Allergy*. Vitamin D has always had a good reputation: it strengthens bones, protects against infections particularly during the cold winter months and aids the nervous and muscular systems.



***Pregnant women should avoid taking vitamin D supplements. Substitution appears to raise the risk of children developing a food allergy after birth. This was the conclusion drawn from a new survey carried out by the Helmholtz Centre for Environmental Research and the Martin Luther University in Halle-Wittenberg in Germany. André Kuenzelmann/UFZ***

Especially in the prevention and treatment of rickets, it has been given to babies and infants around the world for around 50 years. However, recent scientific investigations are increasingly questioning the positive aspect of the "bone vitamin." At the end of the 1990's, for the first time people's attention was drawn to a link between high vitamin D levels and the development of allergies.

To pursue the problem, together with Prof. Gabriele Stangl's group from the Institute of Agricultural and Nutritional Sciences at the Martin-Luther University in Halle-Wittenberg, Dr. Kristin Weiße from the Helmholtz Centre for Environmental Research in Leipzig devoted herself to the following task: can it be proved that there is a correlation between the concentration of vitamin D in the blood of expectant mothers and in cord blood of the babies? The researchers from the UFZ in Leipzig were furthermore interested in the association between vitamin D levels during pregnancy and at birth, the immune status and allergic diseases of the children later in life. Or, in other words: does the vitamin D level of pregnant women affect the allergy risk of their children?

To investigate the question, Dr. Kristin Weiße's team from Leipzig used samples from the LiNA cohort that the Helmholtz Centre for Environmental Research (UFZ) had established together with the St. Georg municipal clinic between 2006 and 2008 headed by Dr. Irina Lehmann. In total, it was possible to include 622 mothers

and their 629 children in the long-term study "Lifestyle and environmental factors and their impact on the newborn allergy risk." The level of vitamin D was tested in the blood of the pregnant mothers and also in the cord blood of the children born. In addition to this, questionnaires were used to assess the occurrence of food allergies during the first two years of the children's lives.

The result was clear: in cases where expectant mothers were found to have a low vitamin D level in the blood, the occurrence of food allergies among their two-year old children was rarer than in cases where expectant mothers had a high vitamin D blood level. In reverse, this means that a high vitamin D level in pregnant women is associated with a higher risk of their children to develop a food allergy during infancy. Furthermore, those children were found to have a high level of the specific immunoglobulin E to food allergens such as egg white, milk protein, wheat flour, peanuts or soya beans. The UFZ scientists also got evidence for the mechanism that could link vitamin D and food allergies. Dr. Gunda Herberth -- also from the Department of Environmental Immunology at the UFZ -- took a closer look at the immune response of the affected children and analysed regulatory T-cells in cord blood in particular. The cells are capable of preventing the immune system from overreacting to allergens, with the result that they protect against allergies. The UFZ researchers know from earlier analyses that the allergy risk increases in cases where too few regulatory T-cells are present in cord blood. The interesting result of the current research project: the higher the level of vitamin D found in the blood of mothers and children, the fewer regulatory T-cells could be detected. The correlation could mean that vitamin D suppresses the development of regulatory T-cells and thus increases the risk of allergy.

Apart from diet, Dr. Kristin Weiße explained that the level of vitamin D is mainly affected by conditions such as season, exposure to the sun and the amount of time spent outdoors -- these factors were also taken into account in the current risk analyses of vitamin D and food allergy. Even though the occurrence of food allergies is undoubtedly affected by many other factors than just the vitamin D level, it is still important to take this aspect into consideration. The UFZ researchers would rather advise pregnant women not to take vitamin D supplements. "Based on our information, an excess of vitamin D can increase the risk of children developing a food allergy in the first two years of their life."

*K. Weisse, S. Winkler, F. Hirche, G. Herberth, D. Hinz, M. Bauer, S. Röder, U. Rolle-Kampczyk, M. von Bergen, S. Olek, U. Sack, T. Richter, U. Diez, M. Borte, G. I. Stangl, I. Lehmann. Maternal and newborn vitamin D status and its impact on food allergy development in the German LINA cohort study. Allergy, 2013; 68 (2): 220 DOI: 10.1111/all.12081*

<http://wapo.st/14cZPkh>

### **Because male breast cancer is rare, many cases aren't caught till later stages**

*For months, Oliver Bogler ignored the lump he felt behind the nipple of his right breast, figuring it was just a weird little nuisance. But on a rafting trip in Idaho last summer, his T-shirt was stained by discharge when he took off his life vest. That got his attention.*

**By Laura Hambleton, Published: February 26**

He went to his doctor, who immediately recommended a mammogram and biopsy. The diagnosis: breast cancer. "I'm kicking myself I had not gone earlier," said Bogler, 46. "I should have gone right away. [But] my major worry during this time - and I wrote this down - is looking foolish and having my wife look at me: 'Are you kidding?' So I didn't say anything to anybody."

Bogler, the senior vice president for academic affairs at MD Anderson Cancer Center at the University of Texas in Houston, is undergoing chemotherapy treatments; so far, his tumor had stopped growing. The next step in his treatment is a modified radical mastectomy, then radiation and five years of tamoxifen, which inhibits estrogen from stimulating the growth of breast cancer cells.

According to the American Cancer Society, Bogler's case is rare: About 2,240 cases of breast cancer are diagnosed in U.S. men a year, compared with about 232,000 cases of invasive cancer among women. And because male breast cancer is rare, most men with the disease do what Bogler did and ignore the symptoms: lumps in a breast, discharge from a breast or other changes in a breast or nipple.

"Both the patient and the doctor often don't have a high level of suspicion it is breast cancer," said Sharon Giordano, Bogler's oncologist. "Some men don't come in, or some doctors don't get biopsies. It is not a common disease, which leads men to being diagnosed at more advanced stages," which are harder to treat. Most of the time, women receive a diagnosis of breast cancer after a mammogram, said Robert Warren, oncologist and professor of medicine at Georgetown Lombardi Comprehensive Cancer Center. "Most male breast cancer is diagnosed with a presence of mass," he said, which means that "right off the bat, the lump or mass is going to be a later-stage tumor."

### **Estrogen as risk factor**

Men rarely get breast cancer because they produce very little estrogen, which is associated with female sexual characteristics.

“Exposure to estrogen is the ultimate risk factor for developing breast cancer,” said Ben Park, a breast cancer specialist and researcher at the Sidney Kimmel Comprehensive Cancer Center of Johns Hopkins Medical School.

Some scientists wonder if some men who develop breast cancer may be producing more estrogen than is normal.

Whether there’s a relationship between estrogen and the male hormone testosterone is unclear, Park said. But when breast cancer develops in men, it more often occurs in older ones, at a time when testosterone production is waning.

According to the American Cancer Society, the average age for the discovery of breast cancer in men is 68; the disease most commonly strikes men (and women) between the ages of 50 and 70.

Other potential risk factors, Park said, include a family history of the disease, obesity (fat cells can convert testosterone into estrogen), and alcohol abuse or cirrhosis of the liver. The liver helps metabolize estrogen. Men born with Klinefelter syndrome, a rare condition where men have an extra X chromosome, may be more susceptible to breast cancer, as well as men who inherit a mutated gene. The most common culprit, for men and women, is the BRCA2 gene mutation.

Most breast cancer cells start in the lining of milk ducts in the breast, and they sometimes spread to lymph nodes or other organs.

The size of the tumor determines the stage of cancer, said Vered Stearns, co-director of the breast cancer program at the Kimmel center. Stage II breast cancer, which Bogler has, indicates that the disease has spread into surrounding breast tissue and the tumor is larger than in Stage I.

Treatment, Stearns said, is “based on the tumor stage,” which is calculated both on the size of tumor and the determination of how far it has spread.

“We look at how quickly the cancer is likely to grow,” she said. “In Grade 3 - that is, a relatively faster-growing tumor - Grade 1 is less likely to come back. In post-menopausal women, the prognosis is a little bit better for older women than younger; same with men.”

Much of the breast cancer found in men is receptive to tamoxifen, which works like a key blocking a keyhole, said Otis Brawley, chief medical officer of the American Cancer Society. Estrogen stimulates the growth of breast cancer cells; by inhibiting the growth of estrogen, the drug causes breast cancer cells to stop multiplying. While tamoxifen is tolerated well by most men, the Lombardi Center’s Warren said, some of his male patients have developed hot flashes, reduced libido, weight gain and changes in moods - the “same kind of menopausal experiences as women.”

### **Male breast cancer deaths**

Men who die from breast cancer - about 400 U.S. men per year (compared with 40,000 women annually), according to the American Cancer Society - often do so because they waited too long to have a troubling symptom checked out.

As a result, “the outcomes seem worse [for men than for women] probably because the breast cancer is often found at a later stage,” said the Kimmel center’s Park. “Male breast cancer is curable if found early enough.” Stearns said most men’s breast cancer is diagnosed at Stage II or III.

Doctors and scientists recommend that men with breast cancer or a family history of the disease undergo testing for the same genetic mutations - BRAC1 and BRAC2 - that put women in higher-risk categories. Knowing family history and genetic makeup can help a patient figure out possible next steps, said Beth Peshkin, a senior genetic counselor and associate professor of oncology at the Lombardi center.

“When [those mutations] are present . . . they affect cells’ ability to repair themselves properly,” she said. “But there is so much about the mechanisms we don’t know.”

That goes for male breast cancer in general. The disease appears to be the same as the female disease and is treated as such.

Yet, “is it the same disease? I don’t know that we know that,” said Giordano of MD Anderson. “The existing data points to more similarity than differences. But men have a different hormonal environment than women.” Giordano and Park are trying to untangle the unknowns surrounding male breast cancer. Giordano is helping collect cancer specimens from male breast cancer patients around the world.

Park is studying differences in DNA in male breast cancers. “It is an orphan disease in terms of research,” he said, because there are so few cases, relatively speaking. “But that is starting to change. It’s all about the numbers.

“It’s a rare disease. We are looking at everything. Starting with the biopsy, as well as the surgical specimen and metastatic disease. How does this cancer adapt and change while a patient is getting therapy? It’s very complex.” Hambleton is a freelance writer and documentary filmmaker.



[http://www.eurekalert.org/pub\\_releases/2013-02/tuhs-nss022513.php](http://www.eurekalert.org/pub_releases/2013-02/tuhs-nss022513.php)

## **New study shows viruses can have immune systems**

### *A pirate phage commandeers the immune system of bacteria*

BOSTON - A study published today in the journal *Nature* reports that a viral predator of the cholera bacteria has stolen the functional immune system of bacteria and is using it against its bacterial host. The study provides the first evidence that this type of virus, the bacteriophage ("phage" for short), can acquire a wholly functional and adaptive immune system.

The phage used the stolen immune system to disable – and thus overcome – the cholera bacteria's defense system against phages. Therefore, the phage can kill the cholera bacteria and multiply to produce more phage offspring, which can then kill more cholera bacteria. The study has dramatic implications for phage therapy, which is the use of phages to treat bacterial diseases. Developing phage therapy is particularly important because some bacteria, called superbugs, are resistant to most or all current antibiotics.

Until now, scientists thought phages existed only as primitive particles of DNA or RNA and therefore lacked the sophistication of an adaptive immune system, which is a system that can respond rapidly to a nearly infinite variety of new challenges. Phages are viruses that prey exclusively on bacteria and each phage is parasitically mated to a specific type of bacteria. This study focused on a phage that attacks *Vibrio cholerae*, the bacterium responsible for cholera epidemics in humans.

Howard Hughes Medical Institute investigator Andrew Camilli, Ph.D., of Tufts University School of Medicine led the research team responsible for the surprising discovery.

First author Kimberley D. Seed, Ph.D., a postdoctoral fellow in Camilli's lab, was analyzing DNA sequences of phages taken from stool samples from patients with cholera in Bangladesh when she identified genes for a functional immune system previously found only in some bacteria (and most Archaea, a separate domain of single-celled microorganisms).

To verify the findings, the researchers used phage lacking the adaptive immune system to infect a new strain of cholera bacteria that is naturally resistant to the phage. The phage were unable to adapt to and kill the cholera strain. They next infected the same strain of cholera bacteria with phage harboring the immune system, and observed that the phage rapidly adapted and thus gained the ability to kill the cholera bacteria. This work demonstrates that the immune system harbored by the phage is fully functional and adaptive.

"Virtually all bacteria can be infected by phages. About half of the world's known bacteria have this adaptive immune system, called CRISPR/Cas, which is used primarily to provide immunity against phages. Although this immune system was commandeered by the phage, its origin remains unknown because the cholera bacterium itself currently lacks this system. What is really remarkable is that the immune system is being used by the phage to adapt to and overcome the defense systems of the cholera bacteria. Finding a CRISPR/Cas system in a phage shows that there is gene flow between the phage and bacteria even for something as large and complex as the genes for an adaptive immune system," said Seed.

"The study lends credence to the controversial idea that viruses are living creatures, and bolsters the possibility of using phage therapy to treat bacterial infections, especially those that are resistant to antibiotic treatment," said Camilli, professor of Molecular Biology & Microbiology at Tufts University School of Medicine and member of the Molecular Microbiology program faculty at the Sackler School of Graduate Biomedical Sciences at Tufts University.

Camilli's previous research established that phages are highly prevalent in stool samples from patients with cholera, implying that phage therapy is happening naturally and could be made more effective. In addition, a study published by Camilli in 2008 determined that phage therapy works in a mouse model of cholera intestinal infection.

The team is currently working on a study to understand precisely how the phage immune system disables the defense systems of the cholera bacteria. This new knowledge will be important for understanding whether the phage's immune system could overcome newly acquired or evolved phage defense systems of the cholera bacteria, and thus has implications for designing an effective and stable phage therapy to combat cholera.

*Additional authors are David W. Lazinski, Ph.D., senior research associate in the Camilli lab at Tufts University School of Medicine, and Stephen B. Calderwood, M.D., Morton N. Swartz, M.D. academy professor of medicine at Harvard Medical School, and chief, division of infectious disease and vice-chair, department of medicine at Massachusetts General Hospital. Research reported in this publication was supported by the National Institute of Allergies and Infectious Diseases of the National Institutes of Health under award numbers R01AI55058, R01AI045746, and R01AI058935.*

*Seed, K.D., Lazinski, D.W., Calderwood, S.B., and Camilli, A. (2013). A bacteriophage encodes its own CRISPR/Cas adaptive response to evade host innate immunity. Nature, vol 494, issue 7438, pp 489 DOI: 10.1038/nature11927*

<http://bit.ly/Z9LNyi>

## US research to be put online for free

*YOU paid for it, so you should be able to see it.*

On Sunday the US government said that all federally funded research results must be available for free online. The UK made a similar decision last year.

Most research papers are behind paywalls. Now all federal agencies that spend \$100 million annually on research and development will have to make their results freely available by a specified time after initial publication. The US government suggests 12 months as a suitable delay. According to John Holdren, director of the US Office of Science and Technology Policy, this will improve access to information while still allowing publishers to charge for early access.

The movement towards open access has been accelerating. Last July the UK government announced that all publicly funded research will be available for free starting in 2014. Furthermore, 13,000 researchers are boycotting the academic publisher Elsevier – owned by the same company as New Scientist – in protest at its high prices.

[http://www.eurekalert.org/pub\\_releases/2013-02/hcfa-sbh022713.php](http://www.eurekalert.org/pub_releases/2013-02/hcfa-sbh022713.php)

## Supermassive black hole spins super-fast

*Imagine a sphere more than 2 million miles across - eight times the distance from Earth to the Moon - spinning so fast that its surface is traveling at nearly the speed of light. Such an object exists: the supermassive black hole at the center of the spiral galaxy NGC 1365.*

Astronomers measured its jaw-dropping spin rate using new data from the Nuclear Spectroscopic Telescope Array, or NuSTAR, and the European Space Agency's XMM-Newton X-ray satellites.

"This is the first time anyone has accurately measured the spin of a supermassive black hole," said lead author Guido Risaliti of the Harvard-Smithsonian Center for Astrophysics (CfA) and INAF - Arcetri Observatory.

This research is being published in the Feb. 28 issue of the journal Nature, and featured in a NASA media teleconference on Feb. 27th.

*In this artist's conception a supermassive black hole is surrounded by a hot accretion disk, while some inspiraling material is funneled into a wispy blue jet. New measurements show that the black hole at the center of galaxy NGC 1365 is spinning at close to the maximum possible rate. This suggests that it grew via "ordered accretion" rather than by swallowing random blobs of gas and stars. NASA/JPL-Caltech*



A black hole's gravity is so strong that, as the black hole spins, it drags the surrounding space along. The edge of this spinning hole is called the event horizon. Any material crossing the event horizon is pulled into the black hole. Inspiring matter collects into an accretion disk, where friction heats it and causes it to emit X-rays. Risaliti and his colleagues measured X-rays from the center of NGC 1365 to determine where the inner edge of the accretion disk was located. This Innermost Stable Circular Orbit - the disk's point of no return - depends on the black hole's spin. Since a spinning black hole distorts space, the disk material can get closer to the black hole before being sucked in.

Astronomers want to know the black hole's spin for several reasons. The first is physical - only two numbers define a black hole: mass and spin. By learning those two numbers, you learn everything there is to know about the black hole.

Most importantly, the black hole's spin gives clues to its past and by extension the evolution of its host galaxy. "The black hole's spin is a memory, a record, of the past history of the galaxy as a whole," explained Risaliti.

Although the black hole in NGC 1365 is currently as massive as several million Suns, it wasn't born that big. It grew over billions of years by accreting stars and gas, and by merging with other black holes.

Spin results from a transfer of angular momentum, like playing on a children's swing. If you kick at random times while you swing, you'll never get very high. But if you kick at the beginning of each downswing, you go higher and higher as you add angular momentum.

Similarly, if the black hole grew randomly by pulling in matter from all directions, its spin would be low. Since its spin is so close to the maximum possible, the black hole in NGC 1365 must have grown through "ordered accretion" rather than multiple random events.

Studying a supermassive black hole also allows theorists to test Einstein's theory of general relativity in extreme conditions. Relativity describes how gravity affects the structure of space-time, and nowhere is space-time more distorted than in the immediate vicinity of a black hole.

The team also has additional observations of NGC 1365 that they will study to determine how conditions other than black hole spin change over time. Those data are currently being analyzed. At the same time, other teams are observing several other supermassive black holes with NuSTAR and XMM-Newton.

[www.eurekalert.org/pub\\_releases/2013-02/plos-has022213.php](http://www.eurekalert.org/pub_releases/2013-02/plos-has022213.php)

### Heading a soccer ball may affect cognitive performance

*In tablet-based experiment, subconcussive head impacts in soccer affect players' performance of certain tasks*

Sports-related head injuries are a growing concern, and new research suggests that even less forceful actions like 'heading' a soccer ball may cause changes in performance on certain cognitive tasks, according to a paper published February 27 in the open access journal PLOS ONE by Anne Sereno and colleagues from the University of Texas Health Science Center at Houston.

The researchers tested the effects of non-injurious head-to-ball impacts on cognitive function using a tablet-based app. They found that high school female soccer players were significantly slower than non-players on a task that required pointing away from a target on the screen, but showed no difference in performance when pointing to the on-screen visual target.

According to the study, tasks that involve pointing away from a target require specific voluntary responses, whereas moving toward a target is a more reflexive response. Based on their observations, the authors conclude that sub-concussive blows to the head may cause changes specifically linked to certain cognitive functions. The authors say that the app used in their research may be a quick and effective way to screen for and track cognitive changes in athletes. They add that a tablet-based application for such quick screens may also have broader applications in the clinic or the field.

*Citation: Zhang MR, Red SD, Lin AH, Patel SS, Sereno AB (2013) Evidence of Cognitive Dysfunction after Soccer Playing with Ball Heading Using a Novel Tablet-Based Approach. PLoS ONE 8(2): e57364. doi:10.1371/journal.pone.0057364*

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[http://www.eurekalert.org/pub\\_releases/2013-02/uoc-fla022713.php](http://www.eurekalert.org/pub_releases/2013-02/uoc-fla022713.php)

### Feeding limbs and nervous system of one of Earth's earliest animals discovered

*One of the earliest evolutionary examples of limbs used for feeding, along with the oldest nervous system*

An extraordinary find allowing scientists to see through the head of the 'fuxianhuiid' arthropod has revealed one of the earliest evolutionary examples of limbs used for feeding, along with the oldest nervous system to stretch beyond the head in fossil record.

Until now, all fossils found of this extremely early soft-bodied animal featured heads covered by a wide shell or 'carapace', obscuring underlying contents from detailed study. But a new fossil-rich site in South China has been found to contain arthropod examples where the carapace has literally been 'flipped' over before fossilisation – allowing scientists to examine the fuxianhuiid head to an unprecedented extent.

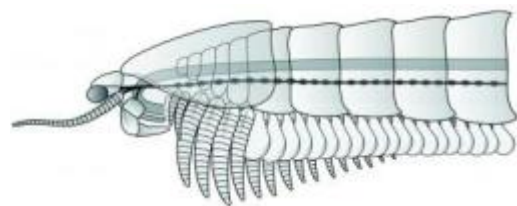
The study, published today in Nature, highlights the discovery of previously controversial limbs under the head, used to shovel sediment into the mouth as the fuxianhuiid crawled across the seabed, millions of years before creatures emerged from the oceans.

Scientists say that this could be the earliest and simplest example of manipulative limbs used for feeding purposes, hinting at the adaptive ability that made arthropods so successful and abundant – evolving into the insects, spiders and crustaceans we know today.

Using a feeding technique scientist's call 'detritus sweep-feeding', fuxianhuiids developed the limbs to push seafloor sediment into the mouth in order to filter it for organic matter – such as traces of decomposed seaweed – which constituted the creatures' food.



*This is a Chengjiangocaris kunmingensis fuxianhuiid fossil revealing inside head. Yie Jang Yunnan University*



*This is a reconstruction of Chengjiangocaris kunmingensis showing feeding limbs. Javier Ortega-Hernández University of Cambridge*

Fossils also revealed the oldest nervous system on record that is 'post-cephalic' – or beyond the head – consisting of only a single stark string in what was a very basic form of early life compared to today.

"Since biologists rely heavily on organisation of head appendages to classify arthropod groups, such as insects and spiders, our study provides a crucial reference point for reconstructing the evolutionary history and relationships of the most diverse and abundant animals on Earth," said Javier Ortega-Hernández, from Cambridge's Department of Earth Sciences, who produced the research with Dr Nicholas Butterfield and colleagues from Yunnan University in Kunming, South China. "This is as early as we can currently see into arthropod limb development."

Fuxianhuiids existed around 520 million years ago, roughly 50 million years before primordial land animals crawled from the sea, and would have been one of the first examples of complex animal life – likely to have evolved from creatures resembling worms with legs. Arthropods were the first jointed animals, enabling them to crawl.

Fuxianhuiid arthropods would have spent most of their time grazing on the sea floor, using these newly discovered limbs to plow sediment into their mouths. They could probably also use their bodies to swim for short distances, like tadpole shrimps.

The fossils date from the early part of the event known as the 'Cambrian explosion', when life on Earth went from multi-cellular organisms we know very little about to a relatively sudden and wide spread explosion of diverse marine animals - the first recognisable evolutionary step for the animal kingdom we know today.

"These fossils are our best window to see the most primitive state of animals as we know them – including us," said Ortega-Hernández. "Before that there is no clear indication in the fossil record of whether something was an animal or a plant – but we are still filling in the details, of which this is an important one."

While still a mystery, theories about the cause of the 'Cambrian Explosion' include possible correlations with oxygen rises, spikes in oceanic nutrient concentration, and genetic complexity reaching critical mass.

But the new site in South China where these fossils were found could prove to be key in uncovering ever more information about this pivotal period in the history of life on Earth. The Xiaoshiba 'biota' - that is the collection of all organisms preserved in the new locality - in China's Yunnan Province is similar to the world-famous Chengjiang biota, which provided many of the best arthropod fossil records to date.

"The Xiaoshiba biota is amazingly rich in such extraordinary fossils of early organisms," said Ortega-Hernández. "Over 50 specimens of fuxianhuiids have been found in just over a year, whereas previous areas considered fossil rich such as Chengjiang it took years - even decades - to build up such a collection."

"So much material is so well preserved. There's massive potential for Xiaoshiba to become a huge deal for new discoveries in early animal evolution".

<http://www.sciencedaily.com/releases/2013/02/130227121908.htm>

## **Good Bacteria May Expunge Vancomycin-Resistant Bacteria from Your Gut**

*Too much antibiotic can decimate the normal intestinal microbiota, which may never recover its former diversity.*

That, in turn, renders the GI tract vulnerable to being colonized by pathogens. Now researchers from Memorial Sloan-Kettering Cancer Center, New York, NY, and Centro Superior de Investigación en Salud Pública, Valencia, Spain, show that reintroducing normal microbial diversity largely eliminated vancomycin-resistant enterococci (VRE) from the intestinal tracts of mice. The investigators showed further that the findings may apply to humans.

The research is published in the March 2013 issue of the journal *Infection and Immunity*.

The reduced diversity of microbiota wrought by antibiotics "allow[s] VRE to invade and thrive in the intestine, suggesting that bacterial species that are wiped out by antibiotics are key to preventing colonization by VRE," says first author Carles Ubeda of the Centro Superior de Investigación en Salud Pública, Valencia, Spain. "We hypothesized that repopulating the mice' intestines with the missing bacteria would promote clearance of the VRE."

In the study, the researchers treated mice with antibiotics. They then gave the mice fecal transplants from untreated mice, or aerobic or anaerobic cultures from the fecal transplants. Following the latter treatments, mice receiving the fecal transplant or the anaerobic culture were able to clear the VRE, while those receiving the aerobic culture failed to do so. The researchers compared the microbiota in each group. The big difference: the mice that had cleared the VRE contained bacteria from the anaerobic genus, *Barnesiella*, while those that had failed to clear the VRE did not.

The researchers then analyzed the fecal microbiota from human patients who had received bone marrow transplants, who were at high risk of being colonized by vancomycin-resistant enterococci. "The presence of *Barnesiella* in fecal samples was associated with protection against VRE, suggesting that in humans, *Barnesiella* may also confer protection against dense VRE colonization," says Ubeda.

"The findings could be very useful for development of novel probiotics," says Ubeda. Additionally, "scientifically, this is a major finding that will help us to understand how the microbiota confer resistance against intestinal colonization by pathogens, an important question that remains incompletely answered."

*C. Ubeda, V. Bucci, S. Caballero, A. Djukovic, N. C. Toussaint, M. Equinda, L. Lipuma, L. Ling, A. Gobourne, D. No, Y. Taur, R. R. Jenq, M. R. M. van den Brink, J. B. Xavier, E. G. Pamer. Intestinal Microbiota Containing Barnesiella Species Cures Vancomycin-Resistant Enterococcus faecium Colonization. Infection and Immunity, 2013; 81 (3): 965 DOI: 10.1128/IAI.01197-12*

<http://www.sciencedaily.com/releases/2013/02/130227151254.htm>

## **Lipid Researcher, 98, Reports On the Dietary Causes of Heart Disease**

***A 98-year-old researcher argues that, contrary to decades of clinical assumptions and advice to patients, dietary cholesterol is good for your heart -- unless that cholesterol is unnaturally oxidized (by frying foods in reused oil, eating lots of polyunsaturated fats, or smoking).***

The researcher, Fred Kummerow, an emeritus professor of comparative biosciences at the University of Illinois, has spent more than six decades studying the dietary factors that contribute to heart disease. In a new paper in the American Journal of Cardiovascular Disease, he reviews the research on lipid metabolism and heart disease with a focus on the consumption of oxidized cholesterol -- in his view a primary contributor to heart disease.

"Oxidized lipids contribute to heart disease both by increasing deposition of calcium on the arterial wall, a major hallmark of atherosclerosis, and by interrupting blood flow, a major contributor to heart attack and sudden death," Kummerow wrote in the review.

Over his 60-plus-year career, Kummerow has painstakingly collected and analyzed the findings that together reveal the underlying mechanisms linking oxidized cholesterol (and trans fats) to heart disease.

Many of Kummerow's insights come from his relentless focus on the physical and biochemical changes that occur in the arteries of people with heart disease. For example, he has worked with surgeons to retrieve and examine the arteries of people suffering from heart disease, and has compared his findings with those obtained in animal experiments.

He and his colleagues first reported in 2001 that the arteries of people who had had bypass operations contained elevated levels of sphingomyelin (SFING-oh-my-uh-lin), one of several phospholipids (phosphate-containing lipids) that make up the membranes of all cells. The bypass patients also had significantly more oxidized cholesterol (oxysterols) in their plasma and tissues than people who had not been diagnosed with heart disease. Human cells incubated with the blood plasma of the cardiac patients also picked up significantly more calcium from the culture medium than cells incubated in the plasma of healthy patients. When the researchers added oxysterols to the healthy plasma, the proportion of sphingomyelin in the cells increased, as did the uptake of calcium.

Earlier research, including studies conducted by medical pioneer Michael DeBakey, noted that the most problematic plaques in patients with heart disease occurred at the branch-points of the arteries of the heart.

Kummerow followed up on these reports by looking at the phospholipid content of the arterial walls in pigs and humans. He found (and reported in 1994) that the branch points of the arteries in humans and in swine also had significantly more sphingomyelin than other regions of the same arteries.

For Kummerow, the increase in sphingomyelin was a prime suspect in the blocked and calcified arteries of the cardiac patients. He had already found that the arteries of the newborn human placenta contained only about 10 percent sphingomyelin and 50 percent phosphatidylcholine (FOSS-fuh-tih-dul-COH-lean), another important phospholipid component of cell membranes.

"But when we looked at the arteries of people who had had bypass operations, we found up to 40 percent sphingomyelin and about 27 percent phosphatidylcholine," Kummerow said. "It took us many more years to discover that when you added large amounts of oxysterols to the cells, then the phosphatidylcholine changed to sphingomyelin."

Further evidence supported sphingomyelin's starring role in atherosclerosis. When Kummerow and his colleagues compared the blocked and unblocked arteries of patients needing second bypass operations, they found that the arteries with blockages contained twice as much sphingomyelin as the unblocked arteries. The calcium content of the blocked arteries (6,345 parts per million) was also much higher than that of the unblocked arteries (182 ppm).

Other studies had demonstrated a link between increases in sphingomyelin and the deposit of calcium in the coronary arteries. The mechanism by which this occurred was unclear, however. Kummerow's team searched the literature and found a 1967 study that showed that in the presence of certain salts (in the blood, for example), lipids like sphingomyelin develop a negative charge. This explains the attraction of the positively charged calcium to the arterial wall when high amounts of sphingomyelin are present, Kummerow said.

"So there was a negative charge on the wall of this artery, and it attracted calcium from the blood until it calcified the whole artery," he said.

Oxidized fats contribute to heart disease (and sudden death from heart attacks) in an additional way, Kummerow said. He and his collaborators found that when the low-density lipoprotein (LDL, the so-called "bad cholesterol") is oxidized, it increases the synthesis of a blood-clotting agent, called thromboxane, in the platelets.

If someone eats a diet rich in oxysterols and trans fats and also smokes, he or she is endangering the heart in three distinct ways, Kummerow said. The oxysterols enhance calcification of the arteries and promote the synthesis of a clotting agent. And the trans fats and cigarette smoke interfere with the production of a compound, prostacyclin, which normally keeps the blood fluid.

"And that causes 600,000 deaths in this country each year," Kummerow said.

Kummerow is the author of "Cholesterol Won't Kill You, But Trans Fats Could."

*Fred A. Kummerow. Interaction between sphingomyelin and oxysterols contributes to atherosclerosis and sudden death. American Journal of Cardiovascular Disease, 2013; 3 (1): 17-26 [link]*

<http://www.bbc.co.uk/news/health-21603235>

### **Thriving cancer's 'chaos' explained**

*The way cancers make a chaotic mess of their genetic code in order to thrive has been explained by UK researchers.*

**By James Gallagher Health and science reporter, BBC News**

Cancer cells can differ hugely within a tumour - it helps them develop ways to resist drugs and spread round the body. A study in the journal Nature showed cells that used up their raw materials became "stressed" and made mistakes copying their genetic code.

Scientists said supplying the cancer with more fuel to grow may actually make it less dangerous.

Most normal cells in the human body contain 46 chromosomes, or bundles of genetic code. However, some cancerous cells can have more than 100 chromosomes. And the pattern is inconsistent - pick a bunch of neighbouring cells and they could each have different chromosome counts.

This diversity helps tumours adapt to become untreatable and colonise new parts of the body. Devising ways of preventing a cancer from becoming diverse is a growing field of research.

#### **Chaos from order**

Scientists at the Cancer Research UK London Research Institute and the University College London Cancer Institute have been trying to crack how cancers become so diverse in the first place.

It had been thought that when a cancer cell split to create two new cells, the chromosomes were not split evenly between the two.

However, lead researcher Prof Charles Swanton's tests on bowel cancer showed "very little evidence" that was the case. Instead the study showed the problem came from making copies of the cancer's genetic code.

Cancers are driven to make copies of themselves, however, if cancerous cells run out of the building blocks of their DNA they develop "DNA replication stress". The study showed the stress led to errors and tumour diversity.

Prof Swanton told the BBC: "It is like constructing a building without enough bricks or cement for the foundations. "However, if you can provide the building blocks of DNA you can reduce the replication stress to limit the diversity in tumours, which could be therapeutic."

He admitted that it "just seems wrong" that providing the fuel for a cancer to grow could be therapeutic.

However, he said this proved that replication stress was the problem and that new tools could be developed to tackle it.

Future studies will investigate whether the same stress causes diversity in other types of tumour.

The research team identified three genes often lost in diverse bowel cancer cells, which were critical for the cancer suffering from DNA replication stress. All were located on one region of chromosome 18.

Prof Nic Jones, Cancer Research UK's chief scientist, said: "This region of chromosome 18 is lost in many cancers, suggesting this process is not just seen in bowel cancers.

"Scientists can now start looking for ways to prevent this happening in the first place or turning this instability against cancers."

<http://www.bbc.co.uk/news/health-21614722>

### **Fukushima: 'Small increased cancer risk'**

*People living near the damaged Fukushima nuclear plant in Japan have an increased risk of developing some cancers, the World Health Organization says.*

The increased risk is limited to communities and some emergency workers exposed to radiation after the 2011 earthquake and tsunami, analysis shows. For those living in the rest of Japan there is no health risk, it said. Experts stressed the increased lifetime risk of cancer remained small. The report is part of an ongoing assessment by international experts on the fallout from severe damage to the Fukushima Daiichi plant. In March 2011, a powerful tsunami generated by a magnitude-9.0 earthquake out at sea slammed into the nuclear power plant in north-eastern Japan, damaging four of six reactors at the site. Around 16,000 people were killed by the impact of the earthquake. A substantial amount of radiation was released into the environment and a 20km (12 miles) evacuation zone was set up.

The latest analysis has found that those living in the most contaminated areas around Fukushima are expected to have a small but higher than expected risk of cancer. The biggest lifetime risks were seen in those exposed as infants, compared with children or adults. For girls exposed to radiation from the accident as infants, the report found a 4% increase above the lifetime expected risk of solid tumours and a 6% increase above that expected for breast cancer. Boys exposed as infants are expected to have a 7% increased risk of leukaemia above that expected in the normal population. The biggest risk was seen in thyroid cancer, which for infant girls could be up to 70% higher than expected over their lifetime.

#### **Demographic factors**

But the WHO was keen to stress that these risks were relative and remained small. For example, the lifetime risk of developing thyroid cancer over a lifetime for women is 0.75% and the additional risk for those exposed as infants in the most affected area is 0.50%. The report also found that a third of emergency workers working in the plant after the disaster are at an increased risk of cancer. Radiation doses from the damaged nuclear power plant are not expected to cause an increase in the incidence of miscarriages, stillbirths or congenital disorders.

Dr Maria Neira, WHO director for public health and environment, said: "The primary concern identified in this report is related to specific cancer risks linked to particular locations and demographic factors." She added that the report underlined the need for long-term health monitoring of those who were at high risk, along with medical follow-up and support. "This will remain an important element in the public health response to the disaster for decades."

Prof Richard Wakeford, visiting professor at Dalton Nuclear Institute at the University of Manchester and contributor to the WHO report, said: "The release of radioactive materials into the environment during the Fukushima nuclear accident was substantial but based on measurement data, the radiation doses received by the surrounding population are small, even for the most exposed communities. "These doses produce an extra risk of cancer over a lifetime of about 1% at most, in addition to background lifetime cancer risks from all other causes of, on average, 40% for men and 29% for women." He added: "Radiation exposure from the Fukushima accident has had only a small impact on the overall health of the nearby population, and much less outside the most affected areas."

[http://www.eurekalert.org/pub\\_releases/2013-02/uo-e-tom022813.php](http://www.eurekalert.org/pub_releases/2013-02/uo-e-tom022813.php)

### **Toxic oceans may have delayed spread of complex life**

*A new model suggests that inhospitable hydrogen-sulphide rich waters could have delayed the spread of complex life forms in ancient oceans.*

A new model suggests that inhospitable hydrogen-sulphide rich waters could have delayed the spread of complex life forms in ancient oceans. The research, published online this week in the journal Nature Communications, considers the composition of the oceans 550-700 million years ago and shows that oxygen-poor toxic conditions, which may have delayed the establishment of complex life, were controlled by the biological availability of nitrogen.

In contrast to modern oceans, data from ancient rocks indicates that the deep oceans of the early Earth contained little oxygen, and flipped between an iron-rich state and a toxic hydrogen-sulphide-rich state. The latter toxic sulphidic state is caused by bacteria that survive in low oxygen and low nitrate conditions. The study shows how bacteria using nitrate in their metabolism would have displaced the less energetically efficient bacteria that produce sulphide – meaning that the presence of nitrate in the oceans prevented build-up of the toxic sulphidic state.

The model, developed by researchers at the University of Exeter in collaboration with Plymouth Marine Laboratory, University of Leeds, UCL (University College London) and the University of Southern Denmark, reveals the sensitivity of the early oceans to the global nitrogen cycle. It shows how the availability of nitrate, and feedbacks within the global nitrogen cycle, would have controlled the shifting of the oceans between the two oxygen-free states – potentially restricting the spread of early complex life.

Dr Richard Boyle from the University of Exeter said: "Data from the modern ocean suggests that even in an oxygen-poor ocean, this apparent global-scale interchange between sulphidic and non-sulphidic conditions is difficult to achieve. We've shown here how feedbacks arising from the fact that life uses nitrate as both a nutrient, and in respiration, controlled the interchange between two ocean states. For as long as sulphidic conditions remained frequent, Earth's oceans were inhospitable towards complex life."

Today, an abundance of nitrate, in the context of an oxygenated ocean, prevents a reversion to the inhospitable environment that inhibited early life. Determining how the Earth's oceans have established long-term stability helps us to understand how modern oceans interact with life and also sheds light on the sensitivity of oceans to changes in composition.

[www.eurekalert.org/pub\\_releases/2013-02/ci-mdc022813.php](http://www.eurekalert.org/pub_releases/2013-02/ci-mdc022813.php)

### **Mineral diversity clue to early Earth chemistry**

*Mineral evolution is a new way to look at our planet's history.*

Washington, D.C. - It's the study of the increasing diversity and characteristics of Earth's near-surface minerals, from the dozen that arrived on interstellar dust particles when the Solar System was formed to the more than 4,700 types existing today. New research on a mineral called molybdenite by a team led by Robert Hazen at Carnegie's Geophysical Laboratory provides important new insights about the changing chemistry of our planet as a result of geological and biological processes.

The work is published by Earth and Planetary Science Letters.

Mineral evolution is an approach to understanding Earth's changing near-surface geochemistry. All chemical elements were present from the start of our Solar System, but at first they formed comparatively few minerals - perhaps no more than 500 different species in the first billion years. As time passed on the planet, novel combinations of elements led to new minerals.

Molybdenite is the most common ore mineral of the critical metallic element molybdenum. Hazen and his team, which includes fellow Geophysical Laboratory scientists Dimitri Sverjensky and John Armstrong, analyzed 442 molybdenite samples from 135 locations and ages ranging from 2.91 billion years old to 6.3 million years old. They specifically looked for trace contamination of the element rhenium in the molybdenite, because rhenium can be used to gauge historical chemical reactions with oxygen from the environment.

They found that concentrations of rhenium, a trace element that is sensitive to oxidation reactions, increased significantly - by a factor of eight - over the past three billion years. The team suggests that this change reflects the increasing near-surface oxidation conditions from the Archean Eon more than 2.5 billion years ago to the Phanerozoic Eon less than 542 million years ago. This oxygen increase was a consequence of what's called the Great Oxidation Event, when the Earth's atmospheric oxygen levels skyrocketed as a consequence of oxygen-producing photosynthetic microbes.

In addition, they found that the distribution of molybdenite deposits through time roughly correlates with five periods of supercontinent formation, the assemblies of Kenorland, Nuna, Rodinia, Pannotia, and Pangea. This correlation supports previous findings from Hazen and his colleagues that mineral formation increases markedly during episodes of continental convergence and supercontinent assembly and that a dearth of mineral deposits form during periods of tectonic stability.

"Our work continues to demonstrate that a major driving force for mineral evolution is hydrothermal activity associated with colliding continents and the increasing oxygen content of the atmosphere caused by the rise of life on Earth," Hazen said.

*Hazen's other co-authors were Joshua Golden, Melissa McMillan, Robert T. Downs, Grethe Hystad, and Ian Goldstein of the University of Arizona; and Holly J. Stein and Aaron Zimmerman of Colorado State University (the former also of the Geological Survey of Norway).*

*Russell Hemley and the Carnegie Institution for Science provided a grant to support the initial development of the Mineral Evolution Database. This work was supported in part by the NASA Astrobiology Institute and the Deep Carbon Observatory, as well as a NSF-NASA collaborative research grant and DOE.*



[http://www.eurekalert.org/pub\\_releases/2013-02/iop-sru022713.php](http://www.eurekalert.org/pub_releases/2013-02/iop-sru022713.php)

## **Space race under way to create quantum satellite**

*A quantum space race is under way to create the world's first global quantum-communication network.*

In this month's special edition of Physics World, focusing on quantum physics, Thomas Jennewein and Brendon Higgins from the Institute for Quantum Computing at the University of Waterloo, Canada, describe how a quantum space race is under way to create the world's first global quantum-communication network. The field of quantum communication – the science of transmitting quantum states from one place to another – has received significant attention in the last few years owing to the discovery of quantum cryptography. Quantum cryptography exploits a unique property of single particles, such as photons: they can exist in two separate states – such as vertically polarized or horizontally polarized – or something in-between, known as a quantum superposition. Upon measuring the state of a particle you instantly change this state, meaning an encryption key made of photons can be passed between two parties safe in the knowledge that if an eavesdropper intercepts it, this would be noticed.

Quantum cryptography has been described as a way of creating "unbreakable" messages and has attracted the attention of major technology companies, governments, banks and other security-focused clients. The transmission of encryption keys over long distances still remains a significant challenge for scientists, however, as the intensity of signals tends to weaken as they travel further because photons get absorbed or scattered off molecules.

Up until now, the furthest that quantum-communication signals have been sent is a few hundred kilometres, which would realistically enable communication between just one or two cities. There is one place, however, where scattering doesn't appear to happen – empty space. Jennewein and Higgins lead just one of several teams around the world looking to take advantage of this by pursuing the concept of a quantum satellite.

A signal travelling from a ground station on Earth to a satellite would spend most of its time in the empty vacuum of space – rather than in Earth's atmosphere, which is crowded with gas molecules – so the signal would travel a lot further without weakening.

A satellite orbiting at around 32000 km above Earth would act as a kind of relay between two ground stations in a way that allows them to establish a secure link by sharing an encryption key made of photons.

In addition to the basic mass and power of the satellite itself, the team led by Jennewein and Higgins has been studying the overall design features of the satellite and ground stations and has emphasized the need for them both to be precisely aligned so they can be certain that what they are measuring correctly corresponds to the photons that are prepared.

"With the prospect of global-scale quantum communications and fundamental quantum science within new, unexplored regimes, the next few years are sure to be exciting," Jennewein and Higgins write.

[http://www.eurekalert.org/pub\\_releases/2013-02/uoc--wis022713.php](http://www.eurekalert.org/pub_releases/2013-02/uoc--wis022713.php)

## **Wolf in sheep's clothing: Uncovering how deadly bacteria trick the immune system**

*UCLA study could provide insight into recent TB outbreak in L.A.'s skid row*

An outbreak of tuberculosis in the skid row area of downtown Los Angeles may have exposed up to 4,500 individuals to the bacterium that causes the deadly disease and has left federal officials scrambling to intervene. The outbreak is occurring during winter, when homeless individuals are driven to crowded shelters, when influenza is peaking and when people's vitamin D levels, typically boosted by sunlight exposure, are low. A new UCLA study offers critical insight into how various bacteria may manipulate such factors to their advantage.

In a study published online Feb. 28 in the journal Science, UCLA researchers demonstrate that certain cunning bacteria — including the type that causes tuberculosis — can pretend to be viruses when infecting humans, allowing them to hijack the body's immune response so that they can hide out, unhindered, inside our cells. The findings may also help explain how viral infections like the flu make us more susceptible to subsequent bacterial infections such as pneumonia.

The study is particularly relevant to tuberculosis, which kills 1.4 million people worldwide each year. In the case of the recent Los Angeles outbreak, the findings could provide clues as to how the flu and a lack of vitamin D may have given the tuberculosis bacterium an edge.

"With 8.7 million in the world falling ill with tuberculosis each year, a better understanding of how these bacteria avoid our immune system could lead to new ways to fight them and to better, more targeted treatments," said senior author Dr. Robert L. Modlin, chief of dermatology at the David Geffen School of Medicine at UCLA and a professor of microbiology, immunology and molecular genetics in the UCLA Division of Life Sciences.

The protection our immune system provides against bacteria-based diseases and infections depends on the critical response of T cells — white blood cells that play a central role in fighting infections — and in particular on the release of a protein called interferon-gamma. Interferon-gamma utilizes the vitamin D hormone to alert and activate cells to destroy invading bacteria.

The research team found that bacteria can pretend to be viruses, triggering the immune system to launch an attack with a different protein, called interferon-beta, which is designed to fight viruses, not bacteria. Not only is interferon-beta ineffective against bacteria, but it can also block the action of interferon-gamma, to the advantage of bacteria. Further, if a real virus were to infect the body, triggering interferon-beta, it would divert the attention of the immune response, preventing an attack on the bacterial invader. The researchers say this may explain why the flu can lead to a more serious bacterial-based infection like pneumonia.

"Like a wolf in sheep's clothing, the bacteria can fool the immune system into launching an attack against the wrong type of infection, thus weakening the response against the bacteria," said first author Rosane M. B. Teles, a researcher in the dermatology division at the Geffen School of Medicine.

For the study, the team examined the mechanisms by which the virus-fighting interferon-beta protein suppresses the interferon-gamma defense response to bacterial infections, tricking the immune system into making the wrong defense choices. The researchers studied leprosy as a model and then applied what they learned to understand tuberculosis, given that leprosy and tuberculosis are caused by related bacteria. Modlin noted that leprosy is an outstanding model for studying immune mechanisms in host defense since it presents as a clinical spectrum that correlates with the level and type of immune response of the pathogen.

The scientists first compared the genetic expression of the virus-fighting interferon-beta protein and the bacteria-fighting interferon-gamma protein in skin lesions from leprosy patients. They found that interferon-gamma was expressed in patients with the milder form of the disease and that interferon-beta was significantly increased in those with the more serious, progressive form of leprosy.

The researchers then compared the genes triggered by interferon-beta in these leprosy skin lesions with those found by two other groups of investigators in the blood of tuberculosis patients. Remarkably, there was a significant overlap. The interferon-beta genes were more frequent in both the skin lesions of leprosy patients with extensive disease and the blood of tuberculosis patients with more severe disease.

"We found this common interferon-beta gene pattern correlated with the greater extent of disease in both leprosy and tuberculosis, which are two very distinct diseases," Teles said.

Previous work by the UCLA team demonstrated that the interferon-gamma defense pathway relies on a specific mechanism involving vitamin D, a natural hormone that plays an essential role in the body's fight against infections. The current study found that interferon-beta suppressed elements involved in the interferon-gamma-triggered vitamin D pathway, preventing the immune system from killing the bacteria.

"The study raises the possibility that a decrease or increase of one of these two interferon proteins could shift the balance from mild to more serious disease," Modlin said. "We may find that therapeutic interventions to block or enhance specific interferon responses may be an effective strategy to alter the balance in favor of protection against bacterial diseases."

The new findings may indicate why, in winter, Los Angeles skid row residents are at an added disadvantage in dealing with tuberculosis — for at least three reasons. First, because of colder weather at night, indigent homeless people tend to stay in shelters, where they live in close proximity with others, facilitating the spread of the infection. Second, due to the seasonal rise in influenza, the body's immune system could be diverted by the flu virus to produce interferon-beta, blocking an effective immune response to the tuberculosis bacteria. And finally, the drop in vitamin D levels associated with a decrease in exposure to sunlight during the winter months could diminish the ability of individuals' immune systems to kill the tuberculosis bacteria.

"With TB on the rise, this scenario could play out not only in cities in the United States but all over the world," Modlin said. "We hope that our findings may provide insight into harnessing new methods to combat TB and other bacterial infections as well."

Modlin noted that 8.7 million become ill with tuberculosis each year, and 1.4 million die from the disease. He added that an increase or decrease in one of the two interferon proteins could help explain why some people may be more resilient against or susceptible to the infection or have a more serious course of the disease.

The next step, according to Teles, is to further understand the mechanisms that bacterial pathogens use to activate interferon-beta and how bacteria can manipulate the immune system to block the potent interferon-gamma host antimicrobial responses in human infections.

*The study was funded by the National Institute of Arthritis and Musculoskeletal Skin Diseases, part of the National Institutes of Health (NIH P50; ARO63020; RO1s AI022553, AR040312 and AI047868; and CTSA Grant UL1TR000124).*

*Additional authors are listed in the manuscript.*

[http://www.eurekalert.org/pub\\_releases/2013-02/nrao-dsi022813.php](http://www.eurekalert.org/pub_releases/2013-02/nrao-dsi022813.php)

## Discoveries suggest icy cosmic start for amino acids and DNA ingredients

### *Important prebiotic chemicals found in interstellar space*

Using new technology at the telescope and in laboratories, researchers have discovered an important pair of prebiotic molecules in interstellar space. The discoveries indicate that some basic chemicals that are key steps on the way to life may have formed on dusty ice grains floating between the stars.

The scientists used the National Science Foundation's Green Bank Telescope (GBT) in West Virginia to study a giant cloud of gas some 25,000 light-years from Earth, near the center of our Milky Way Galaxy. The chemicals they found in that cloud include a molecule thought to be a precursor to a key component of DNA and another that may have a role in the formation of the amino acid alanine.

One of the newly-discovered molecules, called cyanomethanimine, is one step in the process that chemists believe produces adenine, one of the four nucleobases that form the "rungs" in the ladder-like structure of DNA. The other molecule, called ethanamine, is thought to play a role in forming alanine, one of the twenty amino acids in the genetic code.

"Finding these molecules in an interstellar gas cloud means that important building blocks for DNA and amino acids can 'seed' newly-formed planets with the chemical precursors for life," said Anthony Remijan, of the National Radio Astronomy Observatory (NRAO).

In each case, the newly-discovered interstellar molecules are intermediate stages in multi-step chemical processes leading to the final biological molecule. Details of the processes remain unclear, but the discoveries give new insight on where these processes occur.

Previously, scientists thought such processes took place in the very tenuous gas between the stars. The new discoveries, however, suggest that the chemical formation sequences for these molecules occurred not in gas, but on the surfaces of ice grains in interstellar space.

"We need to do further experiments to better understand how these reactions work, but it could be that some of the first key steps toward biological chemicals occurred on tiny ice grains," Remijan said.

The discoveries were made possible by new technology that speeds the process of identifying the "fingerprints" of cosmic chemicals. Each molecule has a specific set of rotational states that it can assume. When it changes from one state to another, a specific amount of energy is either emitted or absorbed, often as radio waves at specific frequencies that can be observed with the GBT.

New laboratory techniques have allowed astrochemists to measure the characteristic patterns of such radio frequencies for specific molecules. Armed with that information, they then can match that pattern with the data received by the telescope. Laboratories at the University of Virginia and the Harvard-Smithsonian Center for Astrophysics measured radio emission from cyanomethanimine and ethanamine, and the frequency patterns from those molecules then were matched to publicly-available data produced by a survey done with the GBT from 2008 to 2011.

A team of undergraduate students participating in a special summer research program for minority students at the University of Virginia (U.Va.) conducted some of the experiments leading to the discovery of cyanomethanimine. The students worked under U.Va. professors Brooks Pate and Ed Murphy, and Remijan. The program, funded by the National Science Foundation, brought students from four universities for summer research experiences. They worked in Pate's astrochemistry laboratory, as well as with the GBT data.

"This is a pretty special discovery and proves that early-career students can do remarkable research," Pate said. The researchers are reporting their findings in the *Astrophysical Journal Letters*.

*The National Radio Astronomy Observatory is a facility of the National Science Foundation, operated under cooperative agreement by Associated Universities, Inc.*

<http://bit.ly/XzW33t>

## Studying Languages Can Grow the Brain

*Researchers have found that people who study languages tend to show significant growth in certain areas of the brain. Christie Nicholson reports*

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Learning a new language can grow one's perspective. Now scientists find that learning languages grows parts of the brain.

Scientists studied the brains of students in the Swedish Armed Forces Interpreter Academy, who are required to learn new languages at an alarmingly fast rate. Many must become fluent in Arabic, Russian and the Persian dialect Dari in just 13 months. The researchers compared the brains of these students to the brains of medical students who also have to learn a tremendous amount in a very short period of time, but without the focus on languages.

The brains of the language learners exhibited significant new growth in the hippocampus and in parts of the cerebral cortex. The medical students' brains showed no observed growth. The study was in the journal *NeuroImage*.

Interestingly, the amount of growth in the brains of the linguists correlated with better skills—so those with better language skills also experienced more growth in the hippocampus and areas of the cerebral cortex that relate to language. For other students who had to work harder to improve their language skills, the scientists found greater growth in the motor area of the cerebral cortex. Where and how much change take place in the brain are linked to how easily one picks up a language. But it remains to be seen why this is.

<http://www.bbc.co.uk/news/health-21613924>

### **Five psychiatric disorders 'linked'**

*Autism, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder and schizophrenia all share several genetic risk factors, according to a major study.*

By James Gallagher Health and science reporter, BBC News

Versions of four genes increased the odds of all five disorders. Researchers hope to move the psychiatry away from describing symptoms towards fundamentally understanding what is going wrong in the brain. The findings were reported in the *Lancet* medical journal.

The international study compared the genetic codes of 33,000 people with a psychiatric disorder with 28,000 people without a psychiatric disorder. Four genetic variants appeared to increase the risk of all five disorders studied. Two genes were involved in the balance of calcium in the brain.

Hundreds of genes and the environment are likely to affect the odds of developing such conditions.

However, the rapidly advancing field of psychiatric genetics is trying to describe these disorders on the basis of what is causing them, rather simply by symptoms.

One of the researchers Nick Craddock, a professor of psychiatry at Cardiff University, said: "It signals the opening of a potential new era for psychiatry and mental illness. "This is a scientific method that helps understand what is going wrong in the brain, the chemicals, the brains systems, that are important in illness." He said that ultimately it could help devise treatments and better ways of diagnosing patients.

Dr Gerome Breen, from the Institute of Psychiatry at King's College London, said: "It points out fairly clearly that there is a common genetic effect between these disorders.

#### **'Breakthrough elusive'**

"These studies give a window into the biology of these disorders, that's really valuable."

Marjorie Wallace, chief executive of mental health charity Sane, said the findings "highlight the need to understand the genetic and biological factors of these life-changing conditions, in order that more effective treatments and therapies may be found".

She added: "While it may take a decade for research studies like this to translate into new drugs and other treatments, we may yet be working towards a breakthrough which has so long eluded scientists working in this field."

<http://www.wired.com/wiredscience/2013/02/fossil-insect-colors/>

### **Resurrecting the Rainbow Colors of Insect Fossils**

*After squeezing and baking beetle wings, or soaking them in mud to let them decay, scientists think they're closer to being able to reconstruct the original brilliant hues of some fossilized insects.*

Some insects keep their colors after they become fossils, in some cases for millions of years. But others turn varying shades of brown and black. Scientists interested in the evolution of insect colors — and their role in things like camouflage, mating, and defense — want to better understand how colors change after fossilization. What really turns a beetle brown, it turns out, is warm temperatures, a team of scientists reported Feb. 20 in *Geology*. "Temperature is the key to destroying the colors of fossils," said paleontologist Maria McNamara, a study coauthor at the University of Bristol. McNamara and her colleagues based their conclusion on a battery of tests known as maturation experiments, during which scientists watched what happened when they subjected beetle bits to a variety of conditions that mimic those a dead insect might encounter after many millennia buried under dirt and debris.

"This opens potential pathways for recovering the color signature from specimens which have since lost their coloration," said paleontologist Michael Engel of the University of Kansas. "In time we may be able to look upon a drawer of fossils rendered black by preservation, but which we know were once colored, and reconstruct their lost hues and patterns."

McNamara has been studying fossil insect colors for years. After identifying some trends in how fossil colors change, she decided to test some of the conditions that could produce color changes after a bug gets buried. To

do this, McNamara and her colleagues took advantage of a Yale University lab equipped to do maturation experiments, a facility normally used by geochemists. Here, the high temperatures and pressures that can affect buried sediments are produced by autoclaves, instruments that heat- and pressure- sterilize lab equipment.

Except McNamara removed the forewings from jewel beetles and weevils and put them in the autoclave.

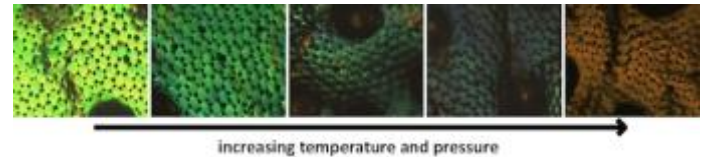
The shiny colors of the beetles' outer cuticles come from microscopic structures. Some beetles, like the green jewel beetle (above left), get their shimmer from multiple layers of reflective compounds. Others, like the weevil (above right), derive their colors from tiny 3-D biophotonic crystals. These crystals, McNamara says, are among the most complex structures known – so complicated that scientists haven't figured out how to replicate them artificially.

Determining when the crystals showed up in the fossil record is a different question, since most fossils show no evidence for the structure.

*Jewel beetles and weevils owe their shiny colors to different structures, but both lose their hues when subjected to high temperatures. Image: Maria McNamara*

The jewel beetle's shiny covering fared well when subjected only to high pressure conditions, McNamara found. But turning up the heat as well as pressure produced a predictable color change, from green, to cyan, to blue, to indigo. And then, brown or black.

"Cook anything long enough and it'll all end up black," McNamara said.



*Jewel beetle cuticle, color change series. An untreated specimen is on the left. Image: Maria McNamara*

The weevil's outer layer responded similarly. Placing both types of insect cuticles in dirt and water for 18 months produced no color change, leading the team to conclude that post-burial temperatures are the most important factor in color change. High temperatures alter color-producing structures, shrinking layers and changing chemical compositions, which causes the tissue to bend light differently. "The color they produce is really dependent on how much the structure bends light," McNamara said.

In support of her conclusion, McNamara points to fossils unearthed from various sites — buried at different depths and under different conditions — whose colors conform to the hypothesis.

Not everyone is convinced, though. Some scientists suggest McNamara is generalizing too much, and that color changes vary on a case-by-case basis, depending in part on species and precise post-burial conditions.

McNamara is working on resolving how these factors can influence a fossil's color, and is planning on testing additional species and tissues. For now, she points to a tantalizing piece of evidence that emerged from her studies: Some of the black fossils she studied retain their original color-producing structures, which means that — with more information — scientists could eventually backtrack from those structures and determine what colors may have adorned paleo-insects.

<http://phys.org/news/2013-02-africa-affects-snowfall-california.html>

### Dust from Africa affects snowfall in California

*One of the driest spots on Earth—the Sahara desert—is increasingly responsible for snow and rain half a world away in the western U.S., a new study released Thursday found.*

It's no secret that winds carrying dust, soot and even germs make transcontinental journeys through the upper atmosphere that can affect the weather thousands of miles (kilometers) away. Yet little is known about the impact of foreign pollutants on the West Coast, which relies on mountain snowmelt for its water needs. Previous studies hinted these jet-setting particles may retard rainfall in the Sierra Nevada mountains in Northern California by reducing the size of water droplets in clouds. But scientists who flew through storm clouds in an aircraft, measured rain and snow and analyzed satellite imagery found the opposite: Far-flung dust and germs can help stimulate precipitation.

During the 2011 winter, a team from the University of California, San Diego and National Oceanic and Atmospheric Administration traced particles suspended in clouds over the Sierra to distant origins—from the skies over the arid Sahara that later mingled with other pollutants in China and Mongolia before crossing the Pacific.

The days with the most particles in the clouds were also "days when we see the most snow on the ground," said study leader Kimberly Prather, an atmospheric chemistry professor at UC San Diego, whose study was published online Thursday in the journal *Science*.

Scientists believe wafting dust, grit and microbes—including bacteria and viruses—can spur the formation of ice crystals in clouds that in turn can influence how much rain or snow falls.

For years, governments and utilities in California and other Western states have used cloud seeding, in which a chemical vapor is sprayed into clouds, in a bid to increase rainfall.

The new study shows how "Mother Nature has figured out how to give us more precipitation" and that may lead to changes in cloud-seeding efforts, which can be hit-or-miss, Prather said.

David J. Smith at the NASA Kennedy Space Center said it was refreshing to see measurements from the ground, air and orbit to tackle how airborne particles affected Northern California snowfall.

"Such a comprehensive approach is the only way to thoroughly examine global transport" of particles, Smith, who had no role in the research, said in an email.

*More information: "Dust and Biological Aerosols from the Sahara and Asia Influence Precipitation in the Western U.S.," by J.M. Creamean et al., Science, 2013.*

<http://bit.ly/Z6YAOG>

## **Prevailing Winds Protected Most Residents from Fukushima Fallout**

*Hotspots of radiation from the nuclear disaster are still likely to cause localized, small increases in cancer risk, according to a new report by the World Health Organization*

**By Declan Butler and Nature magazine | Thursday, February 28, 2013 | 7**

The World Health Organization this morning released a relatively reassuring report suggesting few health impacts from the 2011 disaster at the Fukushima Daiichi nuclear power plant in Japan. But the accident is likely to cause small, but significant, increases in cancers in populations in a few hotspots exposed to higher radioactive doses.

These conclusions regarding the worst nuclear accident since Chernobyl in 1986 could be less comforting than they sound: In fact, Japan dodged a bullet thanks to the weather. The pattern of prevailing winds during the accident meant that most of the radioactive materials released from the plant were blown out to sea. The results therefore say little about the health risks of any future nuclear accidents.

"Had the winds been less favorable, the consequences could have been more serious than Chernobyl," says Keith Baverstock, a radiobiologist at the University of Eastern Finland in Kuopio.

The WHO's assessment last year of the doses of radiation received by the population in the area provided the basis for the health-risk estimates in today's report.

The report, drafted by a panel of international experts in radiation risks and public health, concluded that there was no additional cancer risk for the population in most of Japan — even most parts of Fukushima Prefecture — or in neighboring countries. But the risks were slightly increased in hotspots such as Iitate village and Namie town, which were contaminated by plumes of fallout to the northwest of the plant.

In such hotspots the WHO panel estimated that the fallout has increased the risks of most cancers in children by only a few percent — though for thyroid cancer in young girls the increased risk was put at 70%. These figures are relative risks, however, and the absolute risks are less alarming. For thyroid cancer the baseline lifetime rate in women is 0.75%, so the risk in hotspots would be increased by 0.50%.

"Given the projected very low frequency, 3.2 per 10,000, of radiation-associated thyroid cancer among young people, it is unlikely that any excess would be detectable by the usual epidemiologic approaches," says Roy Shore, head of research at the Radiation Effects Research Foundation in Hiroshima, and a co-author of the WHO report. Most emergency workers were estimated to have minimal increased risks but around one-third had a small but significant increase in cancer risks.

Experts will probably argue intensely over the report during the coming weeks and months. Although many say the report is well done, the exercise largely depended on modeling of radiation doses rather than on direct measurements of population exposures, and the data were often sub-optimal.

"One of the major problems for those of us interested in estimating the public-health consequences of the accident has been the paucity of reliable data," says Baverstock. "That problem still persists. If the WHO data are not better than we have been able to obtain, then the resultant estimates will be of limited value."

Geraldine Thomas, a radiation-health expert at Imperial College London, argues that the report's cancer risks are likely to be overestimates, as its authors openly erred on the side of caution in various assumptions. "Very few members of the population will have been exposed to any more than a lifetime dose equivalent to a single whole-body CT scan," she says.

Greenpeace on the other hand claims that the report is flawed. "The WHO report shamelessly downplays the impact of early radioactive releases from the Fukushima disaster on people inside the 20 km evacuation zone who were not able to leave the area quickly," says Rianne Teule, a nuclear expert at Greenpeace International. But the apparently limited health effects of the accident may have been largely a fluke, Baverstock says. "The health consequences of this accident are smaller than Chernobyl because of the very favorable wind direction, out over the Pacific ocean, and the fact that there are no near neighbors," he says. Tokyo, he adds, is less than 200 km away. "Had the winds prevailed in that direction, Fukushima would have been a whole different story."

<http://arstechnica.com/science/2013/02/lol-texting-and-txt-speak-linguistic-miracles/>

### **LOL, texting, and txt-speak: Linguistic miracles**

*A linguist surprises the TED crowd; apparently txt-speak really is special.*

by Ken Fisher - Mar 1 2013, 6:10am TST

LONG BEACH, CA—Is texting shorthand a convenience, a catastrophe for the English language, or actually something new and special? John McWhorter, a linguist at Columbia University, sides with the latter. According to McWhorter, texting is actually a new form of speech, and [he outlined the reasons why today at the TED2013 conference in Southern California.](#)

We often hear that "texting is a scourge," damaging the literacy of the young. But it's "actually a miraculous thing," McWhorter said. Texting, he argued, is not really writing at all—not in the way we have historically thought about writing. To explain this, he drew an important distinction between speech and writing as functions of language. Language was born in speech some 80,000 years ago (at least). Writing, on the other hand, is relatively new (5,000 or 6,000 years old). So humanity has been talking for longer than it has been writing, and this is especially true when you consider that writing skills have hardly been ubiquitous in human societies.

Furthermore, writing is typically not a reflection of casual speech. "We speak in word packets of seven to 10 words. It's much more loose, much more telegraphic," McWhorter said. Of course, speech can imitate writing, particularly in formal contexts like speechmaking. He pointed out that in those cases you might speak like you write, but it's clearly not a natural way of speaking.

But what about writing like you speak? Historically this has been difficult. Speed is a key issue. "[Texting is] fingered-speech. Now we can write the way we talk," McWhorter said. Yet we view this as some kind of decline. We don't capitalize words, obey grammar or spelling rules, and the like. Yet there is an "emerging complexity...with new structure" at play. To McWhorter, this structure facilitates the speed and packeted nature of real speech.

Take "LOL," for instance. It used to mean "laughing out loud," but its meaning has changed. People aren't guffawing every time they write it. Now "it's a marker of empathy, a pragmatic particle," he said. "It's a way of using the language between actual people."

This is just one example of a new battery of conventions McWhorter sees in texting. They are conventions that enable writing like we speak. Consider the rules of grammar. When you talk, you don't think about capitalizing names or putting commas and question marks where they belong. You produce sounds, not written language. Texting leaves out many of these conventions, particularly among the young, who make extensive use of electronic communication tools.

McWhorter thinks what we are experiencing is a whole new way of writing that young people are using alongside their normal writing skills. It is a "balancing act... an expansion of their linguistic repertoire," he argued.

The result is a whole new language, one that wouldn't be intelligible to people in the year 1993 or 1973. And where it's headed, it will likely be unintelligible to us were we to jump ahead 20 years in time. Nevertheless, McWhorter wants us to appreciate it now: "It's a linguistic miracle happening right under our noses," he said. Forget the "death of writing" talk. Txt-speak is a new, rapidly evolving form of speech.

[http://www.eurekalert.org/pub\\_releases/2013-03/uom-mta022813.php](http://www.eurekalert.org/pub_releases/2013-03/uom-mta022813.php)

### **Mother Teresa: Anything but a saint...**

*Researchers dispell the myth of altruism and generosity surrounding Mother Teresa*

The myth of altruism and generosity surrounding Mother Teresa is dispelled in a paper by Serge Larivée and Genevieve Chenard of University of Montreal's Department of Psychoeducation and Carole Sénéchal of the University of Ottawa's Faculty of Education. The paper will be published in the March issue of the journal *Studies in Religion/Sciences religieuses* and is an analysis of the published writings about Mother Teresa. Like the journalist and author Christopher Hitchens, who is amply quoted in their analysis, the researchers conclude

that her hallowed image—which does not stand up to analysis of the facts—was constructed, and that her beatification was orchestrated by an effective media relations campaign.

"While looking for documentation on the phenomenon of altruism for a seminar on ethics, one of us stumbled upon the life and work of one of Catholic Church's most celebrated woman and now part of our collective imagination—Mother Teresa—whose real name was Agnes Gonxha," says Professor Larivée, who led the research. "The description was so ecstatic that it piqued our curiosity and pushed us to research further."

As a result, the three researchers collected 502 documents on the life and work of Mother Teresa. After eliminating 195 duplicates, they consulted 287 documents to conduct their analysis, representing 96% of the literature on the founder of the Order of the Missionaries of Charity (OMC). Facts debunk the myth of Mother Teresa

In their article, Serge Larivée and his colleagues also cite a number of problems not take into account by the Vatican in Mother Teresa's beatification process, such as "her rather dubious way of caring for the sick, her questionable political contacts, her suspicious management of the enormous sums of money she received, and her overly dogmatic views regarding, in particular, abortion, contraception, and divorce."

### **The sick must suffer like Christ on the cross**

At the time of her death, Mother Teresa had opened 517 missions welcoming the poor and sick in more than 100 countries. The missions have been described as "homes for the dying" by doctors visiting several of these establishments in Calcutta. Two-thirds of the people coming to these missions hoped to find a doctor to treat them, while the other third lay dying without receiving appropriate care. The doctors observed a significant lack of hygiene, even unfit conditions, as well as a shortage of actual care, inadequate food, and no painkillers. The problem is not a lack of money—the Foundation created by Mother Teresa has raised hundreds of millions of dollars—but rather a particular conception of suffering and death: "There is something beautiful in seeing the poor accept their lot, to suffer it like Christ's Passion. The world gains much from their suffering," was her reply to criticism, cites the journalist Christopher Hitchens. Nevertheless, when Mother Teresa required palliative care, she received it in a modern American hospital.

### **Questionable politics and shadowy accounting**

Mother Teresa was generous with her prayers but rather miserly with her foundation's millions when it came to humanity's suffering. During numerous floods in India or following the explosion of a pesticide plant in Bhopal, she offered numerous prayers and medallions of the Virgin Mary but no direct or monetary aid. On the other hand, she had no qualms about accepting the Legion of Honour and a grant from the Duvalier dictatorship in Haiti. Millions of dollars were transferred to the MCO's various bank accounts, but most of the accounts were kept secret, Larivée says. "Given the parsimonious management of Mother Theresa's works, one may ask where the millions of dollars for the poorest of the poor have gone?"

### **The grand media plan for holiness**

Despite these disturbing facts, how did Mother Teresa succeed in building an image of holiness and infinite goodness? According to the three researchers, her meeting in London in 1968 with the BBC's Malcom Muggeridge, an anti-abortion journalist who shared her right-wing Catholic values, was crucial. Muggeridge decided to promote Teresa, who consequently discovered the power of mass media. In 1969, he made a eulogistic film of the missionary, promoting her by attributing to her the "first photographic miracle," when it should have been attributed to the new film stock being marketed by Kodak. Afterwards, Mother Teresa travelled throughout the world and received numerous awards, including the Nobel Peace Prize. In her acceptance speech, on the subject of Bosnian women who were raped by Serbs and now sought abortion, she said: "I feel the greatest destroyer of peace today is abortion, because it is a direct war, a direct killing—direct murder by the mother herself."

Following her death, the Vatican decided to waive the usual five-year waiting period to open the beatification process. The miracle attributed to Mother Theresa was the healing of a woman, Monica Besra, who had been suffering from intense abdominal pain. The woman testified that she was cured after a medallion blessed by Mother Theresa was placed on her abdomen. Her doctors thought otherwise: the ovarian cyst and the tuberculosis from which she suffered were healed by the drugs they had given her. The Vatican, nevertheless, concluded that it was a miracle. Mother Teresa's popularity was such that she had become untouchable for the population, which had already declared her a saint. "What could be better than beatification followed by canonization of this model to revitalize the Church and inspire the faithful especially at a time when churches are empty and the Roman authority is in decline?" Larivée and his colleagues ask.

### **Positive effect of the Mother Teresa myth**

Despite Mother Teresa's dubious way of caring for the sick by glorifying their suffering instead of relieving it, Serge Larivée and his colleagues point out the positive effect of the Mother Teresa myth: "If the extraordinary



image of Mother Teresa conveyed in the collective imagination has encouraged humanitarian initiatives that are genuinely engaged with those crushed by poverty, we can only rejoice. It is likely that she has inspired many humanitarian workers whose actions have truly relieved the suffering of the destitute and addressed the causes of poverty and isolation without being extolled by the media. Nevertheless, the media coverage of Mother Theresa could have been a little more rigorous."

*About the study*

*The study was conducted by Serge Larivée, Department of psychoeducation, University of Montreal, Carole Sénéchal, Faculty of Education, University of Ottawa, and Geneviève Chénard, Department of psychoeducation, University of Montreal.*

*The printed version, available only in French, will be published in March 2013 in issue 42 of Studies in Religion / Sciences religieuses.*

*This study received no specific funding.*

[http://www.eurekalert.org/pub\\_releases/2013-03/sp-umf030113.php](http://www.eurekalert.org/pub_releases/2013-03/sp-umf030113.php)

## **US may face inevitable nuclear power exit**

***In a 2012 report, the Obama administration announced that it was "jumpstarting" the nuclear industry.***

Los Angeles, CA - Because of the industry's long history of permitting problems, cost overruns, and construction delays, financial markets have been wary of backing new nuclear construction for decades.

The supposed "nuclear renaissance" ballyhooed in the first decade of this century never materialized.

And then came Fukushima, a disaster that pushed countries around the world to ask: Should nuclear power be part of the energy future?

In the third and final issue in a series focused on nuclear exits, the Bulletin of the Atomic Scientists, published by SAGE, turns its attention to the United States and looks at whether the country's business-as-usual approach may yet lead to a nuclear phase-out for economic reasons.

The Obama administration injected significant funding into two new nuclear reactor projects in Georgia in 2012. But this investment—the first of its kind in three decades—belies an overall dismal US nuclear power landscape. Where Japan and many European countries responded to the Fukushima disaster with public debate and significant policy shifts in the nuclear arena, the US has scarcely broached the subject.

According to former Nuclear Regulatory Commission Commissioner Peter Bradford, current market forces challenge the economic viability of existing nuclear power plants, with new reactors representing an extremely unattractive investment prospect.

Allowing existing reactors to simply run out their licensed lifetimes in the current scenario, nuclear power may simply disappear, he writes. "Absent an extremely large injection of government funding or further life extensions, the reactors currently operating are going to end their licensed lifetimes between now and the late 2050s," Bradford concludes. "They will become part of an economics-driven US nuclear phase-out a couple of decades behind the government-led nuclear exit in Germany."

Also in this special issue, Sharon Squassoni, a non-proliferation expert at the Center for Strategic and International Studies in Washington, DC, writes that a US nuclear phase out will have only minor international implications. Governmental attempts to buoy the US commercial nuclear industry for national security reasons run the risk of blurring the distinction between civilian and military nuclear programs, undermining public backing for both, she adds.

The Bulletin canvassed opinion on the economic and environmental implications of a US phase from leading institutions. Massachusetts Institute of Technology (MIT) experts Henry D. Jacoby and Sergey Paltsev modeled a number of scenarios, focusing particularly on the effects of greenhouse gas regulations. They also looked at the impacts of a nuclear phase out on greenhouse gas emissions, electricity prices, and the national economy. They conclude that a US exit from nuclear power would impose costs on all three.

Colorado-based Rocky Mountain Institute chairman and chief scientist, Amory Lovins, says that as the US electricity system ages, most of its power plants and transmission grid must be replaced by 2050. The cost will be roughly the same, whether the rebuilt system is fed by new nuclear power plants and "clean coal" facilities or centralized and distributed renewable energy plants: "The inevitable US nuclear phase-out, whatever its speed, is [...] just part of a far broader and deeper evolution from the remarkable electricity system that has served the nation so well to an even better successor now being created," he writes.

The earlier issues in this Nuclear Exit series looked at neighbors France and Germany. Germany is a trailblazer for countries considering an exit from commercial nuclear power, embarking on an ambitious Energiewende, or energy turnaround, that includes a quick nuclear phase-out and an enthusiastic embrace of renewable energy. Just next door, France is taking a more cautious approach, and is currently carrying out an extensive, multi-stakeholder debate on the country's energy future. With three-quarters of France's electricity derived from nuclear power, a rapid or total exit seems unlikely.

The breadth and depth of the data and analysis presented by the authors in all three Nuclear Exit issues make clear that this question has no simple, one-size-fits-all answer. They make something else clear: The question deserves a serious, considered answer in every country with a commercial nuclear power industry.

*"The US Nuclear Exit" by John Mecklin published 01 March 2013 in the Bulletin of the Atomic Scientists.*

*"How to close the US nuclear industry: Do nothing "by Peter. A. Bradford published 01 March 2013 in the Bulletin of the Atomic Scientists.*

*"The economics of a US civilian nuclear phase-out" by Amory b. Lovins published 01 March 2013 in the Bulletin of the Atomic Scientists.*

*"The limited national security implications of civilian nuclear decline" by Sharon Squassoni published 01 March 2013 in the Bulletin of the Atomic Scientists.*

Select articles from the issue will be free to access from a limited time here: <http://bos.sagepub.com/>

[http://www.eurekalert.org/pub\\_releases/2013-03/mtu-tti030113.php](http://www.eurekalert.org/pub_releases/2013-03/mtu-tti030113.php)

### **Turn trash into cash... and save energy**

*New process transforms old milk jugs into everything from lab equipment to cell phone cases*

Suppose you could replace "Made in China" with "Made in my garage." Suppose also that every time you polished off a jug of two percent, you would be stocking up on raw material to make anything from a cell phone case and golf tees to a toy castle and a garlic press.

And, you could give yourself a gold medal for being a bona fide, recycling, polar-bear-saving rock star.

Michigan Technological University's Joshua Pearce is working on it. His main tool is open-source 3D printing, which he uses to save thousands of dollars by making everything from his lab equipment to his safety razor.

Using free software downloaded from sites like Thingiverse, which now holds over 54,000 open-source designs, 3D printers make all manner of objects by laying down thin layers of plastic in a specific pattern.

While high-end printers can cost many thousands of dollars, simpler open-source units run between \$250 and \$500—and can be used to make parts for other 3D printers, driving the cost down ever further.

"One impediment to even more widespread use has been the cost of filament," says Pearce, an associate professor of materials science and engineering and electrical and computer engineering. Though vastly less expensive than most manufactured products, the plastic filament that 3D printers transform into useful objects isn't free.

Milk jugs, on the other hand, are a costly nuisance, either to recycle or to bury in a landfill. But if you could turn them into plastic filament, Pearce reasoned, you could solve the disposal problem and drive down the cost of 3D printing even more.

So Pearce and his research group decided to make their own recycling unit, or RecycleBot. They cut the labels off milk jugs, washed the plastic, and shredded it. Then they ran it through a homemade device that melts and extrudes it into a long, spaghetti-like string of plastic. Their process is open-source and free for everyone to make and use at Thingiverse.com.

The process isn't perfect. Milk jugs are made of high-density polyethylene, or HDPE, which is not ideal for 3D printing. "HDPE is a little more challenging to print with," Pearce says. But the disadvantages are not overwhelming. His group made its own climate-controlled chamber using a dorm-room refrigerator and an off-the-shelf teddy-bear humidifier and had good results. With more experimentation, the results would be even better, he says. "3D printing is where computers were in the 1970s."

The group determined that making their own filament in an insulated RecycleBot used about 1/10th the energy needed to acquire commercial 3D filament. They also calculated that they used less energy than it would take to recycle milk jugs conventionally.

RecycleBots and 3D printers have all kinds of applications, but they would be especially useful in areas where shopping malls are few and far between, Pearce believes. "Three billion people live in rural areas that have lots of plastic junk," he says. "They could use it to make useful consumer goods for themselves. Or imagine people living by a landfill in Brazil, recycling plastic and making useful products or even just 'fair trade filament' to sell. Twenty milk jugs gets you about 1 kilogram of plastic filament, which currently costs \$30 to \$50 online."

*Pearce's research is described in depth in two articles: "Distributed Recycling of Waste Polymer into RepRap Feedstock," coauthored with Christian Baechler and Matthew DeVuono of Queen's University and published in the March issue of Rapid Prototyping; and "Distributed Recycling of Post-Consumer Plastic Waste in Rural Areas," coauthored by Jerry Anzalone, Megan Kreiger, Meredith Mulder and Alexandra Glover of Michigan Tech, which will appear in the Proceedings of the Materials Research Society.*

[http://www.eurekalert.org/pub\\_releases/2013-03/kcl-tdc022613.php](http://www.eurekalert.org/pub_releases/2013-03/kcl-tdc022613.php)

## **Tumors deliberately create conditions that inhibit body's best immune response**

### ***Tumours in melanoma patients deliberately create conditions that knock out the body's 'premier' immune defence***

New research in the Journal of Clinical Investigation reveals that tumours in melanoma patients deliberately create conditions that knock out the body's 'premier' immune defence and instead attract a weaker immune response unable to kill off the tumour's cancerous cells.

The study also highlights a potential antibody biomarker that could help predict prognosis and identify which patients are most likely to respond to specific treatments.

The research, led by Dr Sophia Karagiannis and Professor Frank Nestle at King's College London, UK, was funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London.

Karagiannis and colleagues have previously shown that, in patients with melanoma, antibodies are produced that can attack tumour cells. Despite this, the patient's immune system is often ineffective in preventing the cancer from progressing.

The body's B cells (part of the immune system) produce a total of 5 different antibody classes. The most common, IgG, comprises 4 types (or subclasses) of which the researchers have shown that IgG1 subclass antibodies are the most effective at activating immune cells, while antibodies of the IgG4 subclass are thought to be the least efficient.

In this new research, the authors analysed tumour tissue and blood donated by 80 patients from the melanoma clinic of St John's Institute of Dermatology at Guy's and St Thomas', as well as tissue and blood from healthy volunteers.

By analysing the lesions found in melanoma, the authors show that melanoma tumours not only create conditions that attract IgG4, the weakest possible response, but also that IgG4 antibodies interfere with the action of any IgG1 antibodies circulating.

"We were able to mimic the conditions created by melanoma tumours and showed that B cells can be polarised to produce IgG4 antibodies in the presence of cancer cells," says Dr Karagiannis. In the presence of healthy cells, the body's immune response functions normally, and IgG1 are the main antibodies circulating.

To better understand the functional implications of IgG4 subclass antibodies in cancer, the authors engineered these two antibodies (IgG1, IgG4) against a tumour antigen and demonstrated that unlike IgG1, the IgG4 antibody was ineffective in triggering immune cells to kill cancer cells.

Importantly, IgG4 also blocked the tumour cell killing actions of IgG1, thus preventing this antibody from activating immune cells to destroy tumours.

Additionally, using samples from 33 patients, the authors found that patients with higher IgG4 levels in their blood are more likely to have a less favourable prognosis compared to those whose blood levels of IgG4 are closer to normal levels. This suggests that IgG4 may help assist in predicting disease progression.

"This work bears important implications for future therapies since not only are IgG4 antibodies ineffective in activating immune cells to kill tumours but they also work by blocking antibodies from killing tumour cells," says Dr Karagiannis. "The latter means that IgG4 not only prevents the patient's more powerful antibodies from eradicating cancer, but could also explain why treatments may be hindered by those native IgG4 antibodies found in patients, making therapeutic antibodies less effective."

"Now, with the help of our NIHR Biomedical Research Centre, more work needs to be done on developing IgG4 as a potential clinical and prognostic biomarker which can improve patient care by informing clinical decisions and helping to identify patients most likely to respond to treatments," concludes Professor Nestle. Therefore, these findings are expected to inform the design and help improve the potency and efficacy of future therapies for cancer. "This study can also inform the rational design of novel strategies to counteract IgG4 actions."

The authors are now broadening the study by examining larger groups of patients. The team is analysing blood and sera from patients with melanoma and from patients with other cancers to determine whether the presence of IgG4 could inform patient outcomes or predict responses to therapy. They are also analysing the mechanisms of IgG4 blockade of new and existing therapeutic antibody candidates, and developing new antibody candidates which may be less prone to IgG4 blockade.

*Note to editors: The study additionally benefited from support from Cancer Research UK (CR UK) and CR UK New Agents Committee; and by the CR UK/NIHR Experimental Cancer Medicine Centre.*

<http://bit.ly/WBiLLV>

## Impact craters may have been a toasty home for early life

*Heat from a cosmic crash could have nurtured ancient organisms*

By Erin Wayman

Meteorites smacking into the early Earth could have created warm, watery environments favorable to primordial life. A new study of an impact crater in Finland suggests that such hydrothermal activity could have lasted up to 1.6 million years - at least 10 times longer than theory suggested, providing plenty of time for life to emerge and spread.

Ancient impact craters on Mars were probably also home to hydrothermal activity, making them good places to search for signs of life, the team reports online February 19 in *Geochimica et Cosmochimica Acta*.

The work is “quite exciting,” says Gordon Osinski, a planetary geologist at the University of Western Ontario in Canada. “One of the big unknowns has been how long do these hydrothermal systems last.”

Because hydrothermal systems house life’s most ancient lineages, many biologists think that the first organisms arose there. Volcanoes drive most hydrothermal activity today, such as the hot springs and geysers of Yellowstone. But when life evolved about 3.8 billion years ago, frequent impacts pummeling the planet were the largest source of hydrothermal activity. Energy from such events melted rock and heated water circulating through the Earth’s crust. These hydrothermal environments would have been cozy, protective habitats where life could have emerged, or at least thrived and evolved, Osinski says.

Geologic activity has erased most of the planet’s craters and left the remaining ones poorly preserved, says planetary scientist David Kring of the Lunar and Planetary Institute in Houston. But scientists have managed to estimate that the roughly 250-kilometer-wide Sudbury Crater in Canada hosted hydrothermal activity for a million years or longer after it formed about 1.85 billion years ago.

Smaller impacts, leaving behind holes 20 to 30 kilometers wide, are 10 times as common. So these medium-sized impacts could have played a more important role than big ones in the origins of life, says study coauthor Martin Schmieder, a geologist at the University of Western Australia in Crawley. But theoretical calculations had indicated these craters would have cooled too quickly to sustain hydrothermal activity for more than a few tens of thousands of years—probably not long enough for life to have gotten its start there.

Schmieder and coauthor Fred Jourdan of Curtin University in Perth, Australia, didn’t intend to measure the cooling time of a medium-sized crater. But that’s what happened when they dated Finland’s 23-kilometer-wide Lappajärvi Crater. Using rocks from the crater, the pair determined that the impact occurred about 76.2 million years ago.

But some samples were as much as 1.6 million years younger. Those samples were grains of potassium-feldspar, which is one of the last minerals to crystallize when rock melted by an impact cools. The difference in age between the older rocks and the potassium-feldspar represents the period when the crater was hot enough to support a hydrothermal environment, Schmieder and Jourdan say.

Similar studies of other craters will help determine whether long-lived hydrothermal activity is common to all medium-sized impacts or unique to Lappajärvi, says planetary scientist Jay Melosh of Purdue University in West Lafayette, Ind. Schmieder and Jourdan plan to look at well-preserved craters in Germany or Australia, where they will also investigate properties that influence how long a crater takes to cool.

“I’m happy, if not ecstatic, that people are going to these [smaller] impact craters to collect the data,” Kring says. That will help researchers improve computer simulations of hydrothermal systems in impact craters on Earth and on Mars.

**Citations** G.R. Osinski et al. *Impact-generated hydrothermal systems on Earth and Mars. Icarus.*

doi:10.1016/j.icarus.2012.08.030. [\[Go to\]](#)

M. Schmieder and F. Jourdan. *The Lappajärvi impact structure (Finland): age, duration of hydrothermal crater cooling and implications for life. Geochimica et Cosmochimica Acta.* doi:10.1016/j.gca/2013.02.015. [\[Go to\]](#)

<http://phys.org/news/2013-03-bacteria-clog-medical-devices-quickly.html>

### How do bacteria clog medical devices? Very quickly

*A new study has examined how bacteria clog medical devices, and the result isn't pretty.*

The microbes join to create slimy ribbons that tangle and trap other passing bacteria, creating a full blockage in a startlingly short period of time.

The finding could help shape strategies for preventing clogging of devices such as stents—which are implanted in the body to keep open blood vessels and passages—as well as water filters and other items that are susceptible to contamination. The research was published in *Proceedings of the National Academy of Sciences*. Click on the image to view movie. Over a period of about 40 hours, bacterial cells (green) flowed through a channel, forming a green biofilm on the walls. Over the next ten hours, researchers sent red bacterial cells

through the channel. The red cells became stuck in the sticky biofilm and began to form thin red streamers. Once stuck, these streamers in turn trapped additional cells, leading to rapid clogging. (Image source: Knut Drescher)

Using time-lapse imaging, researchers at Princeton University monitored fluid flow in narrow tubes or pores similar to those used in water filters and medical devices. Unlike previous studies, the Princeton experiment more closely mimicked the natural features of the devices, using rough rather than smooth surfaces and pressure-driven fluid instead of non-moving fluid.

The team of biologists and engineers introduced a small number of bacteria known to be common contaminants of medical devices. Over a period of about 40 hours, the researchers observed that some of the microbes—dyed green for visibility—attached to the inner wall of the tube and began to multiply, eventually forming a slimy coating called a biofilm. These films consist of thousands of individual cells held together by a sort of biological glue.

Over the next several hours, the researchers sent additional microbes, dyed red, into the tube. These red cells became stuck to the biofilm-coated walls, where the force of the flowing liquid shaped the trapped cells into streamers that rippled in the liquid like flags rippling in a breeze. During this time, the fluid flow slowed only slightly.

At about 55 hours into the experiment, the biofilm streamers tangled with each other, forming a net-like barrier that trapped additional bacterial cells, creating a larger barrier which in turn ensnared more cells. Within an hour, the entire tube became blocked and the fluid flow stopped.

The study was conducted by lead author Knut Drescher with assistance from technician Yi Shen. Drescher is a postdoctoral research associate working with Bonnie Bassler, Princeton's Squibb Professor in Molecular Biology and a Howard Hughes Medical Institute Investigator, and Howard Stone, Princeton's Donald R. Dixon '69 and Elizabeth W. Dixon Professor of Mechanical and Aerospace Engineering.

"For me the surprise was how quickly the biofilm streamers caused complete clogging," said Stone. "There was no warning that something bad was about to happen."

By constructing their own controlled environment, the researchers demonstrated that rough surfaces and pressure driven flow are characteristics of nature and need to be taken into account experimentally. The researchers used stents, soil-based filters and water filters to prove that the biofilm streams indeed form in real scenarios and likely explain why devices fail.

The work also allowed the researchers to explore which bacterial genes contribute to biofilm streamer formation. Previous studies, conducted under non-realistic conditions, identified several genes involved in formation of the biofilm streamers. The Princeton researchers found that some of those previously identified genes were not needed for biofilm streamer formation in the more realistic habitat.

*More information: Drescher, Knut, Yi Shen, Bonnie L. Bassler, and Howard A. Stone. 2013. Biofilm streamers cause catastrophic disruption of flow with consequences for environmental and medical systems. Proceedings of the National Academy of Sciences. Published online February 11. Provided by Princeton University*

<http://bit.ly/WBkzV4>

## **Mars trip to use astronaut poo as radiation shield**

***Protection from cosmic rays by lining the spacecraft's walls with water, food and astronauts' faeces.***

**18:45 01 March 2013 by Jacob Aron and Lisa Grossman**

The man and woman aboard the Inspiration Mars mission set to fly-by the Red Planet in 2018 will face cramped conditions, muscle atrophy and potential boredom. But their greatest health risk comes from exposure to the radiation from cosmic rays. The solution? Line the spacecraft's walls with water, food and their own faeces. "It's a little queasy sounding, but there's no place for that material to go, and it makes great radiation shielding," says Taber MacCallum, a member of the team funded by multimillionaire Dennis Tito, who announced the audacious plan earlier this week.

MacCallum told New Scientist that solid and liquid human waste products would get put into bags and used as a radiation shield – as well as being dehydrated so that any water can be recycled for drinking. "Dehydrate them as much as possible, because we need to get the water back," he said. "Those solid waste products get put into a bag, put right back against the wall."

Food too, could be used as a shield, he said. "Food is going to be stored all around the walls of the spacecraft, because food is good radiation shielding," he said. This wouldn't be dangerous as the food would merely be blocking the radiation, it wouldn't become a radioactive source.

### **Water 1 – Metals 0**

The details of Inspiration Mars's plans have yet to be clarified, but the team has said it will be using "state-of-the-art technologies derived from NASA and the International Space Station".

One idea that is already under consideration by the agency's Innovative Advanced Concepts programme, which funds research into futuristic space technology, is a project called Water Walls, which combines life-support and waste-processing systems with radiation shielding.

Water has long been suggested as a shielding material for interplanetary space missions. "Water is better than metals for protection," says Marco Durante of the Technical University of Darmstadt in Germany. That's because nuclei are the things that block cosmic rays, and water molecules, made of three small atoms, contain more nuclei per volume than a metal.

Water shielding also has another benefit – you can drink it. Such dual use is essential aboard a spacecraft, where space is at a premium. Applying this rationale, the Water Walls concept involves polyethylene bags that use osmosis to process clean drinking water from urine and faeces.

### **Sights and smells**

Lining the walls of a spacecraft with layers of these bags creates a 40-centimetre-thick liquid shield. All of the bags would initially be filled with drinking water. The crew would then fill other bags with waste during the trip to Mars and swap them out for the now-empty water bags.

The osmosis-based processing is much simpler than the automated life-support systems aboard the International Space Station, making it less likely to fail during the long ride to Mars.

However, there are problems to be ironed out. The urine-to-water processing bags were tested in orbit on the last ever flight of the space shuttle in 2011 and found to be 50 per cent less efficient in microgravity than in ground-based tests.

Besides testing that the various bags work properly, the Water Walls team points out the more basic worry of dealing with the residual sights and smells. MacCallum made a similar point about the system to be used on Inspiration Mars: "Hopefully they're not clear bags," he said.

### **Solar danger**

Not all bags need be equally unpleasant, though. The Water Walls concept also includes bags that scrub carbon dioxide from air, regulate temperature and grow algae for food – although NASA hasn't yet taken those to space. Inspiration Mars also plans to have an external water tank and the aluminium skin of the spacecraft itself for extra protection. This kind of shielding should keep astronauts safe from lower energy cosmic rays, says Ruth Bamford of the Rutherford Appleton Laboratory in Didcot, UK, who is working on creating magnetic "deflector shields" for spacecraft.

Organic material or aluminium is no defence against the burst of particles that occasionally spew out from the sun during a solar storm, however. "For this, putting three metres of concrete may not be enough to protect the astronauts," says Bamford. Inspiration Mars say they should be able to keep the upper rocket stage of their launch vehicle attached to the spacecraft for the whole of the trip, and point that towards the sun in the event of a flare.

[http://www.eurekalert.org/pub\\_releases/2013-03/uotm-cvs022813.php](http://www.eurekalert.org/pub_releases/2013-03/uotm-cvs022813.php)

## **Cancer vaccines self-sabotage, channel immune attack to injection site**

### ***UT MD Anderson scientists find common vaccine ingredient diverts T cells from tumors***

HOUSTON – Cancer vaccines that attempt to stimulate an immune system assault fail because the killer T cells aimed at tumors instead find the vaccination site a more inviting target, scientists at The University of Texas MD Anderson Cancer Center report in Nature Medicine.

A common substance used in many cancer vaccines to boost immune attack betrays the cause by facilitating a buildup of T cells at the vaccination site, which then summon more T cells to help with the perceived threat.

"Vaccines stimulate production of T cells primed to attack the target cancer, and there are many T cells in the bloodstream after vaccination. We found that only a few get to the tumor while many more are stuck at or double back to the vaccination site," said senior author Willem Overwijk, Ph.D., in MD Anderson's Department of Melanoma Medical Oncology.

The result: largely unscathed tumors while an overstimulated immune response can cause lesions at the injection site. The team found that a major culprit in this failure is incomplete Freund's adjuvant (IFA), a mineral oil-based adjuvant included in many vaccines to stoke the immune response.

"IFA sticks around the vaccination site for up to three months, along with the antigen designed to trigger immunity against the tumor," Overwijk said. "T cells keep attacking and secreting chemokines to call for reinforcements. But it's an unkillable target; T cells can't kill mineral oil."

Eventually, the T cells die. "The vaccination site increasingly resembles a viral infection, with lots of damaged tissue and antigens," Overwijk said.

### **Switch from IFA to saline adjuvant reverses effect**

"Switching to a saline-based adjuvant in a melanoma vaccine reversed the T cell effect in mice," Overwijk said, "Major accumulations of T cells gathered in tumors, shrinking them, with minimal T cell activity at the vaccination site." Peptide antigens are available for almost all types of cancer, Overwijk said. A saline adjuvant could change the poor performance of cancer vaccines.

A clinical trial of the concept is expected to open later this year led by Craig Singluff Jr., M.D., professor of surgery at the University of Virginia Medical School, and Patrick Hwu, M.D., chair of MD Anderson's Department of Melanoma Medical Oncology.

Overwijk and colleagues noted 98 federally approved U.S. clinical trials of vaccines against a variety of cancers have almost all failed, while another 37 trials are open, enrolling patients. The U.S. Food and Drug Administration has approved only one therapeutic vaccine, for treatment of prostate cancer, out of all of those trials.

"Our group and many other researchers have been trying for years to improve the performance of cancer vaccines, to no avail," Overwijk said. "People kept trying because of these beguiling T cell levels in the blood. But our data suggest that the very nature of IFA-based vaccines may make it almost impossible for them to work well."

In past experiments and clinical trials, tumors were rarely examined for evidence of T cell penetration. In people, they are often inoperable, and there was no indication that it needed to be done. "But a few researchers did analyze human tumors for T cell infiltration and largely found what we found in our mouse experiments," he said.

### **Mouse studies reveal vaccine self-sabotage**

The team studied the fate of melanoma-specific CD8-positive T cells after vaccination with the gp100 peptide with and without IFA. Both vaccines increased levels of the desired T cells in the blood, but with IFA, the T cells dropped to nearly undetectable levels after three weeks and did not rebound even with an engineered virus-based booster. The vaccine-lacking IFA produced similar peak amounts of the T cells, a response that persisted over time. The research team fluorescently tagged T cells in the mouse model to see where they went.

*Mice without IFA had the bulk of T cells light up in their tumors with minimal presence at the vaccination site.*

*T cells built up at the injection site in mice that received IFA-based vaccine, with a tiny showing in the tumor.*

Response duration was tested in gp100/IFA and control IFA vaccines. The antigen/IFA combination gathered and persisted at the vaccination site, where it could still stimulate the proliferation of injected T cells 96 days after vaccination. A separate set of experiments showed the antigen/IFA-driven T cells were forced to kill themselves at the vaccination site by a variety of cell suicide-inducing proteins.

### **Reducing vaccine depots at injection site**

Overwijk and colleagues inferred that a possible answer to the problem was to reduce the size and persistence of vaccine "depots" at the injection site.

They tested a vaccine based on a saline solution instead of IFA and found that antigens cleared more quickly but did not spark the desired T cell response. A combination of three stimulatory molecules (covax) was added to the saline/peptide vaccine, producing a strong T cell response. IFA/peptide vaccine produced a strong T cell response but also stronger post-peak T cell suicide.

A comparison of saline/peptide/covax vs. IFA/peptide/covax showed the saline version caused T cells to home to the tumor and destroy them, while the IFA version focused T cells at the vaccination site, killing normal tissue and inducing chemokines that damaged and killed T cells.

"IFA-based vaccination sites essentially outcompete tumor sites for T cell recognition and accumulation, chemokine production and tissue damage," Overwijk said. "It's an engineering flaw in those vaccines that we didn't appreciate until now. Fortunately, our results also directly instruct us how to design new, more powerful vaccine formulas for treating people with cancer."

*Co-authors are first author Yared Hailemichael, Zhimin Dai, Nina Jaffarzarad, Yang Ye, Miguel Medina, Xue-Fei Huang, Stephanie Dorta-Estremera Nathaniel Greeley, , Giovanni Nitti, Weiyi Peng, Chengwen Liu, Yanyan Lou, Brian Rabinovich and Patrick Hwu, all of MD Anderson's Department of Melanoma Medical Oncology; Zhiqiang Wang, Wencai Ma, and Richard Davis, of MD Anderson's Department of Lymphoma and Myeloma; and Kimberly Schluns, of MD Anderson's Department of Immunology.*

*Dorta-Estremera, Greeley, and Nitti are graduate students in The University of Texas Graduate School of Biomedical Sciences, a graduate school operated jointly by MD Anderson and The University of Texas Health Science Center at Houston. Schluns, Davis, Hwu and Overwijk also are on the GSBS faculty.*

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[http://www.eurekalert.org/pub\\_releases/2013-03/uomm-rdf030113.php](http://www.eurekalert.org/pub_releases/2013-03/uomm-rdf030113.php)

## Researchers describe first 'functional HIV cure' in an infant

*A team of researchers from Johns Hopkins Children's Center, the University of Mississippi Medical Center and the University of Massachusetts Medical School describe the first case of a so-called "functional cure" in an HIV-infected infant. The finding, the investigators say, may help pave the way to eliminating HIV infection in children.*

A report on the case is scheduled for presentation at a press conference on Sunday, March 3, at the 20th Conference on Retroviruses and Opportunistic Infections (CROI) in Atlanta. Johns Hopkins Children's Center virologist Deborah Persaud, M.D., lead author on the report, and University of Massachusetts Medical School immunologist and professor Katherine Luzuriaga, M.D., headed a team of laboratory investigators. Pediatric HIV specialist Hannah Gay, M.D., associate professor of pediatrics at the University of Mississippi Medical Center provided treatment to the baby.

The infant described in the report underwent remission of HIV infection after receiving antiretroviral therapy (ART) within 30 hours of birth. The investigators say the prompt administration of antiviral treatment likely led to this infant's cure by halting the formation of hard-to-treat viral reservoirs — dormant cells responsible for reigniting the infection in most HIV patients within weeks of stopping therapy.

"Prompt antiviral therapy in newborns that begins within days of exposure may help infants clear the virus and achieve long-term remission without lifelong treatment by preventing such viral hideouts from forming in the first place," Persaud says.

The researchers say they believe this is precisely what happened in the child described in the report. That infant is now deemed "functionally cured," a condition that occurs when a patient achieves and maintains long-term viral remission without lifelong treatment and standard clinical tests fail to detect HIV replication in the blood. In contrast to a sterilizing cure — a complete eradication of all viral traces from the body — a functional cure occurs when viral presence is so minimal, it remains undetectable by standard clinical tests, yet discernible by ultrasensitive methods.

The child described in the current report was born to an HIV-infected mother and received combination antiretroviral treatment beginning 30 hours after birth. A series of tests showed progressively diminishing viral presence in the infant's blood, until it reached undetectable levels 29 days after birth. The infant remained on antivirals until 18 months of age, at which point the child was lost to follow-up for a while and, the researchers say, stopped treatment. Ten months after discontinuation of treatment, the child underwent repeated standard blood tests, none of which detected HIV presence in the blood. Test for HIV-specific antibodies — the standard clinical indicator of HIV infection — also remained negative throughout.

Currently, high-risk newborns — those born to mothers with poorly controlled infections or whose mothers' HIV status is discovered around the time of delivery — receive a combination of antivirals at prophylactic doses to prevent infection for six weeks and start therapeutic doses if and once infection is diagnosed. But this particular case, the investigators say, may change the current practice because it highlights the curative potential of very early ART.

Specialists say natural viral suppression without treatment is an exceedingly rare phenomenon observed in less than half a percent of HIV-infected adults, known as "elite controllers," whose immune systems are able to rein in viral replication and keep the virus at clinically undetectable levels. HIV experts have long sought a way to help all HIV patients achieve elite-controller status. The new case, the researchers say, may be that long-sought game-changer because it suggests prompt ART in newborns can do just that.

The investigators caution they don't have enough data to recommend change right now to the current practice of treating high-risk infants with prophylactic, rather than therapeutic, doses but the infant's case provides the rationale to start proof-of-principle studies in all high-risk newborns.

"Our next step is to find out if this is a highly unusual response to very early antiretroviral therapy or something we can actually replicate in other high-risk newborns," says Persaud, who is also the scientific chair of the HIV Cure Committee of the International Maternal, Pediatric Adolescent AIDS Clinical (IMPAACT) network, a consortium of researchers and institutions that was critical in spearheading the earliest clinical trials of mother-to-child transmission and early treatment of infants 15 years ago.

A single case of sterilizing cure has been reported so far, the investigators note. It occurred in an HIV-positive man treated with a bone marrow transplant for leukemia. The bone marrow cells came from a donor with a rare genetic mutation of the white blood cells that renders some people resistant to HIV, a benefit that transferred to the recipient. Such a complex treatment approach, however, HIV experts agree, is neither feasible nor practical for the 33 million people worldwide infected with HIV.



"Complete viral eradication on a large scale is our long-term goal but, for now, remains out of reach, and our best chance may come from aggressive, timely and precisely targeted use of antiviral therapies in high-risk newborns as a way to achieve functional cure," says Luzuriaga.

Despite the promise this approach holds for infected newborns, the researchers say preventing mother-to-child transmission remains the primary goal.

"Prevention really is the best cure, and we already have proven strategies that can prevent 98 percent of newborn infections by identifying and treating HIV-positive pregnant women," says Gay, the HIV expert who treated the infant.

*The research was funded by the National Institutes of Health and by the American Foundation for AIDS Research (amfAR).*

<http://www.bbc.co.uk/news/health-21628911>

### **Skin patches 'may beat prostate cancer'**

*Skin patches which deliver oestrogen into the blood may be a cheaper and safer treatment for prostate cancer than current therapies, a study says.*

**By James Gallagher Health and science reporter, BBC News**

The main treatment is injections of a chemical to cut levels of testosterone - the driving force of many prostate cancers - but it causes side effects.

The Imperial College London study in the Lancet Oncology compared patches and injections in 254 patients. It found patches were safe and should avoid menopause-like side effects.

#### **'Effective treatments'**

Using oestrogen to treat prostate cancer is an old treatment.

Both oestrogen and testosterone are very similar chemically, so ramping up the levels of oestrogen in the body can reduce the amount of testosterone produced - and slow prostate cancer growth.

However, taking oral oestrogen pills caused significant health problems by overdosing the liver. The organ then produced chemicals which caused blood clots, heart attacks and strokes.

The preferred treatment is injections of a drug, LHRHa, which reduces the production of both oestrogen and testosterone. However, this has side effects similar to the menopause in women - resulting in poor bone health and diabetes.

Prof Paul Abel, from Imperial College London, said: "We're not claiming this is equivalent to current therapies yet, but it does look like we are getting castration levels of testosterone."

However, the researchers need to follow patients for longer.

"The next step is to test if the oestrogen patches are as effective at stopping the growth of prostate cancer as the current hormone treatments, we're now testing this in over 600 patients."

Kate Law, from the charity Cancer Research UK which part funded the study, said: "More men than ever are surviving prostate cancer thanks to advances in research, but we still urgently need to find more effective treatments and reduce side effects.

"This trial is an important step towards better and kinder treatments that could bring big benefits to men with prostate cancer in the future."

Dr Iain Frame, director of research at Prostate Cancer UK, said: "It is unclear as yet if hormone patches could be an effective alternative to hormone injections, but we await with anticipation the results of the further trials planned which could in time offer men hope for the future."

[http://www.eurekalert.org/pub\\_releases/2013-03/jhm-lo030113.php](http://www.eurekalert.org/pub_releases/2013-03/jhm-lo030113.php)

### **'Shelf life' of blood? Shorter than we think**

*A small study from Johns Hopkins adds to the growing body of evidence that red blood cells stored longer than three weeks begin to lose the capacity to deliver oxygen-rich cells where they may be most needed.*

In a report published online in the journal *Anesthesia & Analgesia*, the Johns Hopkins investigators say red cells in blood stored that long gradually lose the flexibility required to squeeze through the body's smallest capillaries to deliver oxygen to tissue. Moreover, they say, that capacity is not regained after transfusion into patients during or after surgery.

"There's more and more information telling us that the shelf life of blood may not be six weeks, which is what the blood banks consider standard," says study leader Steven M. Frank, M.D., an associate professor of anesthesiology and critical care medicine at the Johns Hopkins University School of Medicine. "If I were having surgery tomorrow, I'd want the freshest blood they could find."

Frank acknowledges that blood banks do not have enough fresh blood for everybody, and that shorter storage periods would result in diminished inventory. But he says that the current practice of transfusing blood stored up to six weeks may need to be reconsidered.

One previous, large study published in the *New England Journal of Medicine* has already shown that cardiac surgery patients who received blood stored longer than three weeks were almost twice as likely to die as patients who got blood that had been stored for just 10 days.

For the new study, Frank and his colleagues enrolled 16 patients scheduled to have spinal fusion surgery, a type of operation that typically requires blood transfusions. Six of the patients received five or more units of blood, while 10 needed three or fewer units. The researchers drew samples from every bag of blood used — 53 in total — and measured the flexibility of the red blood cells. What they found is that blood older than 3 weeks was more likely to have less flexible red blood cell membranes, a condition that may make it more difficult for blood to deliver oxygen, Frank says.

The team also took blood samples from patients in the three days following surgery. Even though the blood cells were out of storage and back in biological environments with proper pH (acidity), electrolytes and oxygen levels, the injury to the red cells was not reversible and appeared to be permanent. The damaged blood cells would likely remain dysfunctional for their life cycle limit, which is up to 120 days, Frank says.

Frank also noted that patients in the study who got fewer units of blood had healthier red cells overall, even though the blood was just as old and showed cell damage. He says it is likely that a small amount of these problem cells make less of a difference than when a large number of damaged cells are present.

According to the research report, the average age of the blood given in the study was more than 3 weeks. Only three samples in the study were 2 weeks old or less. One reason for the lack of availability of fresher bloods for adults, Frank says, is the routine practice of giving pediatric patients priority for the freshest units.

In fact, he notes, blood banks dispense the oldest blood first so that it doesn't exceed its shelf life before it can be used. "As a colleague said, it's like how they sell milk in the grocery store — they put the oldest cartons out front so they can sell them before they expire," Frank says.

Two large randomized controlled studies, one at many centers across the United States, including Johns Hopkins, and one in Canada, are under way to determine the relative safety of older versus newer blood, and the results are expected next year. Frank says blood banks need to be prepared to change practice if those studies show that a six-week shelf life for blood is just too long.

*The study was supported in part by the National Institutes of Health's National Institute on Aging (R01 AG021523) and National Heart, Lung, and Blood Institute (R01 HL092259-01).*

*Other Johns Hopkins researchers involved in the study include Bagrat Abazyan, M.D.; Masahiro Ono, M.D.; Charles W. Hogue, M.D.; David B. Cohen, M.D., M.P.H.; Daniel E. Berkowitz, M.D.; Paul M. Ness, M.D.; and Viachaslau M. Barodka, M.D.*