

[http://www.eurekalert.org/pub\\_releases/2010-11/kri-eb0111910.php](http://www.eurekalert.org/pub_releases/2010-11/kri-eb0111910.php)

**Economic benefits of the global polio eradication initiative estimated at \$40-50 billion**  
***New study in Vaccine offers strong economic justification for finishing the job on polio as quickly as possible***

Boston, MA – A new study released today estimates that the global initiative to eradicate polio could provide net benefits of at least US\$40-50 billion if transmission of wild polioviruses is interrupted within the next five years. The study provides the first rigorous evaluation of the benefits and costs of the Global Polio Eradication Initiative (GPEI)—the single largest project ever undertaken by the global health community. The study comes at a crucial time—following an outbreak in the Republic of the Congo and one in Tajikistan earlier this year—that highlight the risk of delays in finishing the job on polio.

Published in the journal *Vaccine*, the study, "Economic Analysis of the Global Polio Eradication Initiative," considers investments made since the GPEI was formed in 1988 and those anticipated through 2035. Over this time period, the GPEI's efforts will prevent more than 8 million cases of paralytic polio in children. This translates into billions of dollars saved from reduced treatment costs and gains in productivity.

The study also reported that "add-on" GPEI efforts improve health benefits and lead to even greater economic gains during the same time period. Notably, it estimates an additional \$17-90 billion in benefits from life saving effects of delivering vitamin A supplements, which the GPEI has supplied alongside polio vaccines.

"Polio eradication is a good deal, from both a humanitarian and an economic perspective," said Dr. Radboud Duintjer Tebbens of Kid Risk, Inc., the lead author of the study. "The GPEI prevents devastating paralysis and death in children and also allows developing countries and the world to realize meaningful financial benefits."

According to the study, although delays in achieving eradication are costly, even with delays, the GPEI still generates positive net economic benefit estimates.

"Investing now to eradicate polio is an economic imperative, as well as a moral one," said Dr. Tachi Yamada, president of the Bill & Melinda Gates Foundation's Global Health Program. "This study presents a clear case for fully and immediately funding global polio eradication, and ensuring that children everywhere, rich and poor, are protected from this devastating disease."

The GPEI successfully reduced the global incidence of polio by 99 percent since 1988 and eradicated type 2 wild polioviruses in 1999. Intense efforts are underway to stop transmission of types 1 and 3 completely within the next several years, with indigenous transmission remaining only in relatively small areas in Afghanistan, India, Nigeria, and Pakistan and re-established transmission in a few countries, including Angola and the DRC. Until eradication occurs, all countries remain at risk for importation of the virus, as demonstrated by the 2010 polio outbreaks in Tajikistan and the Republic of the Congo. Congo's recent outbreak has resulted in more than 200 cases of acute flaccid paralysis (AFP) since October, mostly affecting people older than 15.

"Studies like this help people put numbers on the value of prevention," said Dr. Kimberly Thompson of Kid Risk, senior author of the study. Nobody questions the value of eradication in developed countries where polio is fortunately just a fading memory, but according to Thompson, "prevention activities like vaccination often go unappreciated, because it is difficult to count cases of a disease that do not occur." The study provides an example of the real value that comes from international cooperation and investment in the health and development of children.

The study examined the 104 countries that directly benefit from the GPEI, which include predominantly lower-income countries. Many higher-income countries eliminated wild polioviruses before the GPEI began. Thus, the estimated net benefits in the study do not include the substantial benefits already accruing in developed countries.

*The study was led by Kid Risk, Inc., an independent non-profit organization started in 2009 as the successor to the Kids Risk Project at the Harvard School of Public Health. Other research partners included the U.S. Centers for Disease Control and Prevention (CDC), Delft University of Technology, and the Global Polio Eradication Initiative. The CDC provided support for the study under a contract to the Harvard School of Public Health.*

[http://www.eurekalert.org/pub\\_releases/2010-11/eaps-nsi112210.php](http://www.eurekalert.org/pub_releases/2010-11/eaps-nsi112210.php)

**New spinal implant will help people with paraplegia to exercise paralyzed limbs**  
***Engineers have developed a new type of microchip muscle stimulator implant that will enable people with paraplegia to exercise their paralysed leg muscles.***

It is the first time that researchers have developed a device of this kind that is small enough to be implanted into the spinal canal and incorporates the electrodes and muscle stimulator in one unit. The implant is the size of a child's fingernail. The Engineering and Physical Sciences Research Council (EPSRC) project is being led by Professor Andreas Demosthenous from University College London. It includes engineers from Freiburg University and the Tyndall Institute in Cork.

"The work has the potential to stimulate more muscle groups than is currently possible with existing technology because a number of these devices can be implanted into the spinal canal", said Professor Andreas Demosthenous. "Stimulation of more muscle groups means users can perform enough movement to carry out controlled exercise such as cycling or rowing."

The devices could also be used for a wide range of restorative functions such as stimulating bladder muscles to help overcome incontinence and stimulating nerves to improve bowel capacity and suppress spasms.

The research team has overcome previous limitations by micro-packaging everything into one tiny unit. Latest laser processing technology has been used to cut tiny electrodes from platinum foil. These are then folded into a 3D shape (which looks like the pages of a book, earning the device the name of the Active Book). The pages close in around the nerve roots. They are micro-welded to a silicon chip which is hermetically sealed to protect against water penetration, which can lead to corrosion of the electronics.

The exciting innovation has been welcomed by Universities and Science Minister David Willetts, who said: "The Active Book is a good example of how UK scientists and engineers are translating research into innovations that deliver real benefits for society. This tiny implant has the potential to make a real difference to the lives and long-term health of people with paraplegia in the UK and around the world."

The Active Book will be made available for pilot studies sometime next year.

*Notes for Editors: The project is co-led by Professor Nick Donaldson of University College London.*

*Although electrical stimulation of leg muscles has been used for some time, it is usually done by attaching electrodes to the outside of the legs and then connecting the electrodes to an external stimulator. This is too time consuming to be used every day so few people with spinal cord injury continue with this method despite the clear health benefits.*

*At the moment electrical stimulation of nerve roots in the spinal canal can be carried out using implanted electrodes and an implanted stimulator connected by a cable. This latest research is the first to combine the electrodes and muscle stimulator in one unit so that more nerves can be stimulated and better function achieved.*

[http://www.eurekalert.org/pub\\_releases/2010-11/uosc-sh112210.php](http://www.eurekalert.org/pub_releases/2010-11/uosc-sh112210.php)

### **Speed heals**

#### ***USC College's Samantha Butler and collaborators show that the rate and direction of axon growth in the spinal cord can be controlled, a discovery that 1 day may help improve treatment for spinal injuries or neurodegenerative diseases***

Both the rate and direction of axon growth in the spinal cord can be controlled, according to new research by USC College's Samantha Butler and her collaborators. The study, "The Bone Morphogenetic Protein Roof Plate Chemorepellent Regulates the Rate of Commissural Axonal Growth," by Butler; lead researcher Keith Phan and graduate students Virginia Hazen and Michele Frendo of USC College; and Zhengping Jia of the University of Toronto, was published online in the November 17 issue of the Journal of Neuroscience.

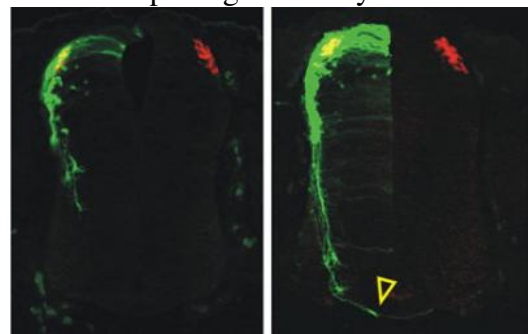
Butler, assistant professor of biological sciences, found that a series of connections at the cellular level produce a guidance cue that tells an axon how fast and in which direction to grow in an embryonic environment. Butler and her team also discovered that by modulating the activity of enzyme LIM domain kinase 1 (Limk1), the rate of axon growth can be stalled or accelerated. Future applications of these findings may include enhancing the ability to regenerate neuronal circuits in patients suffering from spinal cord injuries or neurodegenerative diseases.

Initially, to understand these guidance cues, Butler and her colleagues studied the mechanisms by which neuronal circuits first develop in the embryonic states of rodents and chickens. While researching how an axon is programmed to grow in a particular direction, Butler and her group made a surprising discovery.

"We were expecting that when we perturbed the signaling pathway, the axon would be confused in terms of direction," Butler said. "But we found a much greater effect — the axon grew at a different speed."

Under normal conditions, guidance cues cause a developing neuron to extend an axon into the environment. In a developing spinal cord, the cue comes in the form of a repellent, which acts from behind the cell body to direct the growth of the axon in the opposite direction. This repellent is mediated by bone morphogenetic proteins (BMPs).

*Axons (green) growing around one side of the developing spinal cord in the control (left) and in the experiment (right).*



*In the experiment, by lowering the level of Limk1, the axons have now projected much further (yellow arrow) at the same stage in development. Image courtesy of Samantha Butler.*

In the beginning of the multi-step growth process, BMPs bind to a cell and activate its receptors; then a second messenger is triggered, in this case Limk1. Limk1 modifies the activity of a protein called cofilin. When cofilin is active, the axon grows. If the cofilin becomes inactive, growth comes to a halt.

Butler and her team discovered that by increasing the amount of cofilin, or decreasing the amount of the restricting Limk1, the commissural axon growth accelerated. Likewise, when the amount of cofilin was decreased, or the amount of Limk1 was increased, axon growth stopped.

The axon growth in embryonic spinal cords in which Limk1 was lowered appeared to be more advanced than in controls - the axons grew up to 25 percent faster. Since the axon is growing through an ever-changing environment, if the accelerated rate moves the axon to its subsequent signal destination too fast, that destination may not yet be created. As a result, growth acceleration can lead to errors in the process, Butler said. She hopes to determine the optimal rate of acceleration that prevents these errors but still supports enhanced regeneration.

"That the growth of axons needs to be controlled in time as well as space is something that is an interesting piece of biology," Butler said. "How it can be applied is very exciting."

Butler sees the application of this research as one part of the process for rebuilding damaged circuits in patients who have sustained spinal cord injuries, or those suffering from Parkinson's or Alzheimer's diseases, possibly using stem-cell-derived therapy. The average rate of axon growth is just 1 mm per day, so any increase would improve a patient's treatment. "If we knew how to modulate cofilin to maximize the speed of axon growth," Butler said, "perhaps we could shave time off that process of circuit regeneration."

Read the full text of the article at <http://www.jneurosci.org/cgi/content/full/30/46/15430>

[http://www.eurekalert.org/pub\\_releases/2010-11/bu-sif112210.php](http://www.eurekalert.org/pub_releases/2010-11/bu-sif112210.php)

### **Stability is first step toward treating ALS**

#### ***A team of Brandeis scientists makes breakthrough with mutant gene that causes familial form of Lou Gehrig's disease***

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that eventually destroys most motor neurons, causing muscle weakness and atrophy throughout the body. There is no cure and the current treatment has only a moderate effect on the march of the disease, which typically kills within three to five years. This week in PNAS, a team of Brandeis scientists reports an innovative approach to treating the most common form of familial ALS, commonly known as Lou Gehrig's disease.

In the study, researchers studied mutations in the gene that makes a particular protein, known as SOD1, responsible for causing much of the familial form of ALS, said Brandeis University chemist and study author Jeff Agar. Genetic mutations make the SOD1 protein unstable, causing it to fall apart into two identical pieces called monomers that are sticky and prone to clumping up inside the axon, the long projection of the motor neuron that conducts electrical impulses. Motor neurons are a meter long; when the axon inside the neuron gets clogged, it eventually dies.

"Picture a tennis ball stuck to a small piece of double sided tape. Now picture another. Turn the balls until both pieces of tape come into contact and that's what scientists call a dimer, and it's stable," explained Agar. "It won't stick to anything else. That's what normal SOD1 looks like, and there are billions of SOD1 dimers in every motor neuron.

Now pull the tennis balls apart, turn one 180 degrees, stick them back together and there's a sticky end. That's what ALS-associated SOD1 mutants do. You could stick millions of these balls together if you had them, and a neuron has billions of them. "What we're trying to do is prevent this from happening," said Agar.

Agar, along with post-doctoral fellow Jared Auclair, and biochemists Greg Petsko and Dagmar Ringe, developed an ingenious "chemical rope" to tie the two monomers together, creating a stable dimer. This strategy potentially solves the instability problem, especially since the protein proved able to withstand 40 degrees of heating above body temperature before falling apart again. SOD1 is one of the body's hardest working antioxidants, and its job is to turn a dangerous free radical called superoxide into water. Some ALS mutations stop SOD1 from doing its job, a process called inactivation, and the chemical ropes were even able to reactivate these SOD1 mutants and get them working again.

Next, the scientists had to create a version of their proof-of-concept "chemical rope" that was potentially amenable to development into a therapeutic, because the first one was toxic. Here they adopted a less toxic type of chemistry known as a thiol-disulfide exchange.

"This is only the beginning," said Agar. "It's one thing to do what we've done using purified proteins, but it is orders of magnitude more difficult to accomplish the same thing inside a complex organism. We have a lot more work to do before this could benefit ALS patients."

While the familial form of ALS, known as fALS, affects only about two percent of all ALS cases, there is growing evidence that changes in the same protein can cause some cases of sporadic (non inherited) ALS, and the researchers believe that perhaps 30 to 40 percent of cases where there is no genetic cause could potentially also benefit from the same treatment. The next step is to study SOD1 in cell cultures and in a mouse model to develop a pre-clinical candidate drug using this strategy. *The study was funded by the National Institutes of Health.*



## Toddlers to get 'six in one' jabs

### ***Different immunisations can be administered at the same time***

Young children are to be immunised against six diseases at once, the Government has confirmed.

After their first birthday toddlers will be offered a single appointment to have three injections to guard against measles, mumps, rubella, two types of meningitis and a form of pneumonia.

This replaces the existing NHS policy for England and Wales of spacing the vaccines over a couple of months.

The change is designed to boost vaccination rates. Writing to all GPs concerned, the Chief Medical Officer Professor Dame Sally Davies said the new policy should be "brought in as soon as practicable for your area". Currently around 85% of all toddlers turn up to get immunised.

### **Boosting uptake**

Although this is more than in previous years, experts are still having to work hard to get the figure up to the 95% level that is necessary to effectively stop the spread of the disease in the community.

The vaccination rate has been well below this level for several years, ever since the Lancet medical journal published controversial research about the MMR vaccine in 1998. The study has since been discredited, but confidence has been slow to return in the combined measles, mumps and rubella vaccine.

Government advisors believe simplifying the immunisation schedule will help boost vaccine uptake by making it easier for parents to get their children vaccinated. While some parents will welcome one fewer visit to the doctor, others may be concerned about exposing their children to so many vaccines in one sitting. But experts say combining the vaccines should not pose any additional risk.

A Department of Health spokeswoman said: "Independent scientific research has shown that providing these vaccines at the same time is safe, effective and more convenient for parents." Children will still be offered the usual series of baby vaccinations as well as their pre-school booster jabs after their third birthday.

<http://www.bbc.co.uk/news/magazine-11798317>

## Diagrams that changed the world

***A picture, the old adage goes, is worth 1,000 words. But in science a diagram can describe things that transcend the written word. A single image can convey the simple underlying pattern hidden by words or equations, says Marcus du Sautoy.***

Draw the right picture and you can literally transform the way we see the world. But a diagram is more than just a physical representation of what we see with our eyes.

The power of a diagram is to crystallise a new way of seeing the world.

Often it requires throwing away information, focusing on what is essential.

Other times it changes a scientific idea into a visual language providing a new map where the mathematics of geometry takes over and helps us to navigate the science at hand.

Copernicus certainly understood the power of a good picture. In his great opus *De Revolutionibus Orbium Coelestium* published shortly before his death in 1543 Copernicus takes 405 pages of words, numbers and equations to explain his heliocentric theory.

### **Nine circles**

But it is the diagram that he draws at the beginning of the book that captures in a simple image his revolutionary new idea: it is the Sun that is at the centre of the Solar System, not the Earth.

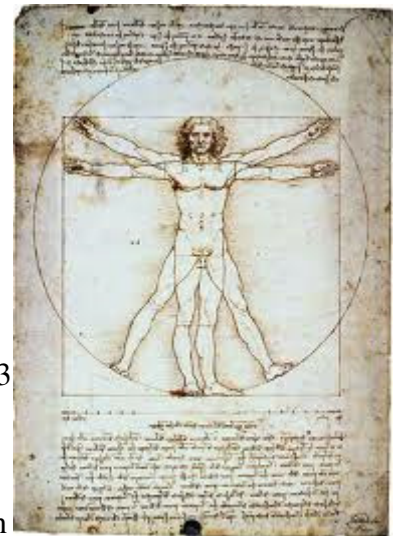
His picture encapsulates some of the essential elements of the best diagrams. The concentric circles are not meant to describe the precise orbits of the planets.

Copernicus knew they weren't circles. The uniform distances between the circles aren't meant to tell you how far the planets are from the sun. Rather this picture conveys the simple yet shocking idea that we aren't at the centre of things. His diagram transformed our view of our place in the universe

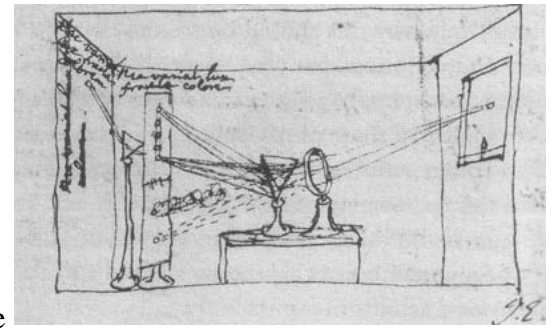
But some diagrams do more than just crystallise the essential underlying structure of a complex system. A diagram has the power to create a whole new visual language to navigate a scientific idea.

Newton's optics diagrams for example transform light into geometry.

By representing light as lines Newton is able to use mathematics and geometry to predict the behaviour of light. It was a revolutionary idea. Look at the light that



illuminates the world around you. There are no lines. Newton's diagram translates the slippery science of optics into the concrete world of geometry where mathematics becomes the eyes to see what is happening to light.



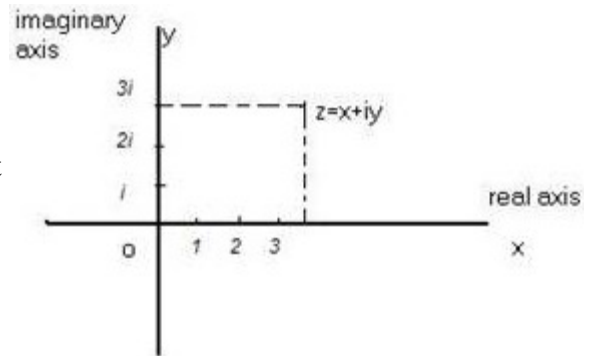
Sometimes a diagram is the crucial step in making people believe in the impossible.

### Diagram of deaths

Mathematicians had been struggling with the idea of the square root of minus one. There seemed to be no number on the number line whose square was negative. Yet experts knew that if such a number existed it would transform their subject.

But where was this number? It was a picture drawn independently by three mathematicians at the beginning of the 19th Century that brought these numbers to life.

They created a two dimensional map of numbers where the numbers we'd known about since the Ancient Greeks ran east-west along the horizontal axis while these new imaginary numbers like the square root of minus one extended vertically in the north-south direction.



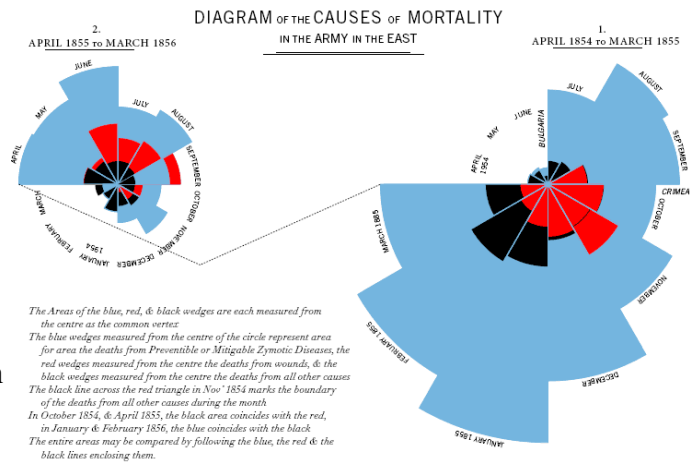
Called the **Argand diagram** after one of its creators, this picture helped mathematicians to believe in these new numbers.

Not only that, the diagram was a potent tool in manipulating these new numbers since the geometry of the diagram reflected the underlying algebra of the numbers they depicted.

One of the most powerful uses of diagrams though has been in visualising data. Given that we live in an age that generates huge reams of numerical information, finding ways to make sense of all these numbers is essential.

### Transcend language

One of the first to use the visual world to navigate numbers was Florence Nightingale. Although better known for her contributions to nursing, her greatest achievements were mathematical. She was the first to use the idea of a pie chart to represent data.



### Florence Nightingale's Crimea diagrams

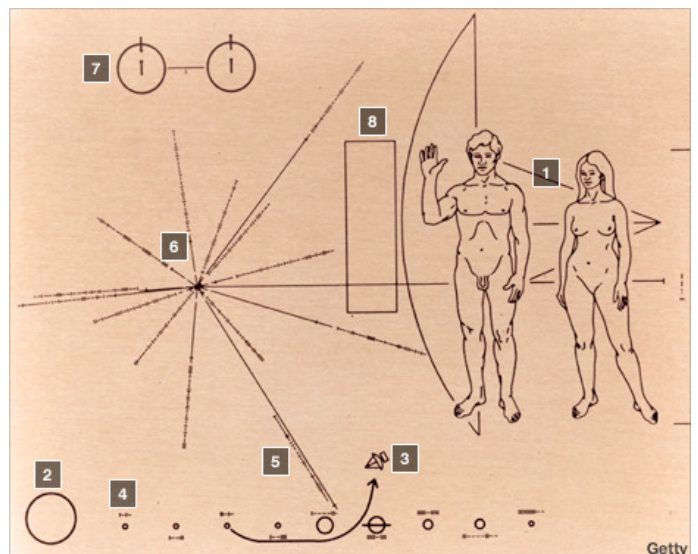
Nightingale had discovered that the majority of deaths in the Crimea were due to poor sanitation rather than casualties in battle. She wanted to persuade government of the need for better hygiene in hospitals.

She realised though that just looking at the numbers was unlikely to impress ministers. But once those numbers were translated into a picture - her Diagram of the Causes of Mortality in the Army in the East - the message could not be ignored. A good diagram, Nightingale discovered, is certainly worth 1,000 numbers.

One of the strengths of all these diagrams is that they transcend language. They can be read and understood by people across the globe.

Which is why when we launched our first space craft out of our Solar System in 1972, scientists recognised that a diagram was probably our best bet at communicating to any intelligent life out there in space.

1. The image of a naked man and woman might prove meaningless scribbles to a life form that looks very different to our own.



2. Echoing Copernicus's picture of the sun-centred solar system, Sagan and Drake drew a picture of the planets and included Pluto.

3. A picture of the Pioneer space probe at the end of a line emanating from the third planet of the Solar System tells aliens where the message comes from.
4. The numbers in the Pioneer plaque are binary - a vertical line for 1 and a horizontal line for 0. The numbers on planets indicate distance from the Sun.
5. There are further binary numbers. We write numbers in decimal because we have 10 fingers. Aliens probably have an entirely different anatomy.
6. The star map locates the Sun. The radial lines locate pulsars, stars emitting a regular electromagnetic pulse. A binary number shows the frequency.
7. This is a unit of measurement of time and distance. The circle represents a hydrogen atom. When the orbiting electron flips states it corresponds to a wave with frequency 1,420 MHz and wavelength 21cm. These are the diagram's units of measurement.
8. The image of the Pioneer space probe gives aliens an idea of the height of humans relative to the probe.
7. The height of the woman is in binary: 1,000 units of length. The unit of length is 21cm given by the wavelength of the hydrogen atom as it flips states. As 1,000 is eight in binary, the woman's height is  $8 \times 21\text{cm} = 168\text{cm}$ .

Frank Drake and Carl Sagan created in some sense the ultimate diagram (see above), an engraving that was attached to the Pioneer space probe which would communicate in visual language who we are and where we come from.

It's unlikely that anyone or thing has received our first message to outer space but when they do, it is the clever use of diagrams that has the best chance of saying hello.

Marcus du Sautoy is the Simonyi Professor for the Public Understanding of Science at the University of Oxford. His new series, *The Beauty of Diagrams*, is on BBC Four at 2030 on Thursdays and also available on iPlayer.

<http://www.physorg.com/news/2010-11-health-improving-tattoos.html>

### **Health-improving tattoos**

***Heather Clark isn't your average tattoo artist. She won't take requests, and her tattoos won't be permanent. They won't even make people look hip — but they will keep them healthier.***

Clark, an associate professor of pharmaceutical sciences in Northeastern University's Bouvé College of Health Sciences, is developing tattoos that involve nanosensors injected into an upper layer of the skin—a far less invasive, and thus less painful, process than a traditional tattoo.

She first conceived this innovative approach to help diabetic patients continuously monitor glucose levels. The problem for many diabetics, she said, is they must measure their blood-sugar levels by pricking a finger several times a day—an agonizing, repetitive process that Clark said becomes more difficult when patients are traveling or trying to find a clean, private environment.

“They are tired of having to take time out of their lives to do this,” said Clark, noting calls she’s received from parents who say they stay up with their diabetic children every night because they are worried about a hypoglycemic event.

Now, she has published a paper in the journal *Integrative Biology* that applies the same concept to monitoring sodium levels, which she said can be useful to check kidney function during prostate surgery, and even to track long-distance runners’ hydration levels. Clark collaborated with Northeastern bioengineering graduate student Matt Dubach on the paper, which they coauthored with colleagues at the California high-tech firm Caliper Life Sciences.

The project, which aligns with Northeastern’s commitment to research that solves global challenges in health, security and sustainability, aims to dramatically improve how certain health conditions are monitored and treated.

Clark said patients would reapply the tattoos about once a week. The process would involve injecting small beads containing fluorescent particles into the epidermal layer of the skin; the fluorescent glow would become more intense — and even change color — as glucose or sodium levels drop. Clark said that ideally, the levels would be monitored with a handheld electronic device.

Clark’s research primarily focuses on developing nanosensors, and the tattoo concept evolved out of her intracellular work at Draper Laboratories. She will continue collaborating closely with Draper researchers while at Northeastern.

“Tattoo artists basically poke holes and inject ink, which is made of particles, into the skin, where they reside for the rest of your life. Our sensors are nanoparticles, so it seemed like a natural choice to use these as a tattoo for monitoring health status,” she said. *Provided by Northeastern University*

<http://www.bbc.co.uk/news/health-11813378>



## **Skin moles link to delayed ageing**

### ***Plentiful skin moles may keep you younger on the inside, say scientists.***

Researchers at Kings College London found that they not only could mean younger skin, but better bone density as well. They said that the cells of people with many moles had properties which allowed them to renew themselves more often. However, there may be a price to pay - more moles have been linked to a higher rate of cancer, both skin and other types. Most people have between 30 and 40 moles, but some have as many as 600.

A series of studies carried out by the King's College team, and Dr Veronique Bataille, a dermatologist based at Hemel Hempstead General Hospital, looked at the relationship between mole numbers and other physical characteristics.

First Dr Bataille noted that people with large numbers of moles appeared less vulnerable to some of the effects of skin ageing, such as wrinkles and blemishes.

The latest study in 1,200 twins suggested that high mole numbers also meant that people were less affected by age-related reductions in bone density, which could mean a lower risk of brittle bone disease and bone fractures later in life. Those with more than 100 moles were half as likely to develop osteoporosis compared with those with 25 moles or fewer.

### **Age-defying**

The reason for these links are unclear, but researchers have noticed that people with large numbers of moles have differences in the strands of DNA in each cell which carry their genetic code.

Sections on the end of these strands are called telomeres, and are effectively a countdown timer governing the number of times a cell can divide to produce new cells. The longer the telomere, the more cell divisions can take place over a lifetime - and more moles were linked to longer telomeres.

Dr Bataille, who presented her findings at a Royal Society of Medicine conference, suggested that moles were a visible product of the underlying system which controls body ageing.

She said: "Some people will have two moles, some people will have 600, but when you have a patient with lots of moles, we noticed they tended to age better."

But she said that tinkering with this system to produce an "elixir of youth" was bound to prove tricky. "We have a DNA system produced over millions of years of evolution - I don't think it will be easy to produce a cream that can alter that."

The underlying ageing mechanism could be a trade-off which allowed longevity without unduly raising the risk of cancer, she said. Those with more cell divisions, and more youthful looks, might be increasing their cancer risk. "As a clinician, when I get a patient with lots of moles, I automatically want to know about their family history of cancer, so I can think about prevention. "This is not just melanoma, but also more common cancers such as breast and colon cancer."

<http://www.bbc.co.uk/news/uk-scotland-tayside-central-11809612>

## **Diabetes drug 'Alzheimer's hope'**

### ***A common diabetes drug could be redeveloped as a new treatment for Alzheimer's, research has suggested.***

Scientists in Dundee have discovered that the drug metformin helps prevent the formation of a key brain abnormality linked to the disease.

Alzheimer's charities said further research was needed to see whether metformin really could help patients.

Because the drug's safety is already proven it could be relatively easy to turn it into an Alzheimer's treatment.

Metformin, which is taken in pill form, belongs to a class of drugs called biguanides that help regulate blood sugar levels. It is widely used by people with Type 2 diabetes and has few side effects.

Experiments on mouse brain cells showed the drug affects the "tau tangles" - filaments of toxic protein that build up in the neurons of Alzheimer's sufferers.

Metformin was shown to activate a natural enzyme that in turn reduced the tangle formation.

The international team of researchers was co-led by Dr Susan Schweiger from the University of Dundee, who wrote about the discovery in the journal Proceedings of the National Academy of Sciences.

### **Clinical trials**

She said the team's data suggested a "potential beneficial role" of metformin in the prevention of Alzheimer's disease.

Rebecca Wood, chief executive of the Alzheimer's Research Trust, said: "The link between diabetes and dementia is well known, and these early results suggest a need for further investigation to see whether this drug has the potential to be developed as an Alzheimer's treatment.

"However, it is important to note that this study looked at cells from mice, not people.

"We need to see the results of pre-clinical and clinical trials before we'll know if the drug could have any benefits for people with Alzheimer's."

Dr Anne Corbett, from the Alzheimer's Society, said: "Previous research has suggested that metformin reduces the risk of dementia in diabetic people, and this study provides some understanding of why this might be."

"The fact that the drug is safe for humans means it could potentially be tested more quickly than a completely new drug."

"However, further research is needed to fully understand the link between diabetes and Alzheimer's."

<http://www.scientificamerican.com/article.cfm?id=solitary-fish-hit-rock-bottom>

## **Solitary fish hit rock bottom**

***'Frozen' zebrafish may be first piscine model for human depression.***

**By David Cyranoski**

Zebrafish that stop swimming when left without company are showing promise as the first fish model of a human mood disorder.

In 2005, when neurobiologist Herwig Baier of the University of California, San Francisco, was screening thousands of zebrafish for vision problems, he found one that seemed a bit "off." If alone, especially after repeated periods of isolation, the fish would "freeze": just sit at the bottom of the tank (see video). If fish that swam normally were put in the tank, the relatively inactive fish became normal and swam around too.

Baier looked at the genetic mutations in the "frozen" fish and found one in the glucocorticoid receptor, a protein that is found in almost every cell and that senses cortisol--a hormone involved in the stress response. In the normal response to a stressful situation, the hypothalamus in the brain sends corticotropin-releasing hormone (CRH) to the pituitary gland, which releases adrenocorticotrophic hormone (ACTH) to the adrenal gland. The adrenal gland in turn produces cortisol. Cortisol then effectively reduces levels of ACTH and CRH, completing the normal response that allows both humans and zebrafish to deal with stress.

In the frozen fish, however, Baier found that levels of all three hormones--CRH, ACTH and cortisol--were higher than normal. He guessed that the animals were unable to respond properly to chronic stress--a problem that is known to trigger anxiety or depression in humans. On the basis of that diagnosis, he started putting the antidepressant fluoxetine (originally marketed as Prozac) in their water. After four days, they started swimming around normally. Other antidepressants and anxiolytics--drugs used to treat anxiety--also worked as a pick-me-up, he says. "There's a long literature on chronic stress being related to depression, but the causal link is unknown," says Baier. "Now we might be able to simulate this in fish and study it."

### **Mutant marvel**

Discussing his results at the Society for Neuroscience meeting in San Diego, Calif., last week, Baier says his mutants could represent the first fish model for a mood disorder and be a useful screening model for drugs.

"The fact that the key elements of stress and stress response are conserved in zebrafish is exciting because of the many experimental advantages of that model organism," says chemical geneticist Randall Peterson of the Massachusetts General Hospital, Harvard Medical School, Charlestown.

Studies this year support the idea that zebrafish can model complex behavior. Earlier this year, Peterson and his collaborator, neuroscientist Alex Schier of Harvard University in Cambridge, Mass., published the first two small-molecule screens based on zebrafish behavior. The studies focused on motor behavior, not mood disorders, but the team found that certain classes of psychotropic drugs, such as the antidepressants known as monoamine oxidase inhibitors, had recognizable, characteristic effects on behavior. "So, the idea of discovering new therapeutic approaches for anxiety or depression may not be so far-fetched," says Peterson.

If that proves true, the finding could accelerate drug-discovery programs. Chemical biology and drug discovery usually depend on screens of cells in lab dishes, for example. "But much of biology can't be easily reduced to an in vitro assay. This is particularly true for nervous-system disorders, where a complex, integrated nervous system is essential for research," says Peterson. Filling thousands of tiny wells on lab plates with zebrafish larvae and dousing them with candidate drug molecules offers the best of both worlds--high-throughput screening in a living system. "When we discover a new small molecule, we have the advantage of knowing that it works in vivo," he says.

### **Larval question**

Baier plans to do the same sort of screening for new antidepressants and anxiolytics using his "frozen" fish. But Peterson does sound a note of caution. Baier's experiments used adult fish, whereas most zebrafish screens use larvae. Using adult for screening would be expensive and laborious. Baier plans to use larval stages but he admits it is not clear yet whether the larval zebrafish will react in the same way as the adult mutants.

The model will also have to convince the pharmaceutical industry that fish depression has significant similarities with the condition in people. This has not always been the case with mice, which as mammals



should be a closer match to humans. "Considering the challenges of using rodents, including genetically engineered mice, to validly model human psychiatric diseases, zebrafish probably have some way to go before they are accepted as a translational model," said conference delegate Jeffrey Kogan, a behavioral neuroscientist working within the pharma industry who studies psychiatric disease.

It might, however, just take some time to sink in. In an e-mail to Nature a few days later, Kogan said that zebrafish might be a useful model organism for psychiatric disease after all. The huge numbers of fish that can be used in such studies would, for example, give the zebrafish mutant an advantage over the mouse. "I may have to reconsider my opinion," he says.

[http://www.eurekalert.org/pub\\_releases/2010-11/irma-ads112210.php](http://www.eurekalert.org/pub_releases/2010-11/irma-ads112210.php)

## **AIDS drug shown to prevent HIV in multinational trial of HIV-negative gay men Data suggest need for rectal gel option**

Chicago, November 23, 2010 – Results of the world's first efficacy trial of an HIV-prevention approach called oral pre-exposure prophylaxis, or PrEP, were released online in the New England Journal of Medicine today. Data from this trial, called iPrEx, indicated an estimated 43.8% reduction of new HIV infections among men who took an antiretroviral tablet daily to prevent HIV, compared to those who took a placebo pill.

"This discovery alters the HIV prevention landscape forever. While this level of efficacy is relatively strong, PrEP is not quite ready for prime time and work remains before this strategy is rolled out. However, we are thrilled to have a new prevention option beyond male and female condoms visible on the horizon," said Jim Pickett, Director of Advocacy at AIDS Foundation of Chicago and Chair of IRMA – International Rectal Microbicide Advocates.

The iPrEx trial evaluated the safety and efficacy of the antiretroviral (ARV) drug TDF/FTC (brand name Truvada) taken once daily for HIV prevention among HIV-negative gay men, transgender women, and other men who have sex with men (MSM).

The participants, 2,499 in all, included individuals from Peru, Ecuador, Brazil, South Africa, Thailand and the United States. Half the men were randomized into the active arm that received Truvada, and the other half were randomized into the placebo arm and received a look-alike pill with no active ingredient. The participants and the researchers did not know who was in either arm. Enrollment for the trial began in June 2007 and was completed in December 2009. The primary analysis of the results released today includes participants who were followed until May 1, 2010, or for an average of 14 months.

Each participant was tested for HIV at monthly trial visits and given intensive pre-and-post test counseling. Additionally, they were regularly screened for sexually transmitted infections and received condoms, making up a very robust prevention package.

At the end of the trial, there were 36 infections in participants who received Truvada and 64 in recipients who took the placebo. Researchers calculated that the use of Truvada reduced new HIV infections by an estimated 43.8% overall when compared to placebo. While there appeared to be few side effects reported by the men who were taking the Truvada tablet, it is clear that much more information is needed regarding long term safety of this drug.

Other PrEP trials are ongoing. Results from studies among heterosexuals in Africa and injection drug users in Thailand are expected next year.

It is important to emphasize the factors that led to successful use of Truvada to prevent HIV in iPrEx. Taking the pill regularly was one of the most important. Efficacy appeared to be higher among those participants who took the study drugs consistently. Men who did not take the pill regularly did not see a protective benefit. Regular HIV testing and ongoing monitoring by a physician was also critical. For this strategy to work, each of these pieces, including a doctor's prescription, need to be in place.

"The study team found that about half of the men in the active arm of the trial were in fact not taking their pills regularly, if at all," said Pickett. "It is not clear why this happened, but it certainly suggests that alternate means of using ARVs to prevent HIV infection may be more acceptable for these men. The primary means of transmission among gay men and other MSM is through unprotected anal intercourse. If we develop an ARV as a gel or lubricant applied rectally – a rectal microbicide – it could be more acceptable for some individuals who don't like taking pills."

Many gay men and other MSM already use lubricants for anal intercourse, so they wouldn't have to modify their behavior to achieve higher levels of protection with a rectal microbicide formulated as a lubricant. Adopting a new behavior—such as taking a pill every day—can be a considerable challenge for some.

Dr. Ian McGowan, one of the principal investigators of the Microbicide Trials Network and Scientific Vice Chair of IRMA agreed. "The data from the iPrEx study are encouraging but the less than ideal adherence rate to

oral PrEP clearly show that we need additional prevention approaches such as rectal microbicides that could be used by men and women at risk of HIV infection through unprotected receptive anal intercourse," he said.

The world's third rectal microbicide trial is currently underway with sites in Pittsburgh, Pennsylvania; Boston, Massachusetts; and Birmingham, Alabama. Scientists are testing the rectal safety and acceptability of tenofovir gel, a microbicide developed for vaginal use that has shown promise for preventing HIV through vaginal intercourse. Depending on the outcome of this new study, tenofovir gel could be further evaluated to determine if it can reduce the risk of HIV among both men and women who engage in receptive anal intercourse.

This new Phase I rectal microbicide study, known as MTN-007, aims to determine if rectal use of tenofovir gel is safe, and in particular, does not cause cells in the rectum to become more vulnerable to HIV. Investigators will also ask trial participants questions regarding the gel's desirability. The trial is planning to recruit a total of 60 men and women.

While the rectal microbicide field has gained significant momentum, more focus and resources are needed. In 2010, U.S. \$7.2 million is being spent globally on rectal microbicide research. IRMA has calculated that annual investments must increase by 40% from 2011 – 2014, to U.S. \$10 million/year and must increase further to U.S. \$44 million (a six-fold increase) in the years 2015 – 2020. These targets need to be met to ensure a minimum of candidate products are moving through the research pipeline into late stage testing for effectiveness.

Just as we use a combination of drugs to treat individuals living with HIV, we need a combination approach to prevention. That approach should include male and female condoms, sterile syringes, and access to treatment as well as new interventions like PrEP, topical microbicides, and vaccines. Adequate funding must continue for all of the methods we currently have, and it must continue for the new strategies that are still being developed as well.

In a global context where millions of individuals do not have access to life saving medications, it is imperative that funding provided for PrEP accessibility not compete with funding for treatment. Treatment funding has not kept pace with the need.

*IRMA congratulates the trial sponsors, scientific collaborators and partners who conducted this landmark trial, with special thanks to the 2,499 participants in the study who volunteered so much of their time and energy. Their extraordinary contribution to HIV prevention science brings us another step closer to a day without AIDS, and for that we are supremely grateful.*

*Based at the AIDS Foundation of Chicago, IRMA is a global network of more than 1,000 advocates, scientists, policy makers and funders from six continents working together to advance a robust rectal microbicide research and development agenda. For further information on IRMA visit [www.rectalmicrobicides.org](http://www.rectalmicrobicides.org) and read IRMA's new report, *From Promise to Product: Advancing Rectal Microbicide Research and Advocacy*.*

<http://www.nytimes.com/2010/11/23/science/23angier.html>

## Reptile's Pet-Store Looks Belie Its Triassic Appeal

By NATALIE ANGIER

***As a femur-shaped island paradise that snapped away from the Gondwana supercontinent some 80 million years ago, New Zealand is famously home to eccentric forms of wildlife that look like pets for a Hobbit.***

There is the kiwi, of course, with its dense, furlike feathers, its catlike whiskers and its long, slender, curving bill tipped by a pair of ultrasensitive nostrils; and the kakapo, a heavy, flightless, nocturnal parrot with the flat-cheeked face of an owl; and the giant weta, a cricket the size of a human hand that displays by waving its formidably serrated rear legs high in the air as if brandishing a pair of saws.

Yet the animal that may well be New Zealand's most bizarrely instructive species at first glance looks surprisingly humdrum: the tuatara. A reptile about 16 inches long with bumpy, khaki-colored skin and a lizardly profile, the tuatara could easily be mistaken for an iguana. Appearances in this case are wildly deceptive. The tuatara - whose name comes from the Maori language and means "peaks on the back" - is not an iguana, is not a lizard, is not like any other reptile alive today.



***TUATARA Native to New Zealand, the tuatara is not like any other vertebrate alive today. Andy Reisinger/Getty Images***

In fact, as a series of recent studies suggest, it is not like any other vertebrate alive today. The tuatara, scientists have learned, is in some ways a so-called living fossil, its basic skeletal layout and skull shape almost identical to that of tuatara fossils dating back hundreds of millions of years, to before the rise of the dinosaurs. Certain tuatara organs and traits also display the hallmarks of being, if not quite primitive, at least closer to evolutionary baseline than comparable structures in other animals.

For example, the tuatara has a third eye at the top of its skull, the legendary if poorly understood pineal eye, which is found in only a sprinkling of reptile species and which vision researchers suspect harks back to nature's original eye — pretty much a few light-sensitive cells on a stalk. A tuatara's teeth likewise follow the no-nonsense design seen in dinosaur dentition, erupting directly from the jawbone and without the niceties of tooth sockets and periodontal ligaments that characterize the teeth of all mammals and many reptiles. Some researchers are looking at tuataras for clues to how dental implants, which are inserted directly into the jaw, might be improved.

Yet in a startling counterpoint to the notion of the tuatara as a holdover from Triassic Park, researchers lately have discovered that a few regions of tuatara DNA appear to be evolving at hyperspeed, possibly the fastest mutation rate yet clocked in a vertebrate genome. The quick-changing sequences are limited to so-called neutral regions of the tuatara's DNA, affecting filler codes, rather than the molecular blueprints for how to build a tuatara. The researchers have yet to determine what the observed hypermutability is all about, but obviously, said David M. Lambert of Griffith University, in Brisbane, Australia, an author of the study, "the processes that govern skeletal morphology are decoupled from the biological processes that govern changes in DNA."

Moreover, while the modern tuatara resembles its distant ancestors anatomically, life aboard a long-isolated land mass clearly has wrought major changes in the reptile's physiology and behavior, pushing the tuatara to Guinness-worthy extremes. A famous Gary Larson cartoon may have featured a crocodile on the witness stand angrily telling the prosecutor, "Well, of course I did it in cold blood, you idiot! I'm a reptile!" but in reality crocodiles and a vast majority of other reptiles do very little when the thermometer drops and their blood runs cold — except maybe die. Not so for tuataras.

"Their biology is quite distinctive," said Charles Daugherty of the Allan Wilson Center for Molecular Ecology and Evolution at Victoria University of Wellington in New Zealand. "They have a unique type of hemoglobin, and their enzymes are set to function at lower temperatures than in most reptiles." As a result, tuataras remain active at night, and in weather just a few degrees above freezing, said Dr. Daugherty, "at temperatures at which most reptiles couldn't survive."

Yes, tuataras are out and about, working the night shift, hunting down other New Zealand fauna similarly adapted for the cold. "They like to eat wetas," said Stephanie S. Godfrey, a postdoctoral researcher at Flinders University in Adelaide, Australia, who has studied parasite transmission among tuataras. "Walking through the forest at night, you can hear the tuataras eating — crunch, crunch, crunch."

Tuataras are living fossils in more than one sense of the term. Through long-term capture, tag and recapture studies that were begun right after World War II, researchers have found that tuataras match and possibly exceed in attainable life span that other Methuselah of the animal kingdom, the giant tortoise. "Tuataras routinely live to 100, and I couldn't tell you they don't live to 150, 200 years or even more," said Dr. Daugherty.

They live, and live it up. "We know there are females that are still reproducing in their 80s," said Dr. Daugherty. At the Southland Museum and Art Gallery in Invercargill, New Zealand, a captive male tuatara named Henry, a local celebrity that had been nasty and unruly for decades until a malignancy was removed from his genitals, mated with an 80-year-old female named Mildred, and last year became a first-time father — at the age of 111.

In every way, tuataras are late bloomers and passionate procrastinators. They don't reach sexual maturity until age 15 to 20. A female needs two or three years to grow a clutch of eggs internally, and takes another seven or eight months after mating before she finally lays those fertilized eggs. Then the eggs incubate in the ground for yet another year before a brood of finger-size baby tuataras will finally hatch. By comparison, the incubation time for the average North American lizard is only four to six weeks. "If these were plants, most lizards would be like weeds, and the tuatara like a sequoia," said Dr. Daugherty. For all the nobility of the comparison, the tuatara's stately pace is also its Achilles' heel, he added. That's why the reptile today is found only on diligently monitored islands away from the New Zealand mainland, protected from mammals like rats, pigs or stoats that within months could reduce every sequoia equivalent and its seedlings to so much sawdust.

The New Zealand tuatara, or *Sphenodon*, is the sole surviving member of a reptilian order that once was as widespread and species-rich as are today's other three reptilian clans — the crocodylians, the snakes and lizards, the turtles and tortoises. Among the tuatara's unusual reptilian traits are the relatively simple structure of its



heart and lungs, the somewhat froggy style of its gait and the absence of any sort of male intromission organ, or penis. A male tuatara manages as a male bird does, by pressing his cloacal opening against the female's.

The tuatara also has a unique approach to mastication. As Neil Curtis and colleagues at the University of Hull in England have shown through computer simulations, the tuatara slides its single row of lower teeth across a groove between a double row of upper teeth, shearing the food, said Dr. Curtis, "like a pair of scissors."

New Zealand's breakaway land mass proved an ideal tuatara sanctuary, for it lacked any terrestrial mammals that would dig up the reptile's slow-cooking eggs or pick off the adolescents before they had a chance to breed. Without mammalian predation pressure, the tuatara life cycle became ever more protracted. The carnivorous reptile thrived, feasting on wetas, worms, nesting seabirds and the occasional baby tuatara, and the population climbed to densities far higher than would be seen for a calorically needier meat-eating mammal.

The edenic age ended some 900 years ago, with the arrival of the first Polynesians and their happenstance co-travelers, the rats. Then came pigs, dogs, cats, goats, Europeans. By the 19th century almost no tuataras survived on the New Zealand mainland.

Today maybe 50,000 survive and are considered a national treasure. A vast majority live on Stephens Island, a mecca for herpetologists, where tuatara densities reach more than 1,000 reptiles per acre and where the animals devote considerable effort to defending their little bit of turf, especially the males and especially during mating season.

"They have crests they can inflate, to make them look big, and they stand very tall and start mouth-gaping at each other," said Dr. Godfrey. "If one male doesn't get the message, it will escalate into a physical fight." They tear at each other's crests and toes, they trade parasites. "During mating season, you can see the bright orange patches of mites on their necks," said Dr. Godfrey. "It's quite spectacular."

They fight for land and fertile females, and if they must fight to the death, well, they are tuataras: they can do it in cold blood.

[http://www.eurekalert.org/pub\\_releases/2010-11/bumc-acd112310.php](http://www.eurekalert.org/pub_releases/2010-11/bumc-acd112310.php)

### **Alcohol consumption decreases with the development of disease**

In a cross-sectional study from the 2004 and 2007 Australian National Drug Strategy Household (NDSH) surveys, respondents were questioned about their current and past drinking, the presence of formal diagnosis for specific diseases (heart disease, type 2 diabetes, hypertension, cancer, anxiety, depression) and self-perceived general health status. The sample sizes for the 2004 and 2007 NDSH surveys were 24,109 and 23,356, respectively.

The authors report that respondents with a diagnosis of diabetes, hypertension, or anxiety were more likely to have reduced or stopped alcohol consumption in the past 12 months. The likelihood of having reduced or ceased alcohol consumption in the past 12 months increased as perceived general health status declined from excellent to poor (although the authors do not point out that lifetime abstainers were more likely than moderate drinkers to report less than excellent health status).

The authors conclude that the experience of ill health is associated with subsequent reduction or cessation of alcohol consumption ("sick quitters"), which is consistent with most prospective epidemiologic studies. The authors also conclude that this may at least partly underlie the observed 'J-shaped' function relating alcohol consumption to premature mortality. On the other hand, most modern epidemiologic studies are careful not to include "sick quitters" within the non-drinking category, and relate health effects of drinkers with those of lifetime abstainers. Further, prospective studies in which alcohol intake is assessed at different times (rather than having "changes" based only on recall at one point in time, as was done in this study) usually indicate that subjects who decrease their intake are more likely to subsequently develop adverse health outcomes, especially related to cardiovascular disease, than those who continue moderate drinking.

*Reference: Liang W, Chikritzhs T. Reduction in alcohol consumption and health status. Addiction 2010; in press (doi:10.1111/j.1360-0443.2010.03164.x).*

[http://www.eurekalert.org/pub\\_releases/2010-11/rb-ust112310.php](http://www.eurekalert.org/pub_releases/2010-11/rb-ust112310.php)

### **Under suspicion: The painkiller ziconotide could increase suicidal ideation Experts recommend more precise diagnosis and closer medical surveillance**

The active agent ziconotide, the synthetic toxin of the cone snail (*Conus magus*), was acclaimed a safe alternative to morphine when it was introduced six years ago. Now it is increasingly suspected of causing patients to commit suicide. Researchers working under the auspices of Prof. Christoph Maier (Director of the Pain Clinic Bergmannsheil at the Ruhr University in Bochum) presume that ziconotide not only suppresses the transmission of pain stimuli, but also deteriorates the frame of mind and could simultaneously reduce anxiety and impulse control. These mechanisms could promote suicidal tendencies in vulnerable patients. The research

scientists thus advise careful diagnosis and monitoring of the psychic condition of patients treated with ziconotide. They have published their findings in the Medical Journal Pain.

### **Alternative to opioids for severe pain**

Ziconotide has numerous advantages, including the fact that it does not have any of the side effects typically associated with opioids, such as respiratory depression (asphyxia). Moreover, it does not lead to tolerance development. It has been on the European and American market since 2004, being administered to patients with intrathecal pumps if opioids do not suffice or if these trigger unacceptable side effects. Recently, the number of reports on the psychic side effects of ziconotide has increased. The researchers in Bochum analysed numerous studies, registering an increasing number of attempted suicides, which the original authors had not attributed to the ziconotide treatment. In PAIN, the physicians from RUB present two new cases, which underscore the suspicion that ziconotide enhances suicidal ideation.

### **Suicide despite pain relief and normal test results**

As Prof. Maier stated, the first case is particularly tragic, the patient concerned, who had had pain in his feet for many years and undergone numerous unsuccessful treatments, having experienced a distinct improvement and pain relief for the first time when treated with ziconotide. There were no side effects. Tests disclosed that his depressiveness, which had also not been particularly marked before the ziconotide treatment commenced, even decreased. After a good three weeks, he appeared to be happy to all concerned. But two months after the ziconotide treatment had commenced he unexpectedly committed suicide. A further patient, a 39-year-old woman, who had undergone pain treatment for backache for 14 years, had had depressive phases 20 years previously and had attempted suicide after a pregnancy. Two months after the ziconotide treatment had commenced – which, according to current recommendations, should never have been administered to her in the first place due to her medical history – she mentioned that she had increased suicidal ideation. Moreover, she complained of other psychic side effects with hallucinations, confusion and partial amnesia, which had resulted in two severe car accidents. It is conceivable that the accidents were also of suicidal character. The physicians stopped the ziconotide treatment. Two weeks later both the suicidal ideation and the hallucinations were history.

### **Pharmaceutical companies and approval authorities must investigate the situation**

Prof. Maier concludes that both cases underscore the assumption that there is a causality between ziconotide and suicidal tendencies. The pain specialist strongly emphasizes that the pharmaceutical companies and approval authorities should urgently investigate this yet again. All patients must be analysed for possible psychic disorders before treatment commences and closely monitored irrespective of pain relief due to the drug. The above-mentioned cases also underscore the fact that an increase in pain treatment when standard drugs fail is not always the correct mode of action. As Prof. Maier so aptly said, it is often even exactly the wrong path. This had already been pointed out a few weeks previously at the Congress of the German Pain Therapists (Kongress der deutschen Schmerztherapeuten)

*Title Christoph Maier, Hans-Helmut Gockel, Kai Gruhn, Elena K. Krumova and Marc-Andreas Edel: Increased risk of suicide under intrathecal ziconotide treatment? – A warning. In: Pain, online 1.11.2010, doi:10.1016/j.pain.2010.10.007, <http://www.painjournalonline.com/article/S0304-3959%2810%2900615-9/abstract>*

[http://www.eurekalert.org/pub\\_releases/2010-11/uoc--brm112310.php](http://www.eurekalert.org/pub_releases/2010-11/uoc--brm112310.php)

## **Biologists report more bad news for polar bears**

### ***Climate change will force them south, where they are unsuited for the diet***

Will polar bears survive in a warmer world? UCLA life scientists present new evidence that their numbers are likely to dwindle.

As polar bears lose habitat due to global warming, these biologists say, they will be forced southward in search of alternative sources of food, where they will increasingly come into competition with grizzly bears.

To test how this competition might unfold, the UCLA biologists constructed three-dimensional computer models of the skulls of polar bears and grizzly bears — a subspecies of brown bears — and simulated the process of biting. The models enabled them to compare the two species in terms of how hard they can bite and how strong their skulls are.

"What we found was striking," said Graham Slater, a National Science Foundation-funded UCLA postdoctoral scholar in ecology and evolutionary biology and lead author of the research. "The polar bear and brown bear can bite equally hard, but the polar bear's skull is a much weaker structure."

The implication is that polar bears are likely to lose out in competition for food to grizzlies as warmer temperatures bring them into the same environments, because grizzlies' stronger skulls are better suited to a plant-rich diet, said Slater and Blaire Van Valkenburgh, UCLA professor of ecology and evolutionary biology and senior author of the research.

"The result for polar bears may be lower weight, smaller and fewer litters, less reproductive success, fewer that would survive to adulthood, and dwindling populations," Van Valkenburgh said. "Then you can get into an extinction vortex, where a small population becomes even smaller in a downward spiral to extinction.

"To people who say polar bears can just change their diet, we are saying they will change their diet - they will have to - but it probably will not be sufficient for them, especially if they are co-existing with grizzly bears. Their skull is relatively weak and not suited to adapting its diet. We did not expect to find what we found."

"This is one additional piece of evidence that things look pretty bleak for the polar bear if current trends continue," Slater said.

The research, federally funded by the National Science Foundation, was published this month in the online journal PLoS ONE, a publication of the Public Library of Science.

Polar bears are a "marvelous example of rapid adaptation to an extreme environment," Slater said. "The fact that we can lose them equally as rapidly as a result of human-mediated climate change is rather striking. Polar bears are very well suited to do what they do, but they are highly specialized and not well suited to doing much else."

It could take quite some time for polar bears to go extinct, Van Valkenburgh said, but they are likely to become much more rare than today.

Polar bears are losing habitat as a result of global warming and the associated loss of arctic sea ice, which they use to hunt for seals, Van Valkenburgh and Slater said. But could they survive on an alternative food source?

"Our results suggest that this is not too likely," Slater said. "The polar bear's skull is a relatively weak structure that is not suited to diets consisting of a lot of plant material like that of the brown bear. As climate change continues, polar bears will be forced to move south in search of resources, while brown bears move north as their climate becomes more mild. When these two species meet, as they have already begun to, it seems that brown bears will easily out-compete polar bears. Our findings should serve as a warning that polar bears may not be flexible enough to survive if current trends continue.

"Chewing a lot of vegetables takes quite a lot of force to grind up," Slater said. "Grizzly bears are well suited to eating these kinds of food, but the polar bear is not well suited for it. The grizzly has a much more efficient skull for eating these kinds of foods."

In Canada, grizzly bears are moving north and are already in polar bear territory, Van Valkenburgh and Slater said.

The life scientists — whose co-authors include UCLA undergraduates Leeann Louis and Paul Yang and graduate student Borja Figueirido from Spain's Universidad de Malaga, Campus Universitario de Teatinos — studied two adult male skulls from museums, one of a polar bear from Canada, the other of a grizzly from Alaska. They built 3-D computer models of the skulls and then analyzed their biomechanics.

"We can apply muscle forces to the skull to simulate biting, and we can measure how hard the animal could bite. We can measure stress and strain in the skull as well," Slater said. "We found that while the stresses in the grizzly bear skull are relatively low, the same bites in the polar bear produce much more stress. Combined with other evidence from Blaire's laboratory, this tells us that the smaller teeth of polar bears are less suited to diets that consist of plants, grass, vegetation and berries."

"Polar bears would not be able to break up the food as well in their mouths and would not digest it as well," Van Valkenburgh said.

In the timeline of evolution, polar bears evolved from the brown bear very recently, and the two are very closely related, Van Valkenburgh and Slater said. Genetic studies indicate that the split between polar bears and brown bears occurred only 500,000 to 800,000 years ago — the most recent split between any of the eight bear species.

Despite the recentness of the split between these two species, their skulls and teeth are extremely different, probably as a result of where they live (arctic versus temperate regions) and the differences in their diets. Grizzly bears have very large molar teeth, while polar bears have teeth that are much smaller. Polar bears eat seal blubber, which is soft and does not require much chewing, while brown bears consume many plants.

The biologists investigated the rate at which skull shape has evolved in the bear family. They found that the rate of evolution in the branch of the bear family tree leading to the polar bear was twice as fast as the rates in other branches of the tree; it appears that skull shape evolved extremely rapidly in polar bears.

Polar bears probably evolved very rapidly in response to glacial climates during the ice ages, Slater said.

"You don't see many bears that look like polar bears, and the difference in skull shape evolved very rapidly," Slater said.



## **Plant-derived scavengers prowl the body for nerve toxins**

***The brain is forever chattering to itself, via electrical impulses sent along its hard-wired neuronal "Ethernet."***

These e-messages are translated into chemical transmissions, allowing communication across the narrow cleft separating one neuron from another or between neurons and their target cells. Of the many kinds of molecules involved in this lively chemical symposium, acetylcholine is among the most critical, performing a host of functions in the central and peripheral nervous system. This delicate cholinergic design however is highly vulnerable. It can fall victim to inadvertent or deliberate poisoning by a class of compounds known as organophosphates—chemicals found in a range of pesticides as well as weaponized nerve agents.

Now Tsafir Mor, a biochemist in the Center for Infectious Diseases and Vaccinology at the Biodesign Institute at Arizona State University has shown that human butyrylcholinesterase (BChE), a so-called bioscavenging molecule, can be produced synthetically—from plants. Further, Mor and his colleagues have demonstrated the effectiveness of plant-derived BChE in protecting against both pesticide and nerve agent organophosphate poisoning.

The group's research, recently reported in the Proceedings of the National Academy of Science (PNAS), shows promise not only for protecting the nervous system from the effects of organophosphates, but also for gaining a firmer understanding of acetylcholine-linked diseases such as Alzheimer's Dementia and possibly for use against drug overdose and addiction, particularly cocaine. PNAS has selected the important paper as an Editor's Choice.

In the developing world, accidental pesticide poisonings are common. Organophosphate compounds are also the method of choice for many suicides in poor, agricultural regions. The development of far more lethal organophosphates engineered to kill humans has continued apace since Nazi Germany invented them and Cold War adversaries, the United States and the Soviet Union refined and stockpiled these agents.

Following the collapse of the USSR, weaponized organophosphate poisons have proliferated, occasionally falling into the hands of rogue states or terrorist organizations, as these lethal nerve toxins are relatively easy and inexpensive to manufacture and store. The threat of a nerve agent assault on civilians, like the sarin attack in the Tokyo subway system in 1995, perpetrated by the religiously-motivated group Aum Shinrikyo, remains a chilling possibility. The need for effective protection and treatment for organophosphate poisoning is hence a vital concern for public health.

Currently, clinical treatment for exposure to organophosphates involves the use of chemicals like atropine, which can save lives and alleviate acute symptoms, but which fail to address long term neurological effects of such poisoning, which may include muscle weakness, seizures and convulsions, permanent brain defects and social or behavioral symptoms.

Bioscavengers, Mor explains, act as sentries in the body, seeking out and binding with unwanted substances and neutralizing or destroying them. The most heavily studied bioscavengers are the two human cholinesterases—acetylcholinesterase (AChE), which is produced by neurons in the brain and BChE, which is produced mainly by the liver and circulates in blood serum. In addition to their role in defending the body from damaging chemicals, cholinesterases perform a vital housekeeping function, mopping up molecules of acetylcholine, once their signaling tasks are complete.

AChE is a key enzyme bioscavenger that terminates transmission of nerve impulses in the cholinergic synapses of the brain and is also active in the neuromuscular junction, where the axons of motoneurons terminate on muscle cells. As Mor explains, "every time that you move a muscle, the transmission is done through acetylcholine, which is released at the end of the nerve cell and taken up by the receptor on the muscle, causing an influx of ions and contraction of the muscle cell." For this to be accomplished in a coordinated way, the nerve impulse must be cut off almost instantly. This is what the cholinesterases do.

While other neurotransmitters like serotonin are eliminated through reuptake, cholinesterases remove molecules of acetylcholine by hydrolyzing them. Hydrolysis is a chemical reaction in which a given molecule is split into two parts through the addition of a water molecule. AChE is supremely efficient in its catalytic activity, degrading about 25,000 molecules of acetylcholine per second.

Without a means of rapidly getting rid of acetylcholine molecules once they have performed their signaling duty, they flood the nervous system and in sufficient quantity, produce neuromuscular paralysis, and unregulated muscle contraction, eventually causing death due to respiratory and cardiac collapse. This fact, Mor says, makes the system something of an Achilles heel. Many organisms make use of this cholinergic matrix for both offensive and defensive purposes. Plants produce potent anti-cholinesterases to try to thwart herbivory by insects, which in some cases have evolved mechanisms to circumvent such defenses.

Mammals and birds have developed their own mechanisms for dealing with cholinesterase blocking agents. In humans, a particular gene codes for BChE, a closely related analogue of AChE, but one that circulates in blood, laying in wait to scavenge anti-cholinesterase molecules like those of organophosphate poisons. The effectiveness of BChE in neutralizing potentially deadly organophosphates has made it a highly attractive candidate for protecting against the effects of pesticides or nerve agents, as well as mitigating their effects post-exposure. While AChE occurs in the brain and is therefore tricky to acquire, BChE can be readily extracted from blood and stockpiled for future use.

The problem however is finding enough BChE. To protect a few thousand troops on the battlefield from nerve agent poisoning, the entire nation's blood supply would be required. Further, Mor points to many other applications in medicine that would make the production of a sizeable stockpile of BChE highly desirable. In addition to possible treatment for cholinergic ailments, BChE could be used post surgery for patients who lack the naturally occurring enzyme and therefore have difficulty recovering from the effects of anesthesia. There is also evidence that BChE may be useful for treating acute cocaine overdose and possibly as a prophylactic that would eliminate cocaine's euphoric effects, making users less likely to seek out the drug. Again, the challenge is producing the enzyme in sufficient quantity.

The solution Mor and his group have come up with is to use transgenic tobacco plants, modified to synthesize human BChE in their leaves. In a series of experiments outlined in the new paper, Mor's group was able to demonstrate successful protection from both pesticide and nerve agent organophosphate poisoning in two animal models. The team was also able to extend the half-life of the plant-derived BChE, more closely replicating the persistence in the bloodstream of naturally occurring BChE, thereby improving its effectiveness. This was accomplished by decorating the outer portion of the enzyme with Polyethylene glycol (PEG).

Mor stresses that much work remains, before synthetic BChE can be applied as a nerve agent antidote or for other clinical purposes. Currently, the plant-derived BChE acts stoichiometrically, meaning that a molecule of the enzyme is needed for every anti-cholinesterase molecule to be degraded. Future work is aimed at developing forms of the enzyme that can act catalytically against organophosphates, which would permit a far lower effective dose of BChE to be used to protect from poisoning or for treatment post-exposure.

*This work was funded in part by the National Institutes of Health CounterACT Program through the National Institute of Neurological Disorders and Stroke under a consortium grant awarded to US Army Medical Research Institute of Chemical Defense and contracted to Dr. Mor under a research cooperative agreement. It is a continuation of earlier work originally under support from the Defense Advanced Research Projects Agency (DARPA).*

*In addition to Dr. Mor's appointment with the Biodesign Institute at Arizona State University he is a professor in the School of Life Sciences.*

*\*Geyer BC, \*Kannan L, \*Garnaud PE, Broomfield CA, Cadieux CL, \*Cherni I, Hodgins SM, Kasten SA, \*Kelley K, \*Kilbourne J, Oliver ZP, Otto TC, \*Puffenberger I, Reeves TE, \*Robbins N, 2nd, \*Woods RR, Soreq H, Lenz DE, Cerasoli DM, \*Mor TS (2010) Plant-derived human butyrylcholinesterase, but not an organophosphorous-compound hydrolyzing variant thereof, protects rodents against nerve agents. Proc Natl Acad Sci U S A, in press (available online at <http://www.pnas.org/content/early/2010/11/05/1009021107>). \*Present or former members of Mor Lab at ASU.*

[http://www.eurekalert.org/pub\\_releases/2010-11/pu-fsn112310.php](http://www.eurekalert.org/pub_releases/2010-11/pu-fsn112310.php)

### **Findings suggest new cause, possible treatment for multiple sclerosis**

**WEST LAFAYETTE, Ind. - Researchers have found evidence that an environmental pollutant may play an important role in causing multiple sclerosis and that a hypertension drug might be used to treat the disease.**

The toxin acrolein was elevated by about 60 percent in the spinal cord tissues of mice with a disease similar to multiple sclerosis, said Riya Shi, a medical doctor and a professor of neuroscience and biomedical engineering in Purdue University's Department of Basic Medical Sciences, School of Veterinary Medicine, Center for Paralysis Research and Weldon School of Biomedical Engineering.

The research results represent the first concrete laboratory evidence for a link between acrolein (pronounced a-KRO-le-an) and multiple sclerosis, he said.

"Only recently have researchers started to understand the details about what acrolein does to the human body," Shi said. "We are studying its effects on the central nervous system, both in trauma and degenerative diseases such as multiple sclerosis."

The compound is an environmental toxin found in air pollutants including tobacco smoke and auto exhaust. Acrolein also is produced within the body after nerve cells are damaged. Previous studies by this research team found that neuronal death caused by acrolein can be prevented by administering the drug hydralazine, an FDA-approved medication used to treat hypertension.

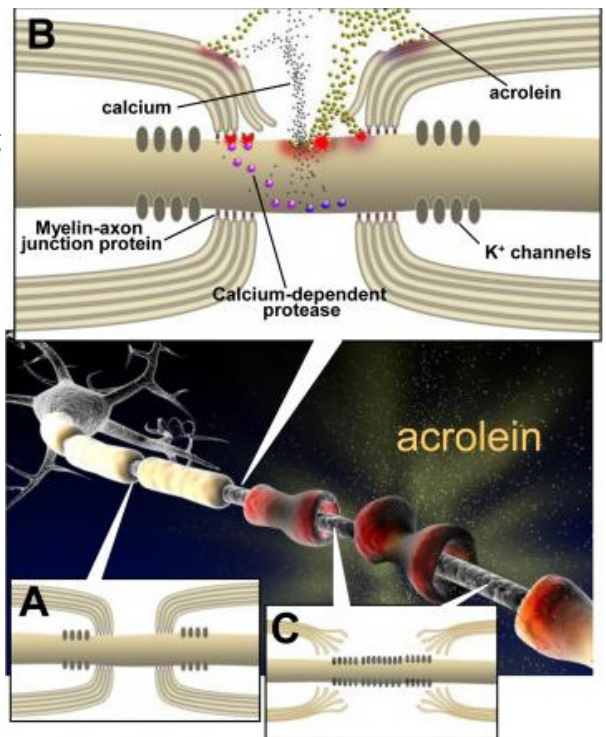
The new findings show that hydralazine also delays onset of multiple sclerosis in mice and reduces the severity of symptoms by neutralizing acrolein.

"The treatment did not cause any serious side effects in the mice," Shi said. "The dosage we used for hydralazine in animals is several times lower than the standard dosing for oral hydralazine in human pediatric patients. Therefore, considering the effectiveness of hydralazine at binding acrolein at such low concentrations, we expect that our study will lead to the development of new neuroprotective therapies for MS that could be rapidly translated into the clinic."

The researchers also learned the specific chemical signature of the drug that binds to acrolein and neutralizes it, potentially making it possible to create synthetic alternatives with reduced side effects. The studies are detailed in a paper appearing online this month in the journal *Neuroscience*. The paper was written by doctoral students Gary Leung, Wenjing Sun and Lingxing Zheng; graduate research assistant Melissa Tully, who is an MD-Ph.D. student at Purdue and the Indiana University School of Medicine; postdoctoral researcher Sarah Brookes; and Shi.

In multiple sclerosis, the myelin insulation surrounding nerve cells is destroyed and the nerve fibers themselves are damaged.

*This drawing depicts how the environmental pollutant acrolein may damage nerve insulation called myelin in multiple sclerosis. "A" represents the normal structure of nerve fibers and myelin; "B" represents how acrolein is thought to damage myelin and cell membranes; and "C" shows how nerves with damaged myelin cannot properly conduct signals. (Purdue University graphic/Michel Schweinsberg)*



"We think that acrolein is what degrades myelin, so if we can block that effect then we can delay the onset of MS and lessen the symptoms," Shi said. Acrolein induces the production of free radicals, compounds that cause additional injury to tissues after disease or physical trauma. "We've discovered that acrolein may play a very important role in free radical injury, particularly in multiple sclerosis," Shi said.

The elevated acrolein levels in the MS mice were cut in half when treated with hydralazine. The drug represents a potential long-term therapy to slow the disease's progress.

"To our knowledge, this is the first evidence that acrolein acts as a neurotoxin in MS and also the first time anyone has demonstrated hydralazine to be a neuroprotective drug," Shi said.

Other researchers had previously shown that acrolein damages liver cells and that the damage can be alleviated by hydralazine, leading the Purdue researchers to study its possible effects on spinal cord tissues.

Further research will be conducted, and Shi's group has identified other potential compounds for binding acrolein. The research team, in a possible future collaboration with the Indiana University School of Medicine, also is working to improve the sensitivity of detection methods to measure acrolein levels in people with multiple sclerosis.

<http://www.physorg.com/news/2010-11-scientists-glimpse-universe-big.html>

### **Scientists glimpse universe before the Big Bang**

**(PhysOrg.com) -- In general, asking what happened before the Big Bang is not really considered a science question. According to Big Bang theory, time did not even exist before this point roughly 13.7 billion years ago.**

But now, Oxford University physicist Roger Penrose and Vahe Gurzadyan from the Yerevan Physics Institute in Armenia have found an effect in the cosmic microwave background (CMB) that allows them to "see through" the Big Bang into what came before.

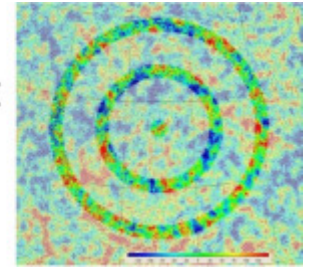
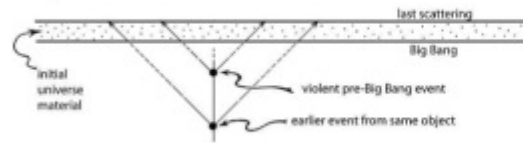
The CMB is the radiation that exists everywhere in the universe, thought to be left over from when the universe was only 300,000 years old. In the early 1990s, scientists discovered that the CMB temperature has anisotropies, meaning that the temperature fluctuates at the level of about 1 part in 100,000. These fluctuations provide one of the strongest pieces of observational evidence for the Big Bang theory, since the tiny fluctuations are thought to have grown into the large-scale structures we see today. Importantly, these fluctuations are considered to be random due to the period of inflation that is thought to have occurred in the fraction of a second after the Big Bang, which made the radiation nearly uniform.

However, Penrose and Gurzadyan have now discovered concentric circles within the CMB in which the temperature variation is much lower than expected, implying that CMB anisotropies are not completely random. The scientists think that these circles stem from the results of collisions between supermassive black holes that



released huge, mostly isotropic bursts of energy. The bursts have much more energy than the normal local variations in temperature. The strange part is that the scientists calculated that some of the larger of these nearly isotropic circles must have occurred before the time of the Big Bang.

The discovery doesn't suggest that there wasn't a Big Bang - rather, it supports the idea that there could have been many of them. The scientists explain that the CMB circles support the possibility that we live in a cyclic universe, in which the end of one "aeon" or universe triggers another Big Bang that starts another aeon, and the process repeats indefinitely. The black hole encounters that caused the circles likely occurred within the later stages of the aeon right before ours, according to the scientists.



***Black hole encounters would have repeated themselves several times, with the center of each event remaining at almost exactly the same point in the CMB sky, even when occurring in different aeons. The huge amounts of energy released would appear as spherical, low-variance radiation bursts in the CMB. Image credit: Gurzadyan and Penrose.***

In the past, Penrose has investigated cyclic cosmology models because he has noticed another shortcoming of the much more widely accepted inflationary theory: it cannot explain why there was such low entropy at the beginning of the universe. The low entropy state (or high degree of order) was essential for making complex matter possible. The cyclic cosmology idea is that, when a universe expands to its full extent, black holes will evaporate and all the information they contain will somehow vanish, removing entropy from the universe. At this point, a new aeon with a low entropy state will begin.

Because of the great significance of these little circles, the scientists will do further work to confirm their existence and see which models can best explain them. Already, Penrose and Gurzadyan used data from two experiments - WMAP and BOOMERanG98 - to detect the circles and eliminate the possibility of an instrumental cause for the effects. But even if the circles really do stem from sources in a pre-Big Bang era, cyclic cosmology may not offer the best explanation for them. Among its challenges, cyclic cosmology still needs to explain the vast shift of scale between aeons, as well as why it requires all particles to lose their mass at some point in the future.

*More information: V.G.Gurzadyan and R.Penrose. "Concentric circles in WMAP data may provide evidence of violent pre-Big-Bang activity." arXiv:1011.3706v1 via: Physics World*

<http://www.bbc.co.uk/news/health-11819901>

### **HIV epidemic 'halted', says UN**

***The number of new HIV infections and deaths from Aids are falling globally, according to new statistics from the UN's programme on HIV/Aids.***

There are now signs the epidemic is declining, it says, however, stigma and discrimination continue to cause problems for the estimated 33m people living with HIV.

Last year there were 2.6m new HIV infections.

This is down almost 20% since the peak of the Aids epidemic in 1999.

In 2009, 1.8m died from Aids-related illnesses, down from 2.1m in 2004.

#### **Mixed progress**

The report says rates of treatment using anti-retroviral drugs have risen from 700,000 in 2004 to over 5m people in 2009.

Sub-Saharan Africa continues to be the region most affected by the epidemic, with around 70% of all new HIV infections occurring here.

But infection rates are falling, particularly in South Africa, Zambia, Zimbabwe and Ethiopia.

Michel Sidibe says the statistics show the spread of HIV has halted in some places

There is a mixed picture in other parts of the world.

Eastern Europe and central Asia show sharp rises in new infections and Aids-related deaths.

And the UN says bad laws and discrimination, particularly in respect to drug users and homosexuals, continue to hamper the fight against Aids.

"We are breaking the trajectory of the Aids epidemic with bold actions and smart choices," said Mr Michel Sidibe, executive director of UNAids.

"Investments in the Aids response are paying off, but gains are fragile - the challenge now is how we can all work to accelerate progress."

## Hardy bugs could survive a million years on Mars

\* 19:48 23 November 2010 by Hazel Muir

It was already nicknamed "Conan the Bacterium" for its ability to withstand radiation. Now it seems *Deinococcus radiodurans* could, in theory, survive dormant on Mars for over a million years.

Lewis Dartnell at University College London and colleagues froze the bugs to -79 °C, the average temperature at Mars's mid-latitudes. Then they zapped them with gamma rays to simulate the dose they would receive under 30 centimetres of Martian soil over long periods of time. The team worked out that it could take 1.2 million years under these conditions to shrink a population of the bacteria to a millionth of its original size.

Earlier studies suggested that the bacterium can endure four times as much radiation in the Martian cold as at room temperature. If a cell is frozen, radiation does less damage to it because the free radicals it creates are much less mobile. "Cold is good in that respect," Dartnell says. "It improves the chances of cells surviving radiation."

### Antarctic bugs

Dartnell's team also isolated three new strains of bacteria from the Dry Valleys of Antarctica, where winter temperatures drop to -40 °C. The hardiest of the bugs, a new strain of *Brevundimonas*, could persist for 117,000 years on Mars before its population would be reduced by a factor of a million, the team's work suggests.

"The more we learn about Earth life, the more likely it appears that it could survive in other parts of the solar system," says Cassie Conley of NASA in Washington DC.

### High vacuum

But even if terrestrial microbes could survive on Mars itself, they might not fare so well on the journey there, she cautions. To simulate spaceflight, she suggests that the experiments be repeated in a high vacuum, which can desiccate microbes. "In space, you suck off nearly all the water molecules," Conley says. This removal of water could make it more difficult for cells to repair radiation damage.

Conley, who makes sure NASA missions minimise the risk of contaminating other worlds with microbes, says the agency's policy on planetary protection already takes into account that some microbes are amazingly radiation resistant.

"The policy is that we won't contaminate other planets or moons, because just one colonising event could screw up our ability to study indigenous life forever," she told *New Scientist*.

*Journal reference: Astrobiology (DOI: 10.1089/ast.2009.0439)*

<http://www.bbc.co.uk/news/world-latin-america-11826323>

## Haiti cholera spreading faster than predicted, UN says

***The cholera epidemic in Haiti is spreading twice as fast as had been estimated and is likely to result in hundreds of thousands of cases in the coming months, the UN says.***

The UN's humanitarian co-ordinator for Haiti, Nigel Fisher, said aid agencies would have to "ratchet up" their response and send more medical staff. The Haitian government says 1415 people are confirmed to have died.

The epidemic has complicated preparations for elections next Sunday.

Mr Fisher said more than 200,000 cases of infection could be recorded in the first three months instead of six months as first estimated. "This epidemic is moving faster and we are in unknown territory in Haiti just because this is moving so fast. There is no immunity to it", he said. Mr Fisher added that the Haitian government would have to increase pressure on local authorities to find places for more treatment centres and to dispose of bodies.

There has been some opposition to the placing of treatment centres from residents who fear they could bring the infection into their neighbourhoods.

The UN under-secretary for humanitarian affairs, Valerie Amos, who is visiting Haiti, told the BBC there was an urgent need to train Haitian health workers, who have no previous experience of dealing with cholera.

"We need to get the message out there to the people that this is something that can be dealt with. We need to make sure they know about hand-washing and proper sanitation, and we need to get supplies in", she said.

### Election challenge

Campaigning is meanwhile in full swing for Sunday's elections, when Haitians will elect a new president and legislative members.

Some human rights groups and four of the 19 presidential candidates have called for the elections to be postponed because of the cholera epidemic.

But the UN mission in Haiti, Minustah, says the conditions for a successful vote are good.

Cholera
<i>Intestinal infection caused by bacteria transmitted through contaminated water or food</i>
<i>Source of contamination usually faeces of infected people</i>
<i>Causes diarrhoea, vomiting, severe dehydration; can kill quickly</i>

"The government and the vast majority of candidates are really determined that these elections be held as planned," said the head of Minustah, Edmond Mulet. "As in the past we might see some intimidation or burning of ballots or polling stations, but we are prepared on the security side to face those challenges".

There have been outbreaks of violence between rival political factions in the run-up to the vote.

On Tuesday two people were shot dead in a clash between supporters of two candidates in the town of Beaumont in south-western Haiti.

Last week there was also rioting directed against UN peacekeepers from Nepal, who some Haitians have accused of bringing cholera into the country. The UN says there is no evidence to support the accusation.

Sunday's elections are seen as a crucial step towards giving Haiti a stable government that can lead recovery efforts after January's massive earthquake, which killed about 230,000 people and shattered the capital, Port-au-Prince. Some 19 candidates are vying to succeed current president, Rene Preval and it is likely that the election will go to a second round run-off on 16 January. Most candidates have insisted that the elections, which will also choose 99 deputies and 10 senators, should go ahead as planned.

[http://www.eurekalert.org/pub\\_releases/2010-11/w-nsr112410.php](http://www.eurekalert.org/pub_releases/2010-11/w-nsr112410.php)

### **New study reveals how cannabis suppresses immune functions**

#### ***Cannabis compounds found to trigger unique immune cells which promote cancer growth***

An international team of immunologists studying the effects of cannabis have discovered how smoking marijuana can trigger a suppression of the body's immune functions. The research, published in the European Journal of Immunology, reveals why cannabis users are more susceptible to certain types of cancers and infections.

The team, led by Dr Prakash Nagarkatti from the University of South Carolina, focused their research on cannabinoids, a group of compounds found inside the cannabis plant, including THC (delta-9 tetrahydrocannabinol) which is already used for medical purposes such as pain relief.

"Cannabis is one of the most widely used drugs of abuse worldwide and it is already believed to suppress immune functions making the user more susceptible to infections and some types of cancer," said Dr Nagarkatti. "We believe the key to this suppression is a unique type of immune cell, which has only recently been identified by immunologists, called myeloid-derived suppressor cells, MDSCs."

While most immune cells fight against infections and cancers to protect the host, MDSCs actively suppress the immune system. The presence of these cells is known to increase in cancer patients and it is believed that MDSCs may suppress the immune system against cancer therapy, actually promoting cancer growth.

Dr Nagarkatti's team demonstrated that cannabinoids can trigger a massive number of MDSCs through activation of cannabinoid receptors. This research reveals, for the first time, that marijuana cannabinoids may suppress the immune system by activating these unique cells.

"These results raise interesting questions on whether increased susceptibility to certain types of cancers or infections caused from smoking marijuana results from induction of MDSCs," said Nagarkatti. "MDSCs seem to be unique and important cells that may be triggered by inappropriate production of certain growth factors by cancer cells or other chemical agents such as cannabinoids, which lead to a suppression of the immune system's response."

In a related study, also published in the European journal of Immunology, Dr Christian Vosschenrich from the Institut Pasteur in Paris, reveals that when cancer cells grow they produce a molecule called interleukin-1  $\beta$  (IL-1 $\beta$ ), which also triggers MDSCs. This study identifies how MDSCs produced during cancer growth also weaken the ability of immune cells to kill cancer cells.

"Marijuana cannabinoids present us with a double edged sword," concluded Dr Nagarkatti. "On one hand, due to their immunosuppressive nature, they can cause increased susceptibility to cancer and infections. However, further research of these compounds could provide opportunities to treat a large number of clinical disorders where suppressing the immune response is actually beneficial."

[http://www.eurekalert.org/pub\\_releases/2010-11/dmc-dsu112410.php](http://www.eurekalert.org/pub_releases/2010-11/dmc-dsu112410.php)

### **Dartmouth study uses the patient's tumor to form vaccine**

#### ***Dendritic cell vaccine induces immune responses in patients***

A new process for creating a personalized vaccine may become a crucial tool in helping patients with colorectal cancer develop an immune response against their own tumors. This dendritic cell (DC) vaccine, developed at Dartmouth and described in a research paper published this week in the journal Clinical Cancer Research, was used after surgical resection of metastatic tumors to try to prevent the growth of additional metastases.

"The results of the study suggest a new way to approach cancer treatment," said Richard Barth Jr., MD, Chief of General Surgery at Dartmouth-Hitchcock Medical Center and a member of the Gastrointestinal Clinical Oncology Group at Dartmouth-Hitchcock Norris Cotton Cancer Center, who is the study's principal

investigator. "Basically, we've worked out a way to use dendritic cells, which initiate immune responses, to induce an antitumor response."

Dendritic cells are critical to the human body's immune system, helping identify targets, or antigens, and then stimulating the immune system to react against those antigens. The new research grew dendritic cells from a sample of a patient's blood, mixed them with proteins from the patient's tumor, and then injected the mixture into the patient as a vaccine. The vaccine then stimulated an anti-tumor response from T-cells, a kind of white blood cell that protects the body from disease.

In the study, Barth first operated on 26 patients to remove tumors that had spread from the colon to the liver. While some of these patients would be expected to be cured with surgery alone, most of them would eventually die from tiny metastases that were undetectable at the time the tumors were removed from the liver. The DC vaccine treatment was given one month after surgery. The results were that T-cell immune responses were induced against the patient's own tumor in more than 60% of the patients. The patients were followed for a minimum of 5.5 years. Five years after their vaccine treatment, 63% of the patients who developed an immune response against their own tumor were alive and tumor-free. In contrast, just 18% of the patients who did not develop an immune response against their own tumor were alive and tumor-free.

"We showed that a tumor lysate-pulsed DC vaccine can induce immune responses against the patient's own tumor in a high proportion of patients," stated Dr. Barth, who has been investigating DC-based vaccines in mice and patients for more than 10 years. "There were two basic questions we wanted to answer: one, can we generate an antitumor response, and two, does it matter? From our research, the answer to both questions is yes."

He said DC vaccines have been a research interest at many institutions, and previous studies showed that DC vaccines could not reduce or eliminate measurable metastatic tumor deposits. "It turned out we were asking the T-cells to do too much," he commented. "The small number of T-cells that are generated by a vaccine can't destroy a large tumor. However, what they may be able to do is search out and destroy tumor cells that exist as only microscopic tumor deposits. Once we brought patients into a measurable tumor-free condition with surgery, the anti-tumor T-cells induced by the DC vaccine may help keep them that way."

Follow-up studies are necessary to more fully understand the mechanisms of the DC vaccine and its impact on long-term survival rates, Dr. Barth said. He believes this study may open the door to a significant change in cancer treatment in the future. The DC vaccine is non-toxic, while traditional chemotherapies are highly toxic. "It's your own immune system doing the fighting," he commented. "I'm optimistic that this really will have an impact."

[http://www.eurekalert.org/pub\\_releases/2010-11/bc-ggs112310.php](http://www.eurekalert.org/pub_releases/2010-11/bc-ggs112310.php)

### **Growth-factor gel shows promise as hearing-loss treatment**

***A new treatment has been developed for sudden sensorineural hearing loss (SSHL), a condition that causes deafness in 40,000 Americans each year, usually in early middle-age.***

Researchers writing in the open access journal BMC Medicine describe the positive results of a preliminary trial of insulin-like growth factor 1 (IGF1), applied as a topical gel.

Takayuki Nakagawa, from Kyoto University, Japan, worked with a team of researchers to test the gel in 25 patients whose SSHL had not responded to the normal treatment of systemic glucocorticoids. He said, "The results indicated that the topical IGF1 application using gelatin hydrogels was safe, and had equivalent or superior efficiency to the hyperbaric oxygen therapy that was used as a historical control; this suggests that the efficacy of topical IGF1 application should be further evaluated using randomized clinical trials".

At 12 weeks after the test treatment, 48% of patients showed hearing improvement, and the proportion increased to 56% at 24 weeks. No serious adverse events were observed. This is the first time that growth factors have been tested as a hearing remedy. According to Nakagawa, "Although systemic glucocorticoid application results in hearing recovery in some patients with SSHL, approximately 20% show no recovery. Topical IGF1 application using gelatin hydrogels is well tolerated and may be efficacious for these patients".

#### ***Notes to Editors***

*1. A Topical insulin-like growth factor 1 treatment using gelatin hydrogels for glucocorticoid-resistant sudden sensorineural hearing loss: a prospective clinical trial*

*Takayuki Nakagawa, Tatsunori Sakamoto, Harukazu Hiraumi, Yayoi S Kikkawa, Norio Yamamoto, Kiyomi Hamaguchi, Kazuya Ono, Masaya Yamamoto, Yasuhiko Tabata, Satoshi Teramukai, Shiro Tanaka, Harue Tada, Rie Onodera, Atsushi Yonezawa, Ken-ichi Inui and Juichi Ito*

*BMC Medicine (in press)*



## **Marsupial carnivores 'as diverse as other mammals once'**

***They are an extraordinary and now rare group of animals but Earth has had some formidable marsupial carnivores.***

These pouched killers have included lions, wolves, and even sabretooths.

Today, the only large marsupial carnivore left in existence is the Tasmanian Devil, and that is on the brink of extinction.

These animals' past success though is illustrated by a new skull study that reveals the creatures to have been just as diverse as their cousins, the placental mammals.

An international team examined the skulls of some 130 carnivores - marsupial and placental, living and extinct - from the past 40 million years. Dr Anjali Goswami and colleagues used a technique known as geometric morphometrics to map the objects.

Their analysis shows the variation in shape in marsupial carnivores' skulls is actually greater than that observed in placentals, such as "ordinary" lions and tigers - even though the marsupial sample was smaller.



***Marsupial lion (SPL) Many of the marsupial carnivores have long been extinct***

The findings are published in the journal Proceedings of the Royal Society B.

The team says the research gives the lie to the idea that marsupial carnivores' method of reproduction, wherein the young are born at a very early stage, somehow limited their ability to adapt to new habits and environments.

"A straightforward example is with the forelimbs," explained Dr Goswami.

"Because marsupials have to crawl really early - they have to develop these crawling, grasping hands to get into the pouch. Once you have to have that kind of structure, it's really hard to then develop a flipper or a bat wing.

"And while it's been shown marsupials do have less diversity in their forelimbs than placental carnivores, our study has shown that's not true of the face.

"I think you can argue that marsupials have gone way beyond what placentals have done in terms of modifying their face and their dentition to be able to eat meat," she told BBC News. "There was a marsupial sabretooth from South America, for example, that had ever-growing canines, and the roots of these teeth went up over the [eye socket]. There's nothing like that in placental carnivores. It's really very extreme."



***An extinct sabretooth marsupial, T. atrox, evolved ever-growing canines***

The reasons for the loss of marsupial carnivores must therefore be more complex than some have recognised, the researchers argue. The group cites competition with placentals during the fusion of North and South America three million years ago, and more recent human hunting as both likely reasons for the creatures' decline.

Co-author Dr Stephen Wroe from the University of New South Wales said: "It seems likely that the diversity in skull shape among marsupial carnivores reflects a diversity in lifestyle that once was quite comparable to that of placentals. "Our results reinforce my own suspicion that the lack of marsupial predators in the world today has more to do with bad luck than bad genes."

<http://www.physorg.com/news/2010-11-sun-comets-stars.html>

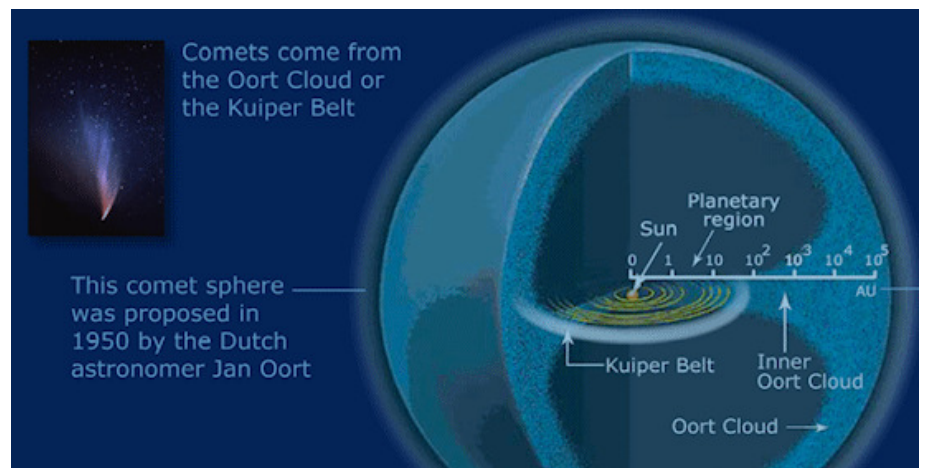
## **The sun steals comets from other stars**

***The next time you thrill at the sight of a comet blazing across the night sky, consider this: it's a stolen pleasure. You're enjoying the spectacle at the expense of a distant star.***

Sophisticated computer simulations run by researchers at the Southwest Research Institute (SWRI) have exposed the crime. "If the results are right, our Sun snatched comets from neighboring stars' back yards," says SWRI scientist Hal Levison. And he believes this kind of thievery accounts for most of the comets in the Oort Cloud at the edge of our solar system.

"We know that stars form in clusters. The Sun was born within a huge community of other stars that formed in the same gas cloud. In that birth cluster, the stars were close enough together to pull comets away from each other via gravity. It's like neighborhood children playing in each others' back yards. It's hard to imagine it not happening."

According to this "thief" model, comets accompanied the nearest star when the birth cluster blew apart. The Sun made off with quite a treasure – the Oort Cloud, which was swarming with comets from all over the "neighborhood."



*An artist's concept of the Oort cloud. Note that the distance scale is logarithmic. Compared to the size of planetary orbits, the Oort cloud is very far away. Indeed, the estimated size of the Oort cloud,  $10^5$  AU, is approximately 1 light year. If the Sun passed within 2 light years of another sun-like star, the stars' Oort clouds would overlap and their comets would intermingle. Image credit: ESO*

The Oort cloud is an immense cloud of comets orbiting the Sun far beyond Pluto. It is named after mid-20th century Dutch astronomer Jan Oort, who first proposed such a cloud to explain the origin of comets sometimes seen falling into the inner solar system. Although no confirmed direct observations of the Oort cloud have been made, most astronomers believe that it is the source of all long-period and Halley-type comets.

The standard model of comet production asserts that our Sun came by these comets honestly.

"That model says the comets are dregs of our own solar system's planetary formation and that our planets gravitationally booted them to huge distances, populating the cloud. But we believe this kind of scenario happened in all the solar systems before the birth cluster dispersed."

Otherwise, says Levison, the numbers just don't add up.

"The standard model can't produce anywhere near the number of comets we see [falling in from the Oort Cloud]. The Sun's sibling stars had to have contributed some comets to the mix."

Comets in the Oort Cloud are typically 1 or 2 miles across, and they're so far away that estimating their numbers is no easy task. But Levison and his team say that, based on observations, that there should be something like 400 billion comets there. The "domestic" model of comet formation can account for a population of only about 6 billion.

"That's a pretty anemic Oort Cloud, and a huge discrepancy – too huge to be explained by mistakes in the estimates. There's no way we could be that far off, so there has to be something wrong with the model itself."

He points to the cometary orbits as evidence. "These comets are in very odd orbits – highly eccentric long-period orbits that take them far from our Sun, into remote regions of space. So they couldn't have been born in orbit around the Sun. They had to have formed close to other stars and then been hijacked here."

This means comets can tell us not only about the early history of the Sun – but also about the history of other stars. "We can study the orbits of comets and put their chemistry into the context of where and around which star they formed. It's intriguing to think we got some of our 'stuff' from distant stars. We're kin."

Provided by Science@NASA

<http://www.stonepages.com/news/archives/004118.html>

### Chinese mine in Afghanistan threatens ancient find

*A Chinese company is eager to begin developing the world's second-biggest unexploited copper mine which lies beneath the ruins of a 2,600-year-old Buddhist monastery in Afghanistan.*

Beijing put \$3.5 billion stake in the mine, the largest foreign investment in Afghanistan by far, and the Afghan government stands to rake in a potential \$1.2 billion a year in revenues from the mine, as well as the creation of much-needed jobs.

In the meantime, archaeologists are racing to salvage what they can from a major seventh century BCE religious site along the famed Silk Road connecting Asia and the Middle East. The ruins, including the monastery and domed shrines known as 'stupas,' will most likely be largely destroyed once construction of the mine begins. The Chinese government-backed China Metallurgical Group Corp., or MCC, planned to start building the mine by the end of 2011, but under an informal understanding with the Kabul government, it has granted archaeologists three years for a salvage excavation.

Archaeologists working on the site since May say that will not be enough time for full preservation. "That site is so massive that it's easily a 10-year campaign of archaeology," stated Laura Tedesco, an archaeologist brought in by the U.S. Embassy to work on sites in Afghanistan. Philippe Marquis, a French archaeologist advising the Afghans, said the salvage effort is piecemeal and 'minimal'; held back by lack of funds and personnel. "This is probably one of the most important points along the Silk Road," revealed Marquis. "What we have at this site, already in excavation, should be enough to fill the (Afghan) national museum."

The monastery complex has been excavated, revealing hallways and rooms decorated with frescoes and filled with clay and stone statues of standing and reclining Buddhas. Some statues reaching as high as 10 feet. An area that was at one time a courtyard is dotted with stupas standing four or five feet high. More than 150 statues have been found to date, though many remain in place. The large ones are too heavy to be moved, and the team lacks the chemicals necessary to keep small ones from disintegrating when extracted.

MCC appears to be pushing the archaeologists to complete the excavation ahead of schedule. The Afghan archaeologist overseeing the dig said he has no idea when MCC representatives might tell him his work is over, so he tries not to think about deadlines. "We would like to work according to our principles. If we don't work according to the principles of archaeology, then we are no different from traffickers," Abdul Rauf Zakir noted.

The team hopes to lift some of the larger statues and shrines out before winter sets in this month, but they still haven't procured the crane and other equipment needed to do so. Funding from foreign governments has been promised, but has yet to materialize. Marquis said MCC has been cooperative and has been helping the archaeologists with dirt removal and asking what more needs to be done. Zakir, the Afghan archaeologist, laughs. "Yes, they are very helpful. They want to help so that we can finish quickly. They want us gone."

*Edited from Associated Press (14 November 2010)*

<http://www.physorg.com/news/2010-11-danish-obesity-riddle.html>

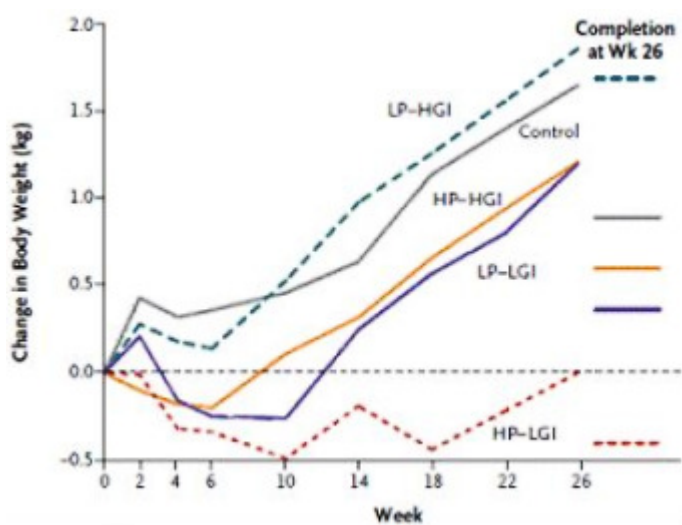
### Danish researchers finally solve the obesity riddle

**Researchers at the Faculty of Life Sciences (LIFE), University of Copenhagen, can now unveil the results of the world's largest diet study: If you want to lose weight, you should maintain a diet that is high in proteins with more lean meat, low-fat dairy products and beans and fewer finely refined starch calories such as white bread and white rice**

With this diet, you can also eat until you are full without counting calories and without gaining weight. Finally, the extensive study concludes that the official dietary recommendations are not sufficient for preventing obesity.

The large-scale random study called Diogenes has investigated the optimum diet composition for preventing and treating obesity. The study was conducted by eight European research centres and headed by Thomas Meinert Larsen, PhD, and Professor Arne Astrup, DrMedSc and Head of Department at the Faculty of Life Sciences (LIFE) and is funded by an EU grant of EUR 14.5 million.

The results were recently published in the distinguished New England Journal of Medicine and have already attracted considerable international attention.



*This chart shows changes in body weight. Credit: Figure*

The objective of the Diogenes study has been to compare the official dietary recommendations in Europe, including the Danish recommendations, with a diet based on the latest knowledge about the importance of proteins and carbohydrates for appetite regulation. A total of 772 European families participated, comprising 938 adult family members and 827 children. The overweight adults initially followed an 800 kcal/day diet for eight weeks, losing an average of 11 kg. They were then randomly assigned to one of five different low-fat diet types which they followed for six months in order to test which diet was most effective at preventing weight regain. Throughout the project, the families received expert guidance from dietitians and were asked to provide blood and urine samples.

#### The five diet types

The design comprised the following five diet types:

- \* A low-protein diet (13% of energy consumed) with a high glycemic index (GI)
- \* A low-protein, low-GI diet



- \* A high-protein (25% of energy consumed), low-GI diet
- \* A high-protein, high-GI diet
- \* A control group which followed the current dietary recommendations without special instructions regarding glycemic index levels

A high-protein, low-GI diet works best. A total of 938 overweight adults with a mean body mass index (BMI) of 34 kg/sq m were initially placed on an 800-kcal-per-day diet for eight weeks before the actual diet intervention was initiated. A total of 773 adult participants completed this initial weight-loss phase and were then randomly assigned to one of five different diet types, where 548 participants completed the six-month diet intervention (completion rate of 71%).

Fewer participants in the high-protein, low-GI groups dropped out of the project than in the low-protein, high-GI group (26.4% and 25.6%, respectively, vs. 37.4%;  $P = 0.02$  and  $P = 0.01$  for the two comparisons, respectively). The initial weight loss on the 800-kcal diet was an average of 11.0 kg.

The average weight regain among all participants was 0.5 kg, but among the participants who completed the study, those in the low-protein/high-GI group showed the poorest results with a significant weight gain of 1.67 kg. The weight regain was 0.93 kg less for participants on a high-protein diet than for those on a low-protein diet and 0.95 kg less in the groups on a low-GI diet compared to those on a high-GI diet.

### The children's study

The results of the children's study have been published in a separate article in the American medical journal *Pediatrics*. In the families, there were 827 children who only participated in the diet intervention. Thus, they were never required to go on a diet or count calories – they simply followed the same diet as their parents. Approx. 45% of the children in these families were overweight. The results of the children's study were remarkable: In the group of children who maintained a high-protein, low-GI diet the prevalence of overweight dropped spontaneously from approx. 46% to 39% – a decrease of approx. 15%.

### Proteins and low-GI foods ad libitum – the way ahead

The Diogenes study shows that the current dietary recommendations are not optimal for preventing weight gain among overweight people. A diet consisting of a slightly higher protein content and low-GI foods ad libitum appears to be easier to observe and has been documented to ensure that overweight people who have lost weight maintain their weight loss. Furthermore, the diet results in a spontaneous drop in the prevalence of overweight among their children.

#### More information: References:

1. "Diets with High or Low Protein Content and Glycemic Index for Weight-Loss Maintenance" Thomas Meinert Larsen, PhD, Stine-Mathilde Dalskov, MSc, Marleen van Baak, PhD, Susan Ann Jebb, PhD, Angeliki Papadaki, PhD, Andreas F.H. Pfeiffer, MD, J. Alfredo Martinez, PhD, Teodora Handjieva-Darlenska, MD, PhD, Marie Kunešová, MD, PhD, Mats Pihlsgård, PhD, Steen Stender, MD, PhD, Claus Holst, PhD, Wim H.M. Saris, MD, PhD, and Arne Astrup, MD, DrMedSc, for the Diet, Obesity, and Genes (Diogenes) Project; *New England Journal of Medicine*, published online 25 Nov. 2010.

2. *The Effect of Protein and Glycemic Index on Children's Body Composition: The DiOGenes Randomized Study*; Angeliki Papadaki Manolis Linardakis, Thomas M. Larsen, Marleen A. van Baak, Anna Karin Lindroos, Andreas F. H. Pfeiffer, J. Alfredo Martinez, Teodora, Handjieva-Darlenska, Marie Kunesová, Claus Holst, Arne Astrup, Wim H. M. Saris and Anthony Kafatos on behalf of the Diogenes Study Group; *Pediatrics*, Vol. 126, 5 Nov. 2010.

Provided by University of Copenhagen

<http://www.newscientist.com/article/dn19771-why-mammals-grew-big--and-then-stopped.html>

### Why mammals grew big – and then stopped

\* 19:00 25 November 2010 by Jeff Hecht

**Land mammals kept getting larger for 35 million years after the dinosaurs were wiped off the planet, then hit a plateau of 15 tonnes around 30 million years ago.**

The first comprehensive study to compare the maximum size of fossils around the world shows how the extinction triggered a growth spurt in the mammals that were left to take over the continents. It reveals that land mammals around the world responded the same way to the death of the dinosaurs 65 million years ago.

There has been a long-running debate over how mammals grew from the tiny shrew-like creatures that hid from dinosaurs to the much larger sizes of recently extinct behemoths such as the woolly mammoth. A decade ago, John Alroy, now at the University of California, Santa Barbara, reported that North American mammals had grown steadily larger for 65 million years after the mass extinction that marked the end of the dinosaurs' reign.

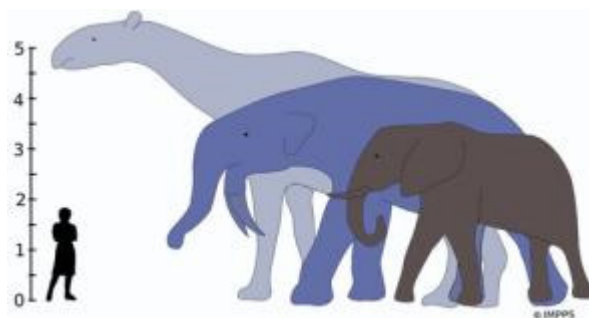
Now Felisa Smith of the University of New Mexico, Albuquerque, and 19 colleagues have looked at mammalian fossils from Africa, Eurasia and South America to see how maximum body size changed with time. The pattern they found "is replicated across space and time, which is just amazing", says Smith.



## Giant herbivore

The fossils show how mammals – which initially weighed in at only 10 to 100 grams – ballooned and eventually reached a maximum of 17 tonnes some 25 million years later. The largest one, Indricotherium transouralicum – which is also the largest mammal to ever walk the earth – was a hornless rhinoceros-like herbivore that stood about 5.5 metres tall at shoulder level.

"Basically, the dinosaurs disappear and all of a sudden there is nobody else eating the vegetation," says co-author Jessica Theodor of the University of Calgary, Alberta, Canada. All of the largest mammals were plant-eaters. "It's more efficient to be a herbivore when you're big," says Theodor.



*The largest land mammals that ever lived, Indricotherium (grey) and Deinotherium (blue) would have towered over modern-day African elephants (Image: IMPPS)*

Mammalian predators never grew to much more than a tonne, about the size of a modern polar bear. Size can be a problem for predators, says Smith, as it makes it easy for potential prey to spot and elude them.

Smith thinks temperature and energy set the upper limits, because massive mammals have a hard time dissipating body heat in warm climates. Even the largest megafauna were not as big as large dinosaurs, and Smith believes dinosaurs could grow much larger because they generated less internal heat.

Others are not convinced. "I don't think we really know why we have larger animals at given times," says palaeontologist Donald Prothero of Occidental College in Los Angeles. Alroy says that evolutionary trends are better revealed by changes in lineages than by looking only at the largest species.

Journal reference: *Science*, DOI: 10.1126/science.1194830

<http://news.nationalgeographic.com/news/2010/11/101125-saturn-moon-oxygen-atmosphere-discovered-science-space/>

## Saturn Moon Has Oxygen Atmosphere

Andrew Fazekas for National Geographic News

***An oxygen atmosphere has been found on Saturn's second largest moon, Rhea, astronomers announced Thursday—but don't hold your breath for colonization opportunities.***

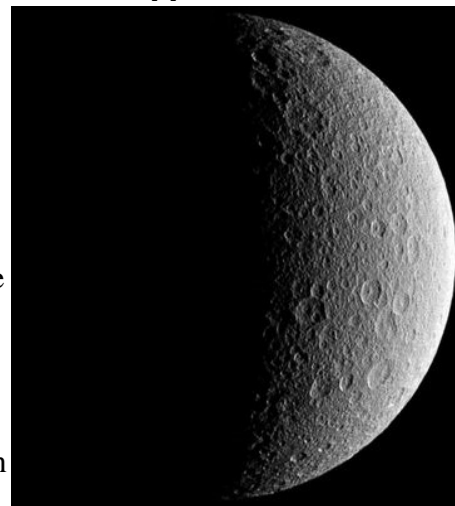
For one thing, the 932-mile-wide (1,500-kilometer-wide), ice-covered moon is more than 932 million miles (1.5 billion kilometers) from Earth. For another, the average surface temperature is -292 degrees Fahrenheit (-180 degrees Celsius).

And at less than 62 miles (100 kilometers) thick, the newfound oxygen layer is so thin that, at Earthlike temperatures and pressure, Rhea's entire atmosphere would fit in a single midsize building.

Still, the discovery implies that worlds with oxygen-filled air may not be so unusual in the cosmos.

At about 327,000 miles (527,000 kilometers) from Saturn, Rhea orbits inside the planet's magnetic field.

Rhea's oxygen atmosphere is believed to be maintained by the ongoing chemical breakdown of water ice on the moon's surface, driven by radiation from Saturn's magnetosphere.



*Saturn's moon Rhea, as seen by the Cassini spacecraft in 2009. Image courtesy NASA*

The Hubble Space Telescope and NASA's Galileo probe found in 1995 that a similar process creates tenuous oxygen atmospheres on Jupiter's ice moons Europa and Ganymede.

"The major implication of this finding at Rhea is that oxygen atmospheres at icy moons, until now only detected at Europa and Ganymede, may in fact be commonplace around those irradiated icy moons throughout the universe with sufficient mass to hold an atmosphere," said study leader Ben Teolis of the Southwest Research Institute in San Antonio, Texas.

Knowing where and how oxygen exists in the universe may in turn help scientists plan future robotic and manned missions.

## Oxygen "Bubbling" From Moon's Surface

NASA's Cassini spacecraft, which has been orbiting the Saturnian system since 2004, detected the oxygen atmosphere around Rhea during a close flyby of the icy moon in March.

Cassini's data show that molecular oxygen (O<sub>2</sub>) forms inside the moon's surface ice when water molecules (H<sub>2</sub>O) are split by energetic ions, a process known as radiolysis. The oxygen then gets ejected from the surface ice and captured by Rhea's gravity to form the atmosphere.

"A loose analogy might be carbon dioxide dissolved, or trapped, in a carbonated beverage, except here we are not talking about liquid water but rather frozen ice at extremely low temperatures," Teolis said.

The amount of oxygen gas produced per second across Rhea's surface weighs about 0.3 pound (130 grams), the study team reports in this week's issue of the journal *Science*. At room temperature and Earth's atmospheric pressure, Teolis estimates, this amount of oxygen would occupy about 3.5 cubic feet (0.1 cubic meter).

That means Rhea's entire atmosphere, under Earthly conditions, would fill a cube about 70 feet (22 meters) long on each side.

### **Oxygen and Carbon: Signs of Underground Life?**

Cassini also identified the distinctive chemical fingerprint of carbon dioxide in Rhea's atmosphere, indicating the presence of carbon on the moon's surface.

The combination of carbon and oxygen holds implications for finding possible life on ice moons, such as Europa, thought to harbor subsurface liquid oceans.

"You would expect a very small amount of gas [around an ice moon], but the fact that there is enough to be measurable is what is surprising and indicates that the energetic processes that must be occurring are more widespread than previously thought," said Robert Carlson, a researcher at NASA's Jet Propulsion Laboratory in Pasadena, California.

"Specifically this indicates that the surface is oxidizing, meaning that you can make alcohols and organic acids if carbon is in the surface materials," said Carlson, who wasn't involved in the study.

"There are also ideas that the oxidants, like O<sub>2</sub>, could be subducting into an ocean below the surface and could be an energy source for any life in these possible oceans."

### **Ice Moons May Be Future Reservoirs**

The new study may have scientists looking with fresh eyes at Rhea-like moons around other gas giant planets.

"This shows how prevalent high-energy chemistry is on icy satellites, not constrained to just Europa," Carlson said. "I expect there will be more Cassini flyby measurements and that many telescopes will be pointed to the icy satellites now, along with a lot of supporting laboratory work."

In the short term, it's possible the discovery on Rhea will help inform plans for robotic probes, such as a proposed mission to Europa currently being considered by NASA.

"The discovery of Rhea's atmosphere is extremely fortuitous, as it will allow us to anticipate what we might expect to find at Jupiter's moons and design the spacecraft instruments accordingly," study leader Teolis said.

And in the longer term, Teolis added, frozen reservoirs of oxygen on moons such as Rhea may one day become pivotal for deep-space exploration involving human missions.

"In some very distant—and highly speculative—future," he said, "one can imagine that the ices on these moons might be heated or melted to extract oxygen and carbon dioxide, both of which are necessities for the survival of plant and animal life."

<http://www.nytimes.com/2010/11/26/health/26alzheimers.html>

## **Children Ease Alzheimer's in Land of Aging**

By PAM BELLUCK

***SEONGNAM, South Korea — They were stooped, hobbled, disoriented, fumbling around the house. They got confused in the bathtub and struggled up stairs that seemed to swim before them.***

"Oh, it hurts," said Noh Hyun-ho, sinking to the ground.

"I thought I was going to die," said Yook Seo-hyun.

There was surprisingly little giggling, considering that Hyun-ho, Seo-hyun and the others were actually perfectly healthy 11- to 13-year-old children. But they had strapped on splints, weighted harnesses and fogged-up glasses, and were given tasks like "Doorknob Experience" and "Bathroom Experience," all to help them feel what it was like to be old, frail or demented.

"Even though they are smiling for us, every day, 24 hours, is difficult for them," Jeong Jae-hee, 12, said she learned. "They lose their memory and go back to childhood."

It is part of a remarkable South Korean campaign to cope with an exploding problem: Alzheimer's disease and other dementias. As one of the world's fastest-aging countries, with nearly 9 percent of its population over 65 already afflicted, South Korea has opened a "War on Dementia," spending money and shining floodlights on a disease that is, here as in many places, riddled with shame and fear.

South Korea is training thousands of people, including children, as “dementia supporters,” to recognize symptoms and care for patients. The 11- to 13-year-olds, for instance, were in the government’s “Aging-Friendly Comprehensive Experience Hall” outside Seoul. Besides the aging simulation exercise, they viewed a PowerPoint presentation defining dementia and were trained, in the hall’s Dementia Experience Center, to perform hand massage in nursing homes.

“ ‘What did I do with my phone? It’s in the refrigerator,’ ” said one instructor, explaining memory loss. “Have you seen someone like that? They may go missing and die on the street.”

In another striking move, South Korea is also pushing to make diagnoses early, despite there being scant treatment.

“This used to be hidden” and “there is still stigma and bias,” said Kim Hye-jin, director of senior policy for the Health and Welfare Ministry. But “we want to get them out of their shells, out of their homes and diagnosed” to help families adjust and give patients “a higher chance of being taken care of at home.”

Hundreds of neighborhood dementia diagnostic centers have been created. Nursing homes have nearly tripled since 2008. Other dementia programs, providing day care and home care, have increased fivefold since 2008, to nearly 20,000. Care is heavily subsidized.

And a government dementia database allows families to register relatives and receive iron-on identification numbers. Citizens encountering wanderers with dementia report their numbers to officials, who contact families.

To finance this, South Korea created a long-term-care insurance system, paid for with 6.6 percent increases in people’s national health insurance premiums. In 2009, about \$1 billion of government and public insurance money was spent on dementia patients. Still, with the over-65 population jumping from 7 percent in 2000 to 14 percent in 2018 to 20 percent in 2026, dementia is straining the country, socially and economically.

“At least one family member has to give up work” to provide caregiving, said Kwak Young-soon, social welfare director for Mapo District, one of Seoul’s 25 geographic districts. Because South Korea encourages people to work well past retirement age, families may also lose dementia sufferers’ incomes.

Most families no longer have generations living together to help with caregiving, and some facilities have long waiting lists, but “we can’t keep building nursing homes,” Mr. Kwak said. “We call it a ghost. It’s basically eating up the whole house.”

### **Dementia Epidemic**

South Korea is at the forefront of a worldwide eruption of dementia, from about 30 million estimated cases now to an estimated 100 million in 2050. And while South Korea’s approach is unusually extensive, even in the United States, the National Alzheimer’s Project Act was introduced this year to establish a separate Alzheimer’s office to create “an integrated national plan to overcome Alzheimer’s.” Supporters of the bill, currently in committee, include Sandra Day O’Connor, whose late husband had Alzheimer’s.

South Korea also worries that dementia, previously stigmatized as “ghost-seeing” or “one’s second childhood” could “dilute respect for elders,” Mr. Kwak said. “There’s a saying that even the most filial son or daughter will not be filial if they look after a parent for more than three years.”

So the authorities promote the notion that filial piety implies doing everything possible for elders with dementia, a condition now called chimae (pronounced chee-may): disease of knowledge and the brain which makes adults become babies. But South Korea’s low birth rate will make family caregiving tougher.

“I feel as if a tsunami’s coming,” said Lee Sung-hee, the South Korean Alzheimer’s Association president, who trains nursing home staff members, but also thousands who regularly interact with the elderly: bus drivers, tellers, hairstylists, postal workers. “Sometimes I think I want to run away,” she said. “But even the highest mountain, just worrying does not move anything, but if you choose one area and move stone by stone, you pave a way to move the whole mountain.”

South Korea is even trying to turn a crisis into a business opportunity. The Aging-Friendly hall, financed by the Ministry of Knowledge Economy, encourages businesses to enter “silver industries,” producing items for feeble elderly people, from chopsticks that are easier to pick up to automated harnesses that hoist people from bed, sliding along a ceiling track, and deposit them onto toilets or living room couches.

College students visit the hall and don blue 3-D glasses for “Dementia Experience” video journeys following people disoriented on streets or seeking bathrooms.

Throughout South Korea, Mrs. Lee leads “dementia supporter” training, arguing against longtime practices of chastising or neglecting patients, and advocating for preserving their skills and self-esteem.

One tip: give demented relatives “a washing pan and washboard” and say, “ ‘The washing machine’s terrible — we need your help’ ” washing clothes, she told 200 senior citizens interested in nursing home jobs or family caregiving advice. If patients say, “ ‘I’m good at making soy soup,’ but forget ingredients,” guide them step by

step, she advised. Otherwise, “They may make it into salt soup, and everyone will say, ‘Oh, this is terrible, you stop doing it.’ ”

Even the youngest are enlisted. Mr. Kwak, the local government official, arranges for nursery school classes to play games with nursing home patients, saying that it destigmatizes dementia and that patients who “regress to earlier days” may “find it easier to relate to young children.”

And Dr. Yang Dong-won, who directs one of many government-run diagnostic centers in Seoul, has visited kindergartens, bringing tofu. “This is very soft, like the brain,” he said, letting it crash down. Now, “the brain is destroyed.”

“Dementia is very bad for you, so protect your brain,” he said, with exercise, “not drinking too much sugar,” and saying, “ ‘Daddy, don’t drink so much because it’s not good for dementia.’ ”

At a Dementia March outside the World Cup Soccer Stadium, children carried signs promoting Dr. Yang’s Mapo district center: “Make the Brain Smile!” and “How is Your Memory? Free diagnosis center in Mapo.”

The Mapo Center for Dementia perches at a busy crossroads of old and new, near a university and a shop selling naturopathic goat extracts. It has exercise machines out front and a van with pictures of smiling elderly people.

Even people without symptoms come, Dr. Yang said. They are “eased by hearing, ‘You do not have dementia and can visit two years later.’ ”

Cha Kyong-ho’s family was wary of getting him tested. “Dementia was a subject to hide,” said his daughter, Cha Jeong-eun. “I worried his pride would be hurt going through this kindergarten experience.”

But when “my mother asked him to get ingredients for curry rice, he came back with mayonnaise,” she said. And one day, Mr. Cha, 74, a retired subway official, could not find his way home. “I was like, ‘Where the hell am I?’ ” he said.

Ultimately, he visited Mapo’s center, finding the testing challenging.

“Sometimes I don’t remember what I read, or I can see it with my eyes and my brain is processing it, but I cannot say it out loud,” he said about the questions. “How can my brilliant brain remember everything? Jeez, it’s so headachy.”

Checking his ability to categorize items, Dr. Yang asked, “What do you call dog and tiger?”

“I call them dog and tiger.”

“Pencil and brush?”

“Oh, there’s a word for that.”

“Airplane and train?”

“I feel embarrassed I don’t know.”

“You have a lot of loss of memory,” Dr. Yang said. “This is the very beginning stages of Alzheimer’s disease.”

He suggested that Mr. Cha get a government-subsidized brain M.R.I. to confirm the diagnosis, and said drugs might delay symptoms slightly. He recommended Mapo’s free programs “to stimulate what brain cells he has.” These include rooftop garden “floral therapy,” art classes making realistic representations of everyday objects, music therapy with bongos sounding “like a heartbeat.”

Mr. Cha sighed.

“I think,” he said, gesturing toward his brain, “that something’s wrong with this, just a little bit.”

### **Students as Helpers**

Schools offer community service credit, encouraging work with dementia patients, whom students call grandmas and grandpas. Teenage girls do foot massage at the Cheongam nursing home, which is run by Mrs. Lee, the Alzheimer’s Association president, for women without sons to care for them. (In South Korea, sons’ families traditionally shoulder caregiving responsibilities.) During one massage session, 16-year-old Oh Yu-mi rubbed a patient’s toes, saying: “I’m doing the heart. The heel is the reproductive system. It will help them excrete better.”

Another girl doing foot massage, Park Min-jung, 17, was shaken to realize that dementia could explain why her grandfather recently grabbed a taxi and circled his old neighborhood seeking his no-longer-existent house. “He used to be very scary to me,” she said, but training made her feel that “I can do things for him.”

A patient wept as the girls left, upsetting 16-year-old Kim Min-joon, the massage group’s leader. She said social workers suggested being less effusive to patients, so the girls’ leaving would be less traumatic: “If there is love or affection of 100 grams, cut it up into 1 gram each” and distribute it over “100 visits, not all at once.” But “I’m not good at controlling that,” Min-joon said. Even at school, “The feeling of their touch remains with me.”



A boys' high school selects top students to help at Seobu Nursing Center, doing art therapy and attempting physical therapy with dances and "balloon badminton" (the racket is pantyhose stretched on a frame). The boys write observations to help Seobu adjust programs.

At school, they wrote questions on the blackboard: "Problems and solutions of communicating with the elderly. Ways to improve and execute exercise routine. How to make sure we're all on time."

"They don't comprehend my words," said Kim Su-hwan, 16.

"Maybe we should get closer to their ears," suggested Kim Jae-kyeum.

Maybe "some of us could massage them," said Su-hwan. "You do that, Su-hwan," snickered Jae-kyeum.

"Smile at them more," another student said. "Some of us look like we don't want to do this."

For Kim Han-bit, 16, the program is intensely personal. Han-bit was 13 when his grandmother, who practically raised him, got Alzheimer's, and "I would just feel it was annoying and walk out of the room," he said. "She would ask to do an activity, and I would say, 'What business do you have doing that?' It was my responsibility to feed her, give her drinks, wash her face. But I even resisted and fought back," he said. When she died, he added, "I couldn't let out tears."

The dementia caregiving program had made him "wonder why I wasn't able to do that with my own grandma, and I think I should do better in the future to compensate for all my wrongdoing," he said. "I could have taken care of my grandmother with a grateful feeling. If only I could have."

Recently, he worked to engage Lee Jeong-hee, a patient half his height with missing teeth who laughed, but spoke incoherently.

"When I come next time," he said tenderly, "please remember me."

Su-Hyun Lee contributed reporting from Seoul, South Korea.

*This article has been revised to reflect the following correction:*

*Correction: November 25, 2010*

*An earlier version of a photo caption with this article misidentified the location where a student was bowing in a hallway. The photo was at the Seobu Nursing Center, not the Mapo Center for Dementia in Seoul.*

[http://www.eurekalert.org/pub\\_releases/2010-11/rson-wsp112410.php](http://www.eurekalert.org/pub_releases/2010-11/rson-wsp112410.php)

### **Walking slows progression of Alzheimer's**

**CHICAGO – Walking may slow cognitive decline in adults with mild cognitive impairment (MCI) and Alzheimer's disease, as well as in healthy adults, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).**

"We found that walking five miles per week protects the brain structure over 10 years in people with Alzheimer's and MCI, especially in areas of the brain's key memory and learning centers," said Cyrus Raji, Ph.D., from the Department of Radiology at the University of Pittsburgh in Pennsylvania. "We also found that these people had a slower decline in memory loss over five years."

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and cognitive skills. According to the National Institute on Aging, between 2.4 million and 5.1 million Americans have Alzheimer's disease. Based on current population trends, that number is expected to increase significantly over the next decade.

In cases of MCI, a person has cognitive or memory problems exceeding typical age-related memory loss, but not yet as severe as those found in Alzheimer's disease. About half of the people with MCI progress to Alzheimer's disease.

"Because a cure for Alzheimer's is not yet a reality, we hope to find ways of alleviating disease progression or symptoms in people who are already cognitively impaired," Dr. Raji said.

For the ongoing 20-year study, Dr. Raji and colleagues analyzed the relationship between physical activity and brain structure in 426 people, including 299 healthy adults (mean age 78), and 127 cognitively impaired adults (mean age 81), including 83 adults with MCI and 44 adults with Alzheimer's dementia.

Patients were recruited from the Cardiovascular Health Study. The researchers monitored how far each of the patients walked in a week. After 10 years, all patients underwent 3-D MRI exams to identify changes in brain volume.

"Volume is a vital sign for the brain," Dr. Raji said. "When it decreases, that means brain cells are dying. But when it remains higher, brain health is being maintained."

In addition, patients were given the mini-mental state exam (MMSE) to track cognitive decline over five years. Physical activity levels were correlated with MRI and MMSE results. The analysis adjusted for age, gender, body fat composition, head size, education and other factors.

The findings showed across the board that greater amounts of physical activity were associated with greater brain volume. Cognitively impaired people needed to walk at least 58 city blocks, or approximately five miles,

per week to maintain brain volume and slow cognitive decline. The healthy adults needed to walk at least 72 city blocks, or six miles, per week to maintain brain volume and significantly reduce their risk for cognitive decline.

Over five years, MMSE scores decreased by an average of five points in cognitively impaired patients who did not engage in a sufficient level of physical activity, compared with a decrease of only one point in patients who met the physical activity requirement.

"Alzheimer's is a devastating illness, and unfortunately, walking is not a cure," Dr. Raji said. "But walking can improve your brain's resistance to the disease and reduce memory loss over time."

*Coauthors are Kirk Erickson, Ph.D., Oscar Lopez, M.D., James Becker, Ph.D., Caterina Rosano, M.D., Anne Newman, M.D., M.P.H., H. Michael Gach, Ph.D., Paul Thompson, Ph.D., April Ho, B.S., and Lewis Kuller, M.D.*

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### **Study suggests that being too clean can make people sick**

***ANN ARBOR, Mich.---Young people who are overexposed to antibacterial soaps containing triclosan may suffer more allergies, and exposure to higher levels of Bisphenol A among adults may negatively influence the immune system, a new University of Michigan School of Public Health study suggests.***

Triclosan is a chemical compound widely used in products such as antibacterial soaps, toothpaste, pens, diaper bags and medical devices. Bisphenol A (BPA) is found in many plastics and, for example, as a protective lining in food cans. Both of these chemicals are in a class of environmental toxicants called endocrine-disrupting compounds (EDCs), which are believed to negatively impact human health by mimicking or affecting hormones.

Using data from the 2003-2006 National Health and Nutrition Examination Survey, U-M researchers compared urinary BPA and triclosan with cytomegalovirus (CMV) antibody levels and diagnosis of allergies or hay fever in a sample of U.S. adults and children over age 6. Allergy and hay fever diagnosis and CMV antibodies were used as two separate markers of immune alterations.

"We found that people over age 18 with higher levels of BPA exposure had higher CMV antibody levels, which suggests their cell-mediated immune system may not be functioning properly," said Erin Rees Clayton, research investigator at the U-M School of Public Health and first author on the paper.

Researchers also found that people age 18 and under with higher levels of triclosan were more likely to report diagnosis of allergies and hay fever.

There is growing concern among the scientific community and consumer groups that these EDCs are dangerous to humans at lower levels than previously thought.

"The triclosan findings in the younger age groups may support the 'hygiene hypothesis,' which maintains living in very clean and hygienic environments may impact our exposure to micro-organisms that are beneficial for development of the immune system," said Allison Aiello, associate professor at the U-M School of Public Health and principal investigator on the study.

As an antimicrobial agent found in many household products, triclosan may play a role in changing the micro-organisms to which we are exposed in such a way that our immune system development in childhood is affected. "It is possible that a person can be too clean for their own good," said Aiello, who is also a visiting associate professor of epidemiology at Harvard.

Previous animal studies indicate that BPA and triclosan may affect the immune system, but this is the first known study to look at exposure to BPA and triclosan as it relates to human immune function, Aiello said.

One surprise finding is that with BPA exposure, age seems to matter, said Rees Clayton. In people 18 or older, higher amounts of BPA were associated with higher CMV levels, but in people younger than 18 the reverse was true.

"This suggests the timing of the exposure to BPA and perhaps the quantity and length of time we are exposed to BPA may be affecting the immune system response," Rees Clayton said.

This is just the first step, she said, but a very important one. Going forward, researchers would like to study the long-term effects of BPA and triclosan in people to see if they can establish a causal relationship.

One limitation of the study is that it measured disease and exposure simultaneously and thus shows only part of the picture, Aiello said.

"It is possible, for example, that individuals who have an allergy are more hygienic because of their condition, and that the relationship we observed is, therefore, not causal or is an example of reverse causation," Aiello said.

*The paper, "The Impact of Bisphenol A and Triclosan on Immune Parameters in the U.S. Population," appears online in Environmental Health Perspectives Nov. 30. See podcast explaining more about Bisphenol A and triclosan (live Nov. 29):*  
<http://ns.umich.edu/podcast/audio.php?id=1286>

## 'My unusual cancer'

By Jane Elliott Health reporter, BBC News

### ***Philippe Parker has a very rare cancer - so rare few have heard of it.***

He was diagnosed with neuroendocrine cancer - which starts in hormone-producing nerve cells. They usually occur in the digestive system but can occur in other parts of the body.

Philippe, who is from London, was lucky. He was diagnosed six months after his first symptoms, including abdominal pains and itching caused by jaundice appeared. But others with the cancer waited around five years to find out what is wrong.

An ultrasound scan revealed Philippe, 39, had a blockage in his pancreas - and most of it had to be removed.

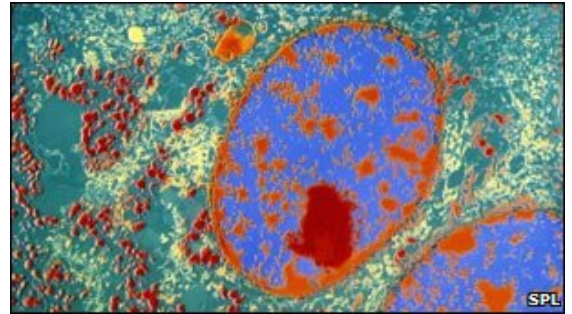
"At first they thought I had contracted something like hepatitis on holiday, or an inflammation," he said.

"But I had a blockage. A tumour.

"The tumour was unusual and difficult to determine. It took quite a while before I could get a biopsy."

When he did it confirmed that Philippe had cancer.

Janet French, of the Association for Multiple Endocrine Neoplasia Disorders (AMEND), agreed that getting an accurate diagnosis is difficult.



*Neuroendocrine tumour Neuroendocrine tumours can be hard to diagnose*

## NEUROENDOCRINE CANCER

\* *Neuroendocrine cancer is rare with up to 2,000 new cases a year in the UK*

\* *It is a cancer of the hormone-producing cells of the body's neuroendocrine system*

\* *Neuroendocrine cells are found throughout the body in organs such as the gastrointestinal tract, and lungs and there are many types of neuroendocrine tumours*

\* *The cancer mainly affects the small intestine, pancreas and lungs. It often spreads to the liver*

"From a recent survey we found that on average patients visited GPs 30 times before getting referral," she said.

"Patients had an average of 15 referrals; saw an average of 10 different consultants or doctors in hospital and required an average of 15 visits to get a diagnosis." She added: "There is a lack of knowledge in all sectors of the NHS, and a patient needs to be treated in a specialist centre where they actually stand a chance of the medical staff having heard of it and know the right things to do and when to do them."

Philippe is now being treated at the Royal Free Hospital in London with interferon therapy, a type of drug therapy which stimulates the body's immune system to fight the cancer.

And although it will not cure his condition, it keeps it at bay.

"It is not really curable and not one of those cancers you can be rid of," he said. "When it is in your endocrine system it is difficult to diagnose it is not like you go into remission you have the treatment and keep going. "It is very intensive treatment. You stop and then repeat."

### **Frustration**

Philippe said that the worst thing for him was not the cancer but its effects. "It is the fact that I have very little pancreas left and have had lots of my intestines cut out and have digestive problems and the interferon has lots of side-effects. "It is a bit like injecting yourself with flu. You get aches and weariness. It was tough the the first couple of years.

"I have been on interferon for four and a half years and almost certainly will be for the rest of my life."

And he said the rarity of the disease had proved to have a double edge: "There is is frustration because it is so rare. Everybody focuses on the effect on people, not the research.

"It does not get funding from the big organisations "But from a patient's perspective, the advantage is that because it is so rare there is not a blanket approach to treatment." And he said this meant a more tailored approach.

Professor Martyn Caplin, a consultant gastroenterologist who heads the Royal Free's neuroendocrine tumour unit, said raising the profile of the disease is important as more than 90% of all patients are incorrectly diagnosed and initially treated for the wrong disease

"By raising awareness, we hope these cancers will be diagnosed earlier. We have many exciting developments in terms of imaging tests and therapies, and it is important for patients with these rarer cancers to be seen in specialist centres so that the correct treatment and support can be given."