Little suckers: Putting leeches on a tight leash

* 04 January 2010 **by Holly Tucker and Jared Katz**

THE cardboard box marked "Emergency Medical Shipment" thumps down on Lillian Jackson's desk in the supplies department at Vanderbilt University Medical Center in Nashville, Tennessee. Inside she finds a sealed plastic bag of water in which dozens of small black creatures are happily swimming around. Leeches, again! Without hesitation, Jackson sends the creatures to the hospital's trauma unit, where nurse Rene Kopp takes charge. Over the next few days, Kopp will apply the leeches to chosen patients - to suck their blood. "We've been doing it for years," says Jackson.

Leeches have indeed been used in medicine for years - for millennia, in fact. They were once believed to remove illness-causing fluids, or "humours", from the blood. In reality they probably had little effect, and by the late 19th century such bloodletting had fallen out of favour. In the early 20th century, however, it occurred to surgeons that the slimy annelids might have a useful medical role after all. Leech bloodlust, they figured, was just the thing to help treat a dangerous complication after surgery to reattach torn or severed body parts such as fingers, ears or flaps of skin. Excess blood can collect in the reattached part, which, if left untreated, can cause tissue death and even be life-threatening.

Leeches are perfect for relieving "venous congestion", as this phenomenon is known. "The leech's primary role is to act as a vein," explains Richard Miller, medical director of the Vanderbilt trauma unit. In addition to the blood it consumes, the leech injects chemicals that stop blood clotting, which keeps blood flowing from the wound after the beast leaves.

The medical leech, Hirudo medicinalis, was approved by the US Food and Drug Administration (FDA) for post-surgical care in 2004 but it's fair to say doctors have not yet completely got to grips with these living medical devices. Leeches can be unpredictable. They may go on strike at the bedside, refusing to latch on where they are needed. Or in the middle of feeding, they may lose interest and creep away. "They do fall into the sheets," Miller admits.

Lending a hand in the hospital **(Image: Sipa Press/Rex Features)**

Sheep-gut condoms

Perhaps their erratic behaviour is understandable, as they travel an awfully long way to lend a hand - or rather a sucker. The leeches that Jackson rushes to the trauma unit start life in the French coastal village of Audenge, close to the city of Bordeaux. Ricarimpex, the company that breeds them, has been in the business since 1845, when leeches were still thought to work by removing bad humours. The firm sells over 250,000 leeches a year to hospitals around the world and is the only FDA-approved supplier.

At the Ricarimpex nurseries, leeches enjoy a pampered existence in artificial ponds designed to mimic the ideal natural habitat. The water is kept at neutral pH and is free of pollutants and predators.

From birth to adulthood, the growing leeches get the royal treatment. Twice a month, Ricarimpex's handlers don rubber waders and gently scoop up newborns from the basins. The leech babies are taken to laboratories where for the next 18 months they dine on chicken blood served in sheep-gut condoms. Once they reach adult size, at about 10 centimetres long, 5000 leeches will be loaded together in damp cotton bags, delivered to pressurised Air France cargo holds, and flown to destinations around the globe.

Leeches headed to the US may have a stopover on Long Island, New York, where they are held in aquariums at Leeches USA, one of the largest US distributors. Here, they pass into the care of Rudy Rosenberg, the company's vice-president. "The leeches are beautiful and graceful," he says, admitting that he sometimes gives them names.

When an order comes in, however, the time for such sentimentality is over, and the creatures are out of the door in moments to be flown to customers around the US. When a patient develops venous congestion, time is of the essence, so the company keeps a contingent of leeches on standby at New York's JFK airport for after-hours emergencies.

Back in Vanderbilt Medical Center, Kopp places her newly arrived charges in a container that looks something like a spaghetti strainer, which drains and collects leeches from their watery residence. The container, known as a leech mobile home, then goes in a fridge at the bedside of a patient with venous congestion.

"Attach one leech to area every 4 hours," might be a typical prescription, and it will usually be accompanied by one for a course of antibiotics. Even leeches raised in tightly controlled conditions harbour Aeromonas hydrophila bacteria in their saliva, which could cause sepsis, a serious blood infection.

Armed with gloves and tweezers, Kopp picks out a leech and places it on the site where blood is collecting. If all goes well, the leech will latch on. Its minuscule teeth puncture the skin, then its circular mouth holds on tight while sucking up its bloody meal.

Despite a popular belief that leeches inject a numbing agent, no such substance has yet been isolated from the creatures' saliva (Comparative Biochemistry and Physiology Part C, vol 88, p 95). Mark Siddall, head of the Leech Lab at the American Museum of Natural History in New York City, is not surprised. He has plenty of personal experience by which to judge the issue: "I've been fed on by these guys enough and, I'll tell you, it hurts."

Despite having been starved for the last three months, there are no guarantees that a leech will latch on, or drink its fill. Perhaps, speculates Siddall, they are disoriented or frightened by being handled. "I like to eat pizza," he muses, "but if a huge pizza several million times my size picked me up, I probably wouldn't turn around and take a bite."

The medical staff take care to account for each and every one of the creatures applied to their patients. In one recorded case, a leech crawled between the stitches of a breast reconstruction incision and lodged itself inside the patient's chest (British Journal of Plastic Surgery, vol 46, p 543). "You've got to know how many go on and how many go off," says Miller.

Surgeons and nurses have come up with several tricks to prevent leeches from straying. In a modern spin on medieval leech cups, some construct a makeshift "leech cage" by cutting a small hole in the bottom of a disposable plastic cup and covering the top with clear film wrap. More sophisticated strategies include trapping the leech in a syringe and focusing it on its fleshy target, using surgical glue, or even stitching the animal to the patient's skin (Plastic and Reconstructive Surgery, vol 122, p 168e). Siddall advocates the gentler approach of tying a lasso around the leech's hind anchor sucker after it latches on.

Fifteen to 20 minutes later, the leech will have gorged itself and swollen to six or seven times its original size. The creature tumbles off the wound. It cannot be reused because of the risk of passing on blood-borne infections, and a brutal fate awaits.

Kopp reaches for her tweezers and drops the leech into a tub of alcohol. Within minutes it is dead. Kopp tosses the shrivelled body into a red bag marked "Medical Waste" and removes her gloves. The leech's long journey is over.

Holly Tucker is a professor in the College of Arts & Science at Vanderbilt University, Nashville, Tennessee.
Jared Katz is a student and research assistant, also at Vanderbilt University

G-spot 'doesn't appear to exist'

The elusive erogenous zone said to exist in some women may be a myth, say researchers who have hunted for it.

Their study in the Journal of Sexual Medicine is the biggest yet, involving 1,800 women, and it found no proof. The King's College London team believe the G-spot may be a figment of women's imagination, encouraged by magazines and sex therapists.

But sexologist Beverley Whipple, who helped popularise the G-spot idea, said the work was "flawed".

She said the researchers had discounted the experiences of lesbian or bisexual women and failed to consider the effects of having different sexual partners with different love-making techniques.

The women in the study, who were all pairs of identical and non-identical twins, were asked whether they had a G-spot. If one did exist, it would be expected that both identical twins, who have the same genes, would report having one. But this pattern did not emerge and the identical twins were no more likely to share a G-spot than non-identical twins who share only half of their genes.

Mythical

Co-author of the study Professor Tim Spector said: "Women may argue that having a G-spot is due to diet or exercise, but in fact it is virtually impossible to find real traits. "This is by far the biggest study ever carried out and shows fairly conclusively that the idea of a G-spot is subjective."

Colleague Andrea Burri was concerned that women who feared they lacked a G-spot might feel inadequate, which she says is unnecessary. "It is rather irresponsible to claim the existence of an entity that has never been proven and pressurise women and men too."

Dr Petra Boynton, a sexual psychologist at University College London, said: "It's fine to go looking for the G-spot but do not worry if you don't find it. "It should not be the only focus. Everyone is different."

The Gräfenberg Spot, or G-Spot, was named in honour of the German gynaecologist Ernst Gräfenberg who described it over 50 years ago. It is said to sit in the front wall of the vagina some 2-5cm up.

Recently Italian scientists claimed they could locate the G-spot using ultrasound scans. They said they had found an area of thicker tissue among the women reporting orgasms.

But specialists warned there could be other reasons for this difference.

Gladstone scientists identify target that may inhibit HIV infectivity

Surfen impairs the action of a factor in semen that greatly enhances the viral infection

Scientists at the Gladstone Institute of Virology and Immunology (GIVI) have discovered a new agent that might inhibit the infectivity of HIV. The agent, surfen, impairs the action of a factor in semen that greatly enhances the viral infection. Surfen might be used to supplement current HIV microbicides to greatly reduce HIV transmission during sexual contact.

The discovery was made by Nadia Roan, PhD, a senior fellow in the laboratory of GIVI Director Warner Greene, MD, PhD. Surfen is a small molecule that inhibits the actions of certain polysaccharide molecules called heparan sulfate proteoglycans (HSPG) that are found on the surface of cells. Importantly for HIV infection, it also interferes with the action of semen-derived enhancer of viral infection (SEVI). The discovery was published in the current issue of the Journal of Biological Chemistry.

"Surprisingly, although HIV readily replicates once inside the body, the virus struggles to establish a beachhead of infection during sexual transmission," said Greene, who is senior author on the study. "We have been studying SEVI, a naturally occurring factor present in semen that can make HIV thousands of times more infectious. Knowing more about surfen, a SEVI inhibitor, might enable us to lower transmission rates of HIV."

SEVI is a breakdown product of prostatic acid phosphatase, a common protein in semen. Under certain conditions, SEVI can increase HIV infectivity 100,000 times by facilitating the attachment of viruses to target cells. Because the majority of all HIV infections are thought to result from sexual contact (during which semen is either the vehicle carrying HIV or is present during the infection process), SEVI might have a significant impact on HIV transmission rates. Surfen interferes with the binding of SEVI to both target cells and HIV-1 virions but does not cause the SEVI fibrils to break up.

"Because SEVI can so greatly enhance HIV infectivity, supplementing current HIV microbicide candidates with SEVI inhibitors, such as surfen, might increase their potency and overall effectiveness," Greene explained.

Previously, the researchers found that negatively charged polymers, such as heparin sulfate, interfere with the binding of SEVI to target cells. This led them to hypothesize that the SEVI fibrils bind target cells by interacting with cell-surface HSPG, naturally occurring anionic carbohydrate polymers with a structure that is closely related to heparin sulfate.

"SEVI has eight basic amino acids which makes this factor very positively charged," said Roan, lead author on the study. "In previous work, we showed that the ability of SEVI to enhance infection was dependent on these positive charges. We reasoned that these positive charges may be interacting with negatively charged groups on HSPG of target cells."

The scientists looked for antagonists of HSPG that might interfere with the binding of SEVI to the virus and target cells. They focused on surfen (bis-2-methyl- 4-amino-quinolyl-6-carbamide), which was first described in 1938 and reported to have anti-inflammatory and anti-bacterial activity. The team found that surfen inhibits enhancement of HIV-1 infection mediated by pure SEVI or semen. They further demonstrated that surfen interferes with the binding of SEVI to both target cells and HIV-1 virions.

"Because SEVI can markedly influence HIV infectivity, it forms a rather attractive target for future therapies" said Greene. "For example, we might be able to create combination microbicides that include agents targeting both the virus and host factors promoting infection. Such combinations might greatly diminish the spread of HIV; it is a target we are energetically pursuing."

Additional contributors to the research include Gladstone's Stefanie Sowinski, and Jan Münch and Frank Kirchhoff from the University Clinic of Ulm, Germany. The work was supported by the Giannini Foundation and the National Institutes of Health/NAIAD grant #P01AI083050.

Dr. Greene's primary affiliation is with the Gladstone Institute of Virology and Immunology where he is senior investigator and the Nick and Sue Hellmann Distinguished Professor of Translational Medicine and where his laboratories are located and his research is conducted. He is also professor of medicine, microbiology and immunology at UCSF and co-director UCSF-GIVI Center for AIDS Research

Exotic stars may mimic big bang

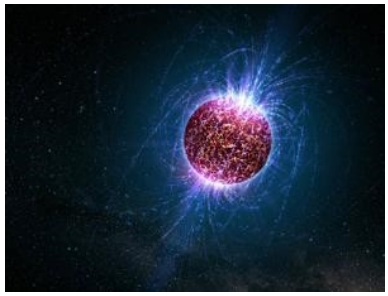
* 17:21 04 January 2010 **by David Shiga**

A new class of star may recreate the conditions of the big bang in its incredibly dense core.

Pack matter tightly enough and gravity will cause it to implode into a black hole. Neutron stars were once thought to be the densest form of matter that could resist such a collapse. More recently, physicists have argued that some supernovae may leave behind even denser quark stars, in which neutrons dissolve into their constituent quarks.

Now, a study led by De-Chang Dai of the State University of New York in Buffalo says the deaths of very massive stars may lead to "electroweak" stars that creep even closer to the black hole limit (arxiv.org/abs/0912.0520).

The cores of these stellar corpses can reach the same density as that of the universe 10-10 seconds after the big bang. At that point, the distinction between the electromagnetic and weak nuclear forces breaks down. This allows quarks to turn into ghostly particles called neutrinos, releasing energy that props up the star against further collapse. The reactions would take place in an apple-sized region in the core weighing about two Earths.



Above the limit

The stars might show up in astronomical data as neutron stars that are heavier than theoretically allowed, the team says. And unlike neutron stars, their internal energy source would prevent them from cooling over time.

'Electroweak' stars may recreate the conditions of the big bang in an apple-sized region in their cores **(Illustration: Casey Reed, courtesy of Penn State)**

The stars could survive for at least 10 million years, the researchers calculate. But Sanjay Reddy of Los Alamos National Laboratory in New Mexico says the stars might not be stable against collapse. "The idea is interesting, but to determine if this is plausible, more work is needed," he told New Scientist.

If the stars do exist, their cores are the only places in the modern universe where matter naturally returns to this primordial state, says team member Glenn Starkman of Case Western Reserve University in Cleveland, Ohio. "Of course, there could be some advanced alien civilisations out there that know how to make it," he says.

Smoking cessation may actually increase risk of developing type 2 diabetes

Johns Hopkins experts suspect weight gain by quitters raises risk in the short term

Cigarette smoking is a well-known risk factor for type 2 diabetes, but new research from Johns Hopkins suggests that quitting the habit may actually raise diabetes risk in the short term.

The researchers suspect the elevated diabetes risk is related to the extra pounds people typically put on after renouncing cigarettes and caution that no one should use the study's results as an excuse to keep smoking, which is also a risk factor for lung disease, heart disease, strokes and many types of cancer.

"The message is: Don't even start to smoke," says study leader Hsin-Chieh "Jessica" Yeh, Ph.D., an assistant professor of general internal medicine and epidemiology at the Johns Hopkins University School of Medicine.

"If you smoke, give it up. That's the right thing to do. But people have to also watch their weight," she adds.

In the study, published in the January 5 issue of Annals of Internal Medicine, researchers found that people who quit smoking have a 70 percent increased risk of developing type 2 diabetes in the first six years without cigarettes as compared to people who never smoked. The risks were highest in the first three years after quitting and returned to normal after 10 years. Among those who continued smoking over that period, the risk was lower, but the chance of developing diabetes was still 30 percent higher compared with those who never smoked.

The study enrolled 10,892 middle-aged adults who did not yet have diabetes from 1987 to 1989. The patients were followed for up to 17 years and data about diabetes status, glucose levels, weight and more were collected at regular intervals.

Type 2 diabetes is a common disease that interferes with the body's ability to properly use sugar, and to regulate and properly use insulin, a substance produced by the pancreas which normally lowers blood sugar during and after eating. In type 2 diabetes, also known as adult-onset diabetes, the pancreas makes plenty of insulin to help the body when food is eaten, but the body cannot use it normally. The result is excess levels of blood sugar, which over time, can lead to blindness, kidney failure, nerve damage and heart disease. Overweight people and those with a family history of the disease have an increased risk for developing it, as do smokers, though the causal relationship is unclear.

According to the study, those who smoked the most and those who gained the most weight had the highest likelihood for developing diabetes after they quit. On average, over the first three years of the study, quitters gained about 8.4 pounds and saw their waist circumferences grow by approximately 1.25 inches.

Yeh and her colleagues want physicians to keep these findings in mind when they are consulting with patients who are giving up cigarettes, especially the heaviest smokers. They recommend considering countermeasures such as lifestyle counseling, aggressive weight management and the use of nicotine-replacement therapy, which seems to blunt the weight gain related to quitting. Another key step is more frequent blood glucose screening to assure the earliest detection of diabetes.

In addition to Yeh, other Hopkins researchers involved in the study include Nae-Yuh Wang, Ph.D., and Frederick L. Brancati, M.D., M.H.S., professor and chief of the division of general internal medicine.

Funding for the study came from the National Heart, Lung and Blood Institute and the National Institute of Diabetes, Digestive and Kidney Disorders, both of the National Institutes of Health.

Autism 'Clusters' Linked To Parents' Education

by Jon Hamilton All Things Considered

** Download* ** Transcript*

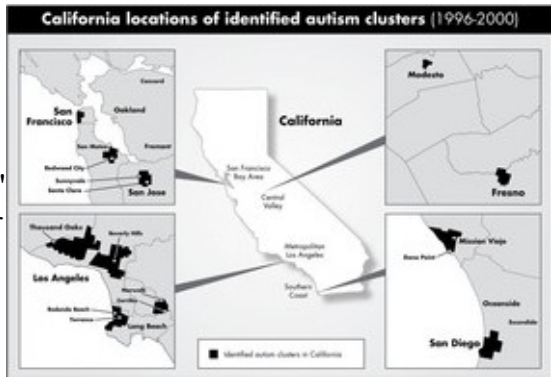
Clusters of children diagnosed with autism tend to occur in places where parents are older, more educated, and white, according to a study by researchers at the University of California, Davis.

The study found no link to local pollution or chemical exposures - which some consumer groups have cited as possible causes of autism clusters.

The results suggest that areas in California with apparently high rates of autism spectrum disorders are probably just places where parents are more likely to obtain a diagnosis for their child, the researchers say.

"It doesn't necessarily mean that higher education causes autism," says Irva Hertz-Picciotto, one of the study's authors and a researcher at the UC Davis MIND Institute. "It gets you the diagnosis more frequently."

Autism "cluster" found in North Los Angeles County. Autism rates here were roughly double that of surrounding areas.



Locations of "clusters" of autism identified in California by researchers at UC Davis. They are found in areas where parents have higher-than-average levels of education. 2010 UC Regents

The UC Davis study looked at the geographic distribution of about 10,000 children who were born in California from 1996 through 2000 and later diagnosed with an autism spectrum disorder.

A cluster was defined as a community in which the proportion of children diagnosed with autism was at least 70 percent higher than in surrounding areas.

The study found that differences in parents' age, education and ethnicity explained the cluster most of the time.

Higher Education, More Diagnosis

For example, it found that children of parents who finished college were at least four times more likely to be diagnosed than children of parents who didn't finish high school.

Children were also more likely to be diagnosed if they were born in a community near a regional service center for people with autism.

Hispanic parents were underrepresented in all 10 of the clusters, according to the study. That could be because some parents are reluctant to seek help from a state agency if they have a member of the family who is undocumented, Hertz-Picciotto says.

***Autism "cluster" found in North Los Angeles County. Autism rates here were roughly double that of surrounding areas.* 2010 UC Regents**

No Evidence Of Environmental Risk

The study may be most interesting because it did not find any environmental explanation for higher autism rates, says Steven Novella, a neurologist at Yale University.

"You can't prove a negative," Novella says. But the results of this and other studies suggest that "if there are environmental factors, they're small," he says.

The California results also show how widely autism diagnosis rates can vary from place to place, Novella says. In some areas of the state, children were four times as likely to be diagnosed as in other areas.

That suggests that in many areas there are still a huge number of children with autism spectrum disorders who are slipping through the cracks, Novella says.

Experimental drug shows promise against brain, prostate cancers

DALLAS – An experimental drug currently being tested against breast and lung cancer shows promise in fighting the brain cancer glioblastoma and prostate cancer, researchers at UT Southwestern Medical Center have found in two preclinical studies.

The drug's actions, observed in isolated human cells in one trial and in rodents in the other, are especially encouraging because they attacked not only the bulk of the tumor cells but also the rare cancer stem cells that are believed to be responsible for most of a cancer's growth, said Dr. Jerry Shay, professor of cell biology and a senior co-author of both papers. The glioblastoma study appears in the January issue of Clinical Cancer Research. The prostate cancer study is available online in the International Journal of Cancer.

In the glioblastoma study, performed in mice, the drug also crossed from the bloodstream into the brain, which is especially important because many drugs are not able to cross the blood-brain barrier.

"Because it attacks a mechanism that's active in most cancers, it might prove to be widely useful, especially when combined with other therapies," said Dr. Shay.

Dr. Shay and his colleagues study telomeres, bits of DNA that help control how many times a cell divides. Telomeres are protective "caps" of DNA on the ends of chromosomes, the structures that contain the body's genes. As long as telomeres are longer than a certain minimum length, a cell can keep dividing. But telomeres shorten with each cell division, so a cell stops dividing once the telomeres are whittled down to that minimum.

In cancer cells, however, an enzyme called telomerase keeps rebuilding the telomeres, so the cell never receives the cue to stop dividing. In essence, they become immortal, dividing endlessly.

The drug used in these studies (imetelstat or GRN163L) blocks telomerase. It is already in clinical trials as a potential treatment for breast and lung cancer, as well as for chronic lymphocytic leukemia.

Glioblastomas are the most common malignant brain tumors in adults, according to the American Cancer Society. They are difficult to treat with drugs because blood vessels in the brain have tightly constructed walls that allow only a few substances to pass through.

The researcher focused on cells called tumor-initiating cells. Some researchers believe that tumors contain a small subset of initiating cells – or cancer stem cells – that are able to initiate and drive tumors and that are often resistant to radiation therapy and chemotherapy.

In the glioblastoma study, Dr. Shay and his colleagues found that imetelstat blocked the action of telomerase in isolated tumor-initiating cells as well as the bulk of the tumor cells, eventually killing the cells. Combining imetelstat with radiation and a standard chemotherapy drug made imetelstat even more effective. When the researchers implanted human tumor-initiating cells into rodents, they found that imetelstat was able to enter brain tissue and inhibit telomerase activity.

In the prostate cancer study, the researchers isolated tumor-initiating cells from human prostate cancer cells. The cells showed significant telomerase activity. Imetelstat blocked the enzyme's activity, and telomeres shortened greatly.

Other UT Southwestern researchers involved in the glioblastoma study were lead author Dr. Calin Marian, postdoctoral researcher in cell biology; Dr. Steve Cho, postdoctoral researcher in neurology; graduate student Brian McEllin; Dr. Elizabeth Maher, associate professor of internal medicine; Dr. Kimmo Hatanpaa, assistant professor of pathology; Dr. Christopher Madden, associate professor of neurological surgery; Dr. Bruce Mickey, professor of neurological surgery; Dr. Woodring Wright, professor of cell biology; and co-senior author Dr. Robert Bachoo, assistant professor of neurology.

Other UT Southwestern researchers involved in the prostate cancer study were lead author Dr. Marian and Dr. Wright.

Geron Corporation, which manufactures GRN163L under the name imetelstat, provided the drug for both studies. The glioblastoma study was supported by the National Institutes of Health. The prostate cancer study was supported by a Department of Defense Prostate Cancer Training Award and the Southland Financial Corporation.

Spectacular Mars images reveal evidence of ancient lakes

Spectacular satellite images suggest that Mars was warm enough to sustain lakes 3 billion years ago

Spectacular satellite images suggest that Mars was warm enough to sustain lakes three billion years ago, a period that was previously thought to be too cold and arid to sustain water on the surface, according to research published today in the journal Geology.

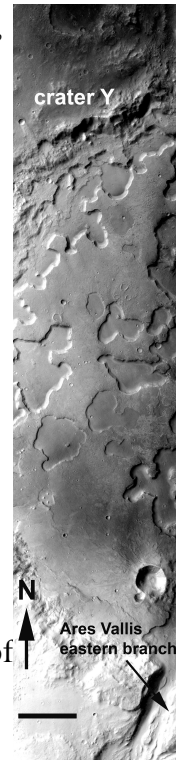
The research, by a team from Imperial College London and University College London (UCL), suggests that during the Hesperian Epoch, approximately 3 billion years ago, Mars had lakes made of melted ice, each around 20km wide, along parts of the equator.

Earlier research had suggested that Mars had a warm and wet early history but that between 4 billion and 3.8 billion years ago, before the Hesperian Epoch, the planet lost most of its atmosphere and became cold and dry. In the new study, the researchers analysed detailed images from NASA's Mars Reconnaissance Orbiter, which is currently circling the red planet, and concluded that there were later episodes where Mars experienced warm and wet periods.

The researchers say that there may have been increased volcanic activity, meteorite impacts or shifts in Mars' orbit during this period to warm Mars' atmosphere enough to melt the ice. This would have created gases that thickened the atmosphere for a temporary period, trapping more sunlight and making it warm enough for liquid water to be sustained.

Lead author of the study, Dr Nicholas Warner, from the Department of Earth Science and Engineering at Imperial College London, says: "Most of the research on Mars has focussed on its early history and the recent past. Scientists had largely overlooked the Hesperian Epoch as it was thought that Mars was then a frozen wasteland. Excitingly, our study now shows that this middle period in Mars' history was much more dynamic than we previously thought."

The researchers used the images from the Mars Reconnaissance Orbiter to analyse several flat-floored depressions located above Ares Vallis, which is a giant gorge that runs 2,000 km across the equator of Mars. Scientists have previously been unable to explain how these depressions formed, but believed that a process known as sublimation may have created the depressions, where ice changes directly from its solid state into a gas without becoming liquid water. The loss of ice would have created cavities between the soil particles, which would have caused the ground to collapse into a depression.



In the new study, the researchers analysed the depressions and discovered a series of small sinuous channels that connected them together. The researchers say these channels could only be formed by running water, and not by ice turning directly into gas.

The scientists were able to lend further weight to their conclusions by comparing the Mars images to images of thermokarst landscapes that are found on Earth today, in places such as Siberia and Alaska. Thermokarst landscapes are areas where permafrost is melting, creating lakes that are interconnected by the same type of drainage channels found on Mars.

The team believe the melting ice would have created lakes and that a rise in water levels may have caused some of the lakes to burst their banks, which enabled water to carve a pathway through the frozen ground from the higher lakes and drain into the lower lying lakes, creating permanent channels between them.

Professor Jan-Peter Muller, Mullard Space Science Laboratory, Department of Space Climate Physics at University College London, was responsible for mapping the 3D shape of the surface of Mars. He adds: "We can now model the 3D shape of Mars' surface down to sub-metre resolution, at least as good as any commercial satellite orbiting the Earth. This allows us to test our hypotheses in a much more rigorous manner than ever before."

Image 1 NASA Context Camera image of crater near Ares Vallis. The floor of the crater shows several irregular, flat-floored depressions that are interpreted as ancient lake basins. Scale bar is 10 km.
Download image: https://fileexchange.imperial.ac.uk/files/6e8a67a9d25/Fig.1_Lakes.jpg

The researchers determined the age of the lakes by counting crater impacts, a method originally developed by NASA scientists to determine the age of geological features on the moon. More craters around a geological feature indicate that an area is older than a region with fewer meteorite impacts. In the study, the scientists counted more than 35,000 crater impacts in the region around the lakes, and determined that the lakes formed approximately three billion years ago. The scientists are unsure how long the warm and wet periods lasted during the Hesperian epoch or how long the lakes sustained liquid water in them.

The researchers say their study may have implications for astrobiologists who are looking for evidence of life on Mars. The team say these lake beds indicate regions on the planet where it could have been warm and wet, potentially creating habitats that may have once been suitable for microbial life. The team say these areas may be good targets for future robotic missions.

The next step will see the team extend their survey to other areas along the equator of Mars so that they can ascertain how widespread these lakes were during the Hesperian Epoch. The team will focus their surveys on a region at the mouth of Ares Vallis called Chryse Planitia, where preliminary surveys of satellite images have suggested that this area may have also supported lakes.

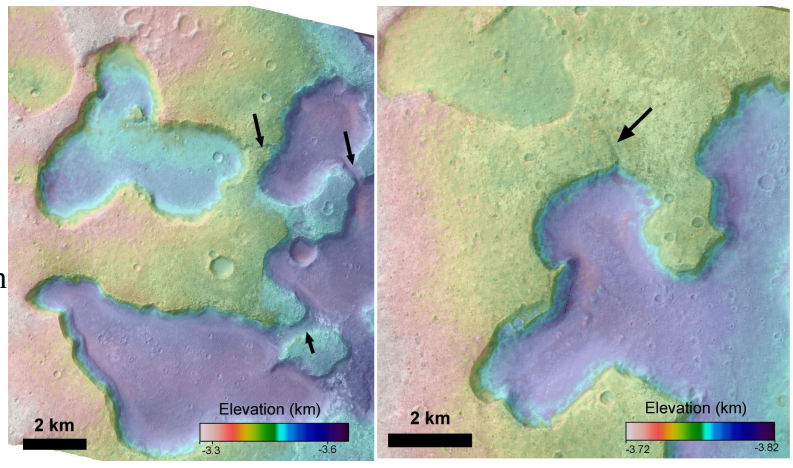


Image 6 PLEASE NOTE THAT COLOURS REPRESENT ELEVATION.
These images show topographic data for depressions interpreted as ancient lakes. Topography data illustrate that channels connect depressions of different depths suggesting lakes drained from shallower to deeper depressions. Main depression in right hand image is ~40 metres deep.
Main depression at top left in left image is ~100 metres deep.
Download image: https://fileexchange.imperial.ac.uk/files/b64830dde6d/Fig.6_Topographic_image.jpg

The study was a collaboration between the Department of Earth Science and Engineering at Imperial College London and Space Physics at UCL. The project was funded by the Science and Technology Facilities Council, the Royal Society and the Leverhulme Trust.

Images are from the Context Camera (CTX) onboard NASA's Mars Reconnaissance Orbiter (MRO).

A trip to the candy store might help ward off rare, but deadly infections

New research in the Journal of Leukocyte Biology shows that glycyrrhizin extracted from licorice root helps the body defend against Pseudomonas aeruginosa infection

As it turns out, children were not the only ones with visions of sugar plums dancing in their heads over this past holiday season. In a new research report published in the January 2010 issue of the Journal of Leukocyte Biology (http://www.jleukbio.org), a team of scientists from the University of Texas Medical Branch and Shriners Hospitals for Children show how a compound from licorice root (glycyrrhizin from Glycyrrhiza glabra) might be an effective tool in battling life-threatening, antibiotic-resistant infections resulting from severe burns. Specifically, they found that in burned mice, glycyrrhizin improved the ability of damaged skin to create small proteins that serve as the first line of defense against infection. These proteins, called antimicrobial peptides, work by puncturing the cell membranes of bacteria similar to how pins pop balloons.

"It is our hope that the medicinal uses of glycyrrhizin will lead to lower death rates associated with infection in burn patients," said Fujio Suzuki, Ph.D., one of the researchers involved in the work. Suzuki also said that more research is necessary to determine if this finding would have any implications for people with cystic fibrosis, who can develop Pseudomonas aeruginosa infections in their lungs.

To make this discovery, Suzuki and colleagues used three groups of mice. The first group was normal, the second group was burned and untreated, and the third group was burned and treated with glycyrrhizin. The skin of the untreated burned mice did not have any detectable antimicrobial peptides that prevent bacteria from growing and spreading, but the normal mice did. The skin of the untreated burned mice also had immature myeloid cells, which indicate an inability of the skin to produce antimicrobial peptides needed to prevent infection. The mice treated with glycyrrhizin, however, were more like the normal mice as they had the antimicrobial peptides and no immature myeloid cells.

"Burns are the most painful of all injuries," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "and the deadly Pseudomonas infections that can result from severe burns do more than add insult to those injuries. This research should serve as an important stepping stone toward helping develop new drugs that help prevent or treat Pseudomonas."

Details: *Tsuyoshi Yoshida, Shohei Yoshida, Makiko Kobayashi, David N. Herndon, and Fujio Suzuki. Glycyrrhizin restores the impaired production of β-defensins in tissues surrounding the burn area and improves the resistance of burn mice to Pseudomonas aeruginosa wound infection. J Leukoc Biol 2010 87: 35-41. http://www.jleukbio.org/cgi/content/abstract/87/1/35*

St. John's wort not helpful treatment for irritable bowel syndrome, Mayo Clinic researchers say

ROCHESTER, Minn. -- A Mayo Clinic research study published in the January issue of the American Journal of Gastroenterology finds that St. John's wort is not an effective treatment for irritable bowel syndrome (IBS). While antidepressants are frequently used to treat IBS, to date, no study has examined the success of using the herbal supplement St. John's wort in treating IBS.

"Our study investigated if herbal antidepressants such as St. John's wort could benefit irritable bowel disease patients," says Yuri Saito, M.D., M.P.H., gastroenterologist and lead physician scientist on the study. "Several of the chemical neurotransmitters that are in the brain are also in the colon. Therefore, it's been thought that antidepressants may affect sensation in the colon in a similar way to how they affect sensation in the brain. Our goal was to evaluate the usefulness of St John's wort in treating IBS."

In this placebo-controlled trial, 70 participants with IBS were randomized where half the patients received St. John's wort and the other half received a placebo for three months. In all, 86 percent of the participants were women, and the median age was 42 years. After three months of observing symptoms such as stomach pain, diarrhea, constipation and bloating, Mayo researchers found that the placebo group had a better response than the group taking the herbal supplement, St. John's wort.

"Because people tend to struggle with IBS for several years, patients are really looking for inexpensive, over-the-counter treatments such as St. John's wort," says Dr. Saito. "Unfortunately, our study showed that St. John's wort was not successful in helping IBS patients."

St. John's wort is an herbal supplement derived from the St. John's wort plant. It has been shown to be helpful in several medical conditions such as depression as well as other pain syndromes. Research has shown it to be as effective as conventional, prescription anti-depressants in treating mild to moderate depression.

"The challenge with IBS is that there is no cure, no one treatment tends to be wholly effective and some treatments come with significant side effects," explains Dr. Saito. "However, well-designed studies of herbal supplements are important so that physicians and patients can make informed decisions about which supplements to recommend or try. Studies of alternative treatments are generally lacking and patients are forced to use a "trial and error" approach to over-the-counter treatments for their IBS."

IBS is a common disorder that affects the colon and commonly causes cramping, abdominal pain, bloating, gas, diarrhea and constipation. Approximately 58 million people struggle with IBS, mostly women.

Running shoes may cause damage to knees, hips and ankles

Greater stresses on joints than running barefoot or walking in high-heeled shoes observed

New York, NY – Knee osteoarthritis (OA) accounts for more disability in the elderly than any other disease. Running, although it has proven cardiovascular and other health benefits, can increase stresses on the joints of the leg. In a study published in the December 2009 issue of PM&R: The journal of injury, function and rehabilitation, researchers compared the effects on knee, hip and ankle joint motions of running barefoot versus running in modern running shoes. They concluded that running shoes exerted more stress on these joints compared to running barefoot or walking in high-heeled shoes.

Sixty-eight healthy young adult runners (37 women), who run in typical, currently available running shoes, were selected from the general population. None had any history of musculoskeletal injury and each ran at least 15 miles per week. A running shoe, selected for its neutral classification and design characteristics typical of most running footwear, was provided to all runners. Using a treadmill and a motion analysis system, each subject was observed running barefoot and with shoes. Data were collected at each runner's comfortable running pace after a warm-up period.

The researchers observed increased joint torques at the hip, knee and ankle with running shoes compared with running barefoot. Disproportionately large increases were observed in the hip internal rotation torque and in the knee flexion and knee varus torques. An average 54% increase in the hip internal rotation torque, a 36% increase in knee flexion torque, and a 38% increase in knee varus torque were measured when running in running shoes compared with barefoot.

These findings confirm that while the typical construction of modern-day running shoes provides good support and protection of the foot itself, one negative effect is the increased stress on each of the 3 lower extremity joints. These increases are likely caused in large part by an elevated heel and increased material under the medial arch, both characteristic of today's running shoes.

Writing in the article, lead author D. Casey Kerrigan, MD, JKM Technologies LLC, Charlottesville, VA, and co-investigators state, "Remarkably, the effect of running shoes on knee joint torques during running (36%-38% increase) that the authors observed here is even greater than the effect that was reported earlier of high-heeled shoes during walking (20%-26% increase). Considering that lower extremity joint loading is of a significantly greater magnitude during running than is experienced during walking, the current findings indeed represent substantial biomechanical changes." Dr. Kerrigan concludes, "Reducing joint torques with footwear completely to that of barefoot running, while providing meaningful footwear functions, especially compliance, should be the goal of new footwear designs."

The article is "The Effect of Running Shoes on Lower Extremity Joint Torques" by D. Casey Kerrigan, MD, Jason R. Franz, MS, Geoffrey S. Keenan, MD, Jay Dicharry, MPT, Ugo Della Croce, PhD, and Robert P. Wilder, MD. It appears in PM&R: The journal of injury, function and rehabilitation, Volume 1, Issue 12 (December 2009), published by Elsevier. The article has been made freely available and may be accessed at: http://www.pmrjournal.org/article/S1934-1482(09)01367-7/fulltext

Before or after birth, gene linked to mental health has different effects

Mouse study links timing of expression to various abnormalities

Scientists have long eyed mutations in a gene known as DISC1 as a possible contributor to schizophrenia and mood disorders, including depression and bipolar disorder. Now, new research led by Johns Hopkins researchers suggests that perturbing this gene during prenatal periods, postnatal periods or both may have different effects in mice, leading to separate types of brain alterations and behaviors with resemblance to schizophrenia or mood disorders.

The findings, reported online Jan. 5 in Molecular Psychiatry, could eventually help researchers treat mental illness in people or even prevent it.

To manipulate DISC1 expression during different periods, the researchers, led by Associate Professor Mikhail Pletnikov, M.D., Ph.D., crafted a novel mouse model in which a mutant form of the gene could be turned off by feeding the animals small amounts of the antibiotic doxycycline in their chow. The animals could get the drug directly by eating it or through their mothers during gestation. Withdrawing doxycycline turned this gene on. (All the animals also carried the normal DISC1 gene, which wasn't affected by the drug.)

Using this model, Pletnikov's team generated four groups of mice: those that expressed mutant DISC1 prenatally (Pre), those that expressed mutant DISC1 postnatally (Post), those that expressed it during both periods (Pre+Post), and those that never expressed it (NO).

When the mice were about 2 months old, the researchers put the animals through a battery of behavioral tests designed to measure characteristics similar to schizophrenia and depression in humans, such as abnormal social

interactions and heightened aggression under stress, comparing these animals with "control" animals that didn't express the mutant gene.

Because previous studies have shown that male mice with mutant DISC1 have such altered traits, the researchers tested male mice in each of the groups by placing them in a cage with a normal male mouse and allowing them to mingle for 10 minutes. They counted various social behaviors, including sniffing, following and attacks. Pletnikov and his colleagues found that the Pre+Post and Post groups spent significantly less time in non-aggressive social interaction with their partners than the mice of the NO group. Those in the Pre+Post group also demonstrated significantly more aggressive attacks on their partners than control mice that did not express mutant DISC1.

To look for behaviors reflecting depression, the researchers gave animals of both sexes in all the groups a forced swim test and a tail suspension test. In both tests, the animals participated in unpleasant activities - being made to swim in a pool, or being lifted by their tails - and were timed for how long they struggled. Mice thought to exhibit depression-like behavior spend more time immobile than non-depressed mice.

Pletnikov's team found that only female mice of the Post group spent significantly more time immobile in the forced swim test than mice that did not express mutant DISC1. Female mice in the Pre+Post group spent significantly more time immobile in the tail suspension test than control mice . Male mice in each of the groups displayed similar behavior in these tests.

Finally, when the researchers examined the brains of the mice, they found significant differences between animals in different groups. Those in the Pre group had significantly smaller brain volume than the other mice. Mice in the Post and Pre+Post groups had significantly larger lateral ventricles and decreased content of dopamine, a pleasure-producing brain chemical, in the frontal cortex. Both female and male mice in the Pre, Post and Pre+Post groups had fewer neurons that produce GABA, a brain chemical that regulates nerve cell firing, than mice in the NO group.

The researchers say both the behavioral and physiological findings suggest that expressing mutant DISC1 at different time points during fetal or early childhood development can lead to different outcomes. While selective prenatal expression led to smaller brain volumes but mild behavioral effects, pre- and postnatal expression led to behaviors and brain alterations in male mice similar to schizophrenic humans, and postnatal expression produced abnormalities in female mice similar to depression.

The researchers aren't sure why the animals varied according to sex. However, Pletnikov notes, schizophrenia and depression also vary between the sexes in humans, with schizophrenia more prevalent in males and depression more prevalent in females. He and his team plan to study these sex-related differences in future studies.

The team also plans to try to narrow the time periods in which mutant DISC1 is turned on in their model to study particular stages, such as early postnatal development, sexual maturity, adulthood and aging, since triggers at each of these stages might bring on mental illness.

The goal, says Pletnikov, is to use these findings to develop new therapies to treat psychiatric disorders.

"Right now," he says, "we cannot treat or reverse all the abnormalities associated with schizophrenia or major mood disorders, but our research gives us hope that we can eventually target some of these abnormalities that are currently considered incurable. If we catch these problems early enough, we may someday be able to prevent schizophrenia or depression from developing."

This study was supported by grants from the National Institute of Mental Health, Autism Speaks, the National Alliance for Research on Schizophrenia and Depression, and the Mortimer W. Sackler Foundation.

Other Johns Hopkins researchers who participated in this study include Yavuz Ayhan, M.D.; Bagrat Abazyan, M.D.; Jun Nomura, Ph.D.; Roy Kim; Akira Sawa, M.D., Ph.D.; Russell L. Margolis, M.D; and Christopher A. Ross, M.D., Ph.D.

New virus is not linked to chronic fatigue syndrome, suggests UK research

New UK research, published today in PLoS ONE, has not reproduced previous findings that suggested Chronic Fatigue Syndrome may be linked to a recently discovered virus. The authors of the study, from Imperial College London and King's College London, say this means that anti-retroviral drugs may not be an effective treatment for people with the illness.

An estimated three in 1000 people have Chronic Fatigue Syndrome (CFS), or myalgic encephalomyelitis (ME), experiencing severe physical and mental fatigue that is not alleviated by rest, together with other symptoms such as muscle pain, headache, joint pain and depression. Diagnosing CFS is difficult, as symptoms vary and there is no standard test. The fundamental cause of CFS is unknown and it is usually treated using rehabilitation techniques such as cognitive behavioural therapy or graded exercise therapy.

In October 2009, a group of US scientists published research in the journal Science that suggested that a recently discovered virus called XMRV could be linked to CFS. In their study, 68 out of 101 patients with the illness and 8 out of 218 healthy controls appeared to be infected with the virus.

However, in today's study, researchers found no evidence that patients with CFS had the XMRV virus, after analysing tissue samples from 186 patients with CFS using sensitive molecular testing techniques.

This more recent analysis showed no molecular evidence for XMRV in any of the samples from CFS patients. The researchers say this means that anti-retrovirals should not be used to treat CFS, as they would be unlikely to have an effect on the symptoms. However, several labs in the US now offer CFS patients treatments based on the earlier findings that linked the condition with XMRV.

Professor Myra McClure, one of the authors of the study from the Division of Medicine at Imperial College London, said: "Our research was carried out under rigorous conditions - we looked at samples from well-studied patients, and we used very sensitive testing methods to look for the virus. If it had been there, we would have found it. The lab in which we carried out the analysis had never housed any of the murine leukaemia viruses related to XMRV, and we took great care to ensure there was no contamination.

"We are confident that our results show there is no link between XMRV and Chronic Fatigue Syndrome, at least in the UK. The US study had some dramatic results that implied people with the illness could be treated with anti-retrovirals. Our recommendation to people with Chronic Fatigue Syndrome would be not to change their treatment regime, because our results suggest that anti-retrovirals would not be an effective treatment for the condition," added Professor McClure.

After reading the US study, clinical researchers from King's College London sent blood samples from 186 CFS patients to the Imperial Retrovirology Laboratory team. King's has been running an NHS service for CFS patients for nearly twenty years, and the previously stored samples came from patients had been fully investigated and examined, meaning that CFS was the correct diagnosis.

The Imperial scientists extracted the DNA from the samples and analysed it using a sensitive technique, called Polymerase Chain Reaction (PCR), which can locate tiny fragments of virus DNA. The scientists analysed control samples of water at the same time to ensure there was no contamination. They also looked for a specific marker fragment of human DNA in the sample to make sure the technique was working.

The water controls contained no DNA, showing that the samples were not contaminated. All the test samples, from patients and healthy controls, contained the human DNA they looked for, suggesting the technique was working well.

Dr Anthony Cleare, Reader in Psychiatric Neuroendocrinology, one of the authors of the study from the Chronic Fatigue Syndrome Clinic at King's College London, said: "Chronic Fatigue Syndrome is a serious and debilitating condition. It can also be extremely frustrating for people with the illness, as we have yet to identify its fundamental cause, or come up with any definitive treatments. The recent US study generated real excitement among doctors and patients alike as it seemed to open up a new line of research. Unfortunately, we have not been able to replicate those findings."

"It is important to emphasise that today's findings do not invalidate all previous research, some of which has shown that CFS can be triggered by other infective agents, such as Epstein Barr Virus or Giardia parasites. As ever in science, no single study is conclusive and there are lots of other research groups working on this at the moment. We await their results with interest," added Professor Simon Wessely, another author of the study from the Chronic Fatigue Syndrome Clinic at King's College London.

Study Says Women With Mate Get Heavier

By NICHOLAS BAKALAR

It is widely known that women tend to gain weight after giving birth, but now a large study has found evidence that even among childless women, those who live with a mate put on more pounds than those who live without one.

The differences, the scientists found, were stark.

After adjusting for other variables, the 10-year weight gain for an average 140-pound woman was 20 pounds if she had a baby and a partner, 15 if she had a partner but no baby, and only 11 pounds if she was childless with no partner. The number of women with a baby but no partner was too small to draw statistically significant conclusions.

There is no reason to believe that having a partner causes metabolic changes, so the weight gain among childless women with partners was almost surely caused by altered behavior. Moreover, there was a steady weight gain among all women over the 10 years of the study.

This does not explain the still larger weight gain in women who became pregnant. The lead author, Annette J. Dobson, a professor of biostatistics at the University of Queensland in Australia, suggested that physiological changes might be at work.

"Women's bodies may adjust to the increased weight associated with having a baby," Dr. Dobson said. "There may be a metabolic adjustment that goes on when women are pregnant that is hard to reverse. This would be more consistent with our findings than any other explanation."

The study covered more than 6,000 Australian women over a 10-year period ending in 2006.

At the start, the women ranged in age from 18 to 23. Each woman periodically completed a survey with more than 300 questions about weight and height, age, level of education, physical activity, smoking status, alcohol consumption, medications used and a wide range of other health and health care issues.

By the end of the study, published in the January issue of The American Journal of Preventive Medicine, more than half the women had college degrees, about three-quarters had partners and half had had at least one baby. Almost all of the weight gain happened with the first baby; subsequent births had little effect.

Also by the end of the study period, there were fewer smokers and risky drinkers than at the beginning, more women who exercised less and a larger proportion without paid employment.

But even after adjusting for all of these factors and more, the differences in weight gain among women with and without babies, and among women with and without partners, remained.

Despite the study's limitations - weight was self-reported, for example, and the sample size diminished over time because people dropped out - other experts found the results valuable.

"It's interesting and brings out some important points," said Maureen A. Murtaugh, an associate professor of epidemiology at the University of Utah who has published widely on weight gain in women. Perhaps, she suggested, a more active social life may help explain why women with partners gain more weight.

"Think of going to a restaurant," Dr. Murtaugh said. "They serve a 6-foot man the same amount as they serve me, even though I'm 5 feet 5 inches and 60 pounds lighter."

The study included only women, but the researchers cited one earlier study that showed an increase in obesity among men who had children, adding further evidence that social and behavioral factors are part of the explanation.

Dr. Dobson said the finding of weight gain among all the women, with families or without, was troubling.

"This is a general health concern," she said. Getting married or moving in with a partner and having a baby are events that trigger even further weight gain. "From a prevention point of view, one can look at these as particular times when women need to be especially careful."

Report suggests similar effectiveness among options for managing low-risk prostate cancer

Institute for Clinical and Economic Review summary incorporates findings from 3 separate appraisals of 6 treatment options

A comprehensive appraisal of the management and treatment options for low-risk prostate cancer found that the rates of survival and tumor recurrence are similar among the most common treatment approaches, although costs can vary considerably. The report was prepared by the Institute for Clinical and Economic Review (ICER), a leader in comparative effectiveness research based at the Massachusetts General Hospital's Institute for Technology Assessment.

Bringing together the findings from three previous reviews completed by ICER, the final summary report, "Management Options for Low-Risk Prostate Cancer: A Report on Comparative Effectiveness and Value," compares multiple approaches to managing the most common non-skin cancer among U.S. men:

* Active surveillance, a "watch and wait" strategy with careful monitoring and referral for surgery or radiation if necessary;
* Radical prostatectomy, surgical removal of the prostate via traditional "open" or robot-assisted approaches;
* Brachytherapy, implantation of radioactive seeds in the prostate;
* Intensity-modulated radiation therapy (IMRT) and proton therapy, two forms of external radiation therapy.

The ICER review found that there are no definitive head-to-head studies comparing these options, but that accumulated evidence from multiple studies over the years suggests that overall survival and the rate of cancer recurrence are quite similar among all options, including active surveillance. There are different risks for certain side effects and complications, but no treatment option stands out as superior overall. Because low-risk prostate cancer is typically slow-growing and may not cause any symptoms, active surveillance is a reasonable option, particularly for men 65 and older, approximately half of whom will never have their cancer progress to the point of requiring treatment.

"ICER's review provides a welcome objective summary of what we know and what we don't know that can help men in conversations with their doctor," stated David Most, PhD, prostate cancer survivor and Founder and President of Health Information Research, Inc., who was a member of the Evidence Review Group that participated in the ICER appraisal process. "Given the numerous sources of information we have on the different management options, it really can be difficult to know what to do. Having a report like this from ICER will help patients make informed healthcare decisions that reflect their values about the risks and benefits among the different options."

The ICER report included a review of published literature on the treatment of low-risk prostate cancer as well as simulation modeling to project the long-term effects of each treatment approach. The evidence on radical prostatectomy, brachytherapy, and IMRT was judged to demonstrate comparable overall clinical effectiveness for most men, while there was not enough evidence to date to make a comparison on proton therapy. The evidence on active surveillance was stronger for older men, and therefore ICER rated its clinical effectiveness as comparable to immediate treatment for men 65 and over. Long-term outcomes with active surveillance are not yet available, but for younger men active surveillance may still be a reasonable option given that surgery or radiation can be done if regular blood tests and prostate biopsies suggest the cancer is growing. The ICER report also found that, based on Medicare payments, active surveillance costs approximately $300-$1,000 per year, while brachytherapy and radical prostatectomy procedures cost approximately $10,000. IMRT and proton therapy are more expensive, costing $20,000 and $35,000 per treatment course, respectively.

"ICER works hard to create unbiased, fully-informed appraisals of disease management and treatment options so that patients, clinicians, and payers can trust the information produced," stated Steven D. Pearson, MD, MSc, FRCP, President of ICER. "The results of the summary report on low-risk prostate cancer are an example of how scientifically-sound comparative effectiveness research can be presented in an actionable way for multiple audiences. Ultimately, this type of research can help improve patient outcomes and overall value in the healthcare system. "

Atul Gawande's 'Checklist' For Surgery Success

Morning Edition

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Atul Gawande is a staff member of Brigham and Women's Hospital and the Dana Farber Cancer Institute. His other books include Better and Complications **Fred Field**

Speaking about dealing with unexpected challenges in medicine, Atul Gawande - a surgeon who writes for The New Yorker when he's not at his day job at Harvard Medical School - relates a story about a man who came into an emergency room with a stab wound.

"It was a single wound, about an inch in size, in his belly," Gawande tells Morning Edition host Steve Inskeep.

The man's injuries didn't appear life-threatening, but his condition quickly turned.

"About 10 minutes later, he crashed," Gawande says. "When they got him open they found that the wound had gone - this is a pretty big guy - straight through more than a foot into him, all the way into his back and sliced open his aorta. And so afterwards they asked a few more questions of the family. 'How did this happen?' 'Well, it was a Halloween party.' 'What exactly went on?' And then they learned that the guy who had stabbed him was dressed as a soldier carrying a bayonet. And if they had understood it was a bayonet, they would have thought about it quite differently."

Gawande uses this anecdote, a simple miscommunication with the potential to cause so much tragedy, to illustrate an argument he makes in a new book called The Checklist Manifesto: How to Get Things Right.

"Our great struggle in medicine these days is not just with ignorance and uncertainty," Gawande says. "It's also with complexity: how much you have to make sure you have in your head and think about. There are a thousand ways things can go wrong."

At the heart of Gawande's idea is the notion that doctors are human, and that their profession is like any other.

"We miss stuff. We are inconsistent and unreliable because of the complexity of care," he says. So Gawande imported his basic idea from other fields that deal in complex systems.

"I got a chance to visit Boeing and see how they make things work, and over and over again they fall back on checklists," Gawande says. "The pilot's checklist is a crucial component, not just for how you handle takeoff and landing in normal circumstances, but even how you handle a crisis emergency when you only have a couple of minutes to make a critical decision."

This isn't the route medicine has traveled when dealing with complex, demanding situations.

"In surgery the way we handle this is we say, 'You need eight, nine, 10 years of training, you get experience under your belt, and then you go with the instinct and expertise that you've developed over time. You go with your knowledge.' "

To see if surgeons might perform better if the intricate steps necessary to avoid catastrophe were made explicit, Gawande and a team of researchers studied what happened when doctors used a reminder - what Gawande calls "a bedside aide" - to navigate complex procedures. (Click to see a sample "Surgical Safety Checklist".)

"We brought a two-minute checklist into operating rooms in eight hospitals," Gawande says. "I worked with a team of folks that included Boeing to show us how they do it, and we just made sure that the checklist had some basic things: Make sure that blood is available, antibiotics are there." How did it work?

"We get better results," he says. "Massively better results.

"We caught basic mistakes and some of that stupid stuff," Gawande reports. But the study returned some surprising results: "We also found that good teamwork required certain things that we missed very frequently."

Like making sure everyone in the operating room knows each other by name. When introductions were made before a surgery, Gawande says, the average number of complications and deaths dipped by 35 percent.

"Making sure everybody knew each other's name produced what they called an activation phenomenon," Gawande explains. "The person, having gotten a chance to voice their name, let speak in the room - were much more likely to speak up later if they saw a problem."

How did surgeons respond to the suggestion that they should change the way they operate? Says Gawande, many were resistant at first.

"You can imagine the response" to the idea of running through a checklist before surgery, Gawande says. But when his team surveyed the doctors who used the checklist, "There was about 80 percent who thought that this was something they wanted to continue to use. But 20 percent remained strongly against it. They said, 'This is a waste of my time, I don't think it makes any difference.' And then we asked them, 'If you were to have an operation, would you want the checklist?' Ninety-four percent wanted the checklist."

(Click to see a sample "Surgical Safety Checklist".)

So why does Gawande think professionals have such a hard time admitting that having a reminder might be a good idea?

"Partly I think we have a hard time admitting weakness," he says. "And one of the things we have to grapple with is that we have to assume we are fallible, even as experts."

That's a tough pill to swallow, and one made even harder given the way in which the media and entertainment industry present profiles of people who succeed in demanding situations.

"One of the things that struck me about the 'Miracle on the Hudson,' when 'Sully' Sullenberger brought the plane down that saved 155 people after it was hit by geese over Manhattan and landed it in the river," Gawande says, was that "over and over again we wanted to say, 'Look at this hero who piloted this plane down,' and the striking thing was how much over and over again he said, 'There was nothing that hard about the physical navigation of this plane.' Instead he kept saying 'it was teamwork and adherence to protocol.' "

Gawande says he experiences a similar displacement of credit when he performs a surgery.

"I come out of my operations and then I go out and talk to the family and they say 'Doctor, thank you for saving my husband!' " Gawande says. "You feel a little bit like a fraud because you know how much you were dependent on everybody getting this right. And when we acknowledge it, that's when we come back to ideas like checklists."

Despite all the evidence, Gawande admits that even he was skeptical that using a checklist in everyday practice would help to save the lives of his patients.

"I didn't expect it," Gawande says with a chuckle. "It's massively improved the kind of results that I'm getting. When we implemented this checklist in eight other hospitals, I started using it because I didn't want to be a hypocrite. But hey, I'm at Harvard, did I need a checklist? No." Or so he thought.

"I was in that 20 percent. I have not gotten through a week of surgery where the checklist has not caught a problem."

Read the entire article

New Health Rule: Quit Worrying About Your Health

By TARA PARKER-POPE

Have you had your five to nine servings of vegetables today? Exercised for an hour? Cut back on saturated fat and gotten eight hours of sleep?

Dictating the rules for healthful living has become a cottage industry, with Web sites, talk shows and books (and health columns like this one) devoted to the dos and don’ts of staying healthy.

But when it comes to achieving these goals, many of us feel we are falling far short. Whether you're a busy parent who can't find time for exercise, a chronic dieter struggling to lose 20 pounds or a multitasker who gets by on six hours of sleep, it is virtually impossible to follow the rules.

Now Dr. Susan M. Love, one of the country's most respected women's health specialists, offers a new rule: stop worrying about your health.

In the new book, "Live a Little! Breaking the Rules Won't Break Your Health" (Crown), Dr. Love makes the case that perfect health is a myth and that most of us are living far more healthful lives than we realize.

Dr. Love, a clinical professor of surgery at the David Geffen School of Medicine at the University of California, Los Angeles, says that failing to live by the various health rules is a major source of stress and guilt, particularly for women. For most of us, "pretty healthy" is healthy enough.

"Is the goal to live forever?" she said in a recent interview. "I would contend it's not. It's really to live as long as you can with the best quality of life you can. The problem was all of these women I kept meeting who were scared to death if they didn't eat a cup of blueberries a day they would drop dead."

The book, written with Alice D. Domar, a Harvard professor and senior staff psychologist at Beth Israel Deaconess Medical Center, explores the research and advice in six areas of health - sleep, stress, prevention, nutrition, exercise and relationships. In all six, they write, the biggest risks are on the extremes, and the middle ground is bigger than we think.

"Everything is a U-shaped curve," Dr. Love said. "There may be times in your life when you've gotten too much of this or too little of that, but being in the middle is better, and most of us are probably there already."

Take the issue of sleep. Most people believe that it's best to get at least eight hours a day. But the studies on which this belief is based look at how much men and women sleep under ideal conditions - silence, darkness and no responsibilities other than taking part in a sleep study. These studies tell us how much people will sleep when they have nothing else to do, but they don't tell us anything about how much sleep we really need on a daily basis or what will happen if we get less.

A 2002 report in Archives of General Psychiatry tried to address those issues by comparing sleep habits and mortality risk. The study found that people who slept seven hours a night were the least likely to die during the six-year study period. Sleeping more than seven hours or less than five increased mortality risk. It wasn't clear from the study whether more or less sleep increased risk or whether an underlying health problem was affecting sleep habits, but the findings did call the old "eight hours" rule into question.

The reality is that individual sleep needs can vary. Some people need very little while others need more than the average. "The issue of sleep causes a lot of guilt by women," Dr. Love said. "We need to be more realistic. If you're sleepy all the time, you're not getting enough sleep for you. If you're fine on six hours, don't worry about it."

Likewise, while exercise is important, many people don't place enough value on the fitness that comes from everyday tasks like lifting and chasing children, lugging groceries and cleaning house.

And there is nothing magic about losing weight. People who are obese or underweight have higher mortality rates, but people who are overweight are just as healthy as those of normal weight - and sometimes healthier. "The goal is to be as healthy and have as good of a quality of life as you can have," Dr. Love said. "It's not to be thin."

Health experts agree that moderation is important and that people should not panic about their health habits. But Dr. Elizabeth Barrett-Connor, professor of family medicine at the University of California, San Diego, cautions against interpreting a relaxed health message as an excuse to overeat or stay sedentary. "I think the problem is the slippery slope," Dr. Barrett-Connor said. "In the process of translating this message simply to the masses, they may feel they've been forgiven. They shouldn't feel like they're sinning, but they shouldn't feel like this is a license not to try to do better."

Miriam E. Nelson, director of the John Hancock Research Center on Physical Activity, Nutrition and Obesity Prevention at Tufts University, who has read the book, says it may help people realize that it is easier to be healthy than they thought. "There is a large part of the population that doesn't do anything because they've been overwhelmed," Dr. Nelson said. "This book could get them interested because it's not so complicated anymore."

Dr. Love said she and Dr. Domar decided to write the book because many people seemed to have lost sight of what it meant to be healthy. "The point of this is to use your common sense, and if you feel good, then you're fine," she said. "The goal is not to get to heaven and say, 'I'm perfect.' It's to use your body, have some fun and to live a little."

Using a Virus's Knack for Mutating to Wipe It Out

By CARL ZIMMER

Evolution is a virus's secret weapon. The virus can rapidly slip on new disguises to evade our immune systems, and it can become resistant to antiviral drugs.

But some scientists are turning the virus's secret weapon against it. They hope to cure infections by forcing viruses to evolve their way to extinction.

Viruses can evolve because of the mistakes they make when they replicate. All living things can mutate, but viruses are especially prone to these genetic errors. In fact, some species of viruses mutate hundreds of thousands of times faster than we do.

Many of the mutations that strike new viruses are fatal. Others only slow down their growth, and still others have no effect at all. A few mutations are beneficial, and the viruses that inherit those good mutations can swiftly dominate a viral population.

Viruses depend on this rapid evolution to infect a host successfully. Poliovirus, for example, enters the body in the gut and then moves into the bloodstream, muscles and, in a small fraction of cases, the nervous system.

Each time the virus moves into a new kind of tissue, natural selection favors those best suited to growing there. "The virus needs to have this genetic flexibility to adapt to its environments," said Raul Andino, a virologist at the University of California, San Francisco.

But if a virus's rate of mutation gets too high, mathematical studies suggest, it will suffer. "Most mutations are bad," said Claus O. Wilke, an evolutionary biologist at the University of Texas. "And so by increasing the amount of mutations, you can decrease the number of good offspring."

The defective offspring reproduce slower than their ancestors. After enough mutations pile up, the viruses can no longer replace their numbers. The entire population vanishes.

If increasing mutation rates can wipe out viruses, does that mean a mutation-increasing drug could cure a case of the flu? "People have thought about this idea for many years," said Louis M. Mansky, a virologist at the University of Minnesota.

A decade ago, scientists began running experiments that suggested the idea just might work. In one study, Dr. Lawrence A. Loeb, a University of Washington geneticist, and his colleagues eradicated H.I.V. in vitro by applying a mutation-increasing drug to infected cells. Reporting their results, Dr. Loeb's group dubbed this kind of attack "lethal mutagenesis."

Lethal mutagenesis appealed to many scientists at first, because it seemed to be a radically new way to fight viruses. But 10 years after its initial successes, lethal mutagenesis has not made its way to the drug store. Scientists have had to grapple with difficult questions about whether lethal mutagenesis can be safe and effective.

"That's a common thing in biomedical research," Dr. Mansky said. "People get ideas, but then there are roadblocks and the excitement dies down."

One roadblock was the fact that many of the drugs scientists used to cause lethal mutagenesis were too toxic to give to patients. And there was also something inherently risky about the very idea of lethal mutagenesis. After all, a drug that speeds up mutations in a virus might also speed up the mutations in its host cell. As a result, lethal mutagenesis could conceivably raise the risk of cancer.

Another problem with lethal mutagenesis is that viruses may be able to evolve resistance to it. Some studies suggest that viruses can evolve so that mutation-increasing drugs cannot interfere with them.

Dr. Andino and his colleagues have discovered another kind of resistance in polioviruses: they become more careful. These resistant strains have a lower mutation rate because their enzymes make fewer mistakes as they build new genes. "The enzymes take more time at each step," he said.

A new paper to be published in the journal Genetics shows just how mysterious lethal mutagenesis remains. Researchers at the University of Texas tried to use lethal mutagenesis to kill off a virus called T7, which infects only E. coli. The scientists understand T7 very well thanks to two decades of careful research on the virus. They were able to make precise predictions about the effects of a mutation-increasing drug.

But T7 did not wither away as they had predicted. After evolving for 200 generations in the presence of the drug, the viruses ended up replicating 90 percent faster than their ancestors.

James Bull, a co-author of the new study, thinks it shows how unexpected virus evolution can be under lethal mutagenesis. Whether that evolution could pose a risk to patients is an open question. "I'm on the fence on whether that really is a problem," Dr. Bull said. "But I think it's worth looking at."

Despite these challenges, a number of researchers see reason for optimism about lethal mutagenesis. Dr. Mansky, for example, has been inspired by studies in the last few years that revealed how our own bodies use a

natural kind of lethal mutagenesis. People produce proteins, known by the acronym Apobec, that fight off H.I.V. infections. They do so by adding mutations to the viruses as they replicate.

"To me that was important," Dr. Mansky said. "It said that cells have evolved a mechanism for fending off viruses with lethal mutagenesis."

In recent years Dr. Mansky has been seeking to overcome one of the big hurdles with lethal mutagenesis: toxic side effects. In November, he and his colleagues reported wiping out H.I.V. in infected cells with a drug called 5-AZC. He chose the drug to test because doctors regularly prescribe it for precancerous blood disorders. Now that Dr. Mansky has demonstrated that an approved drug can cause lethal mutagenesis in H.I.V., he is moving forward with preclinical trials on people.

Other scientists are confident they will be able to find solutions to the other problems with lethal mutagenesis. One way to avoid the risk of cancer, for example, would be to design drugs that interfere only with replicating viruses but not host cells.

To eliminate the threat from evolving viruses, Dr. Wilke, of the University of Texas, advises a swift and brutal attack. "If you hit the virus hard and everything dies out in a couple generations, then everything is fine," he said.

Lethal mutagenesis would be able to hit viruses even harder, Dr. Wilke argues, if it is part of a one-two punch. He points to studies like one published in November by Estaban Domingo of Autonomous University in Madrid and his colleagues.

Dr. Domingo first treated foot-and-mouth viruses with a drug that slowed their growth. Once the population had shrunk, he and his colleagues then gave the viruses a second drug to set off lethal mutagenesis. The viruses vanished much faster than they did when the scientists used lethal mutagenesis alone.

For Dr. Domingo, who has been studying mutation rates in viruses for more than three decades, the latest results suggest lethal mutagenesis will become a medical reality - at least someday.

"We're still really just halfway in the development of all these strategies," he said. "But I'm hopeful that it can be done."

Circumcision associated with significant changes in bacteria

Changes in bacteria within the penis microbiome documented for the first time

PHOENIX, Ariz. - Circumcision, which substantially lowers HIV risk in men, also dramatically changes the bacterial communities of the penis, according to a study led by scientists at the Translational Genomics Research Institute (TGen) and Johns Hopkins University and published Jan. 6 in the scientific journal PLoS ONE.

And these bacterial changes may also be associated with earlier observations that women whose male partners are circumcised are less likely to develop bacterial vaginosis, an imbalance between good and harmful bacteria.

The study - The Effects of Circumcision on the Penis Microbiome - could lead to new non-surgical HIV preventative strategies for the estimated 70 percent of men worldwide (more than 2 billion) who, because of religious or cultural beliefs, or logistic or financial barriers, are not likely to become circumcised.

"It has important public-health ramifications," said Dr. Lance B. Price, Director of TGen's Center for Metagenomics and Human Health and co-lead author of the scientific paper, which describes the world's first molecular assessment of the bacterial diversity of the male reproductive organ.

This new study is part of a larger effort by the U.S. National Institutes of Health to study and describe the "human microbiome" - the microbes that exist collectively on and in the human body. Other projects are focused on microbiomes involving the skin, nose, mouth, digestive and female genitourinary tract. Jointly, the goal of these projects is to define the various roles of microbes in human health and disease.

In investigating the impact of male circumcision on the penis microbiome, a collaborative team from TGen and the Johns Hopkins Bloomberg School of Public Health found for the first time that circumcision significantly changes the bacterial community of the penis.

Other epidemiological studies have shown that male circumcision is associated with significant reductions in HIV acquisition in men.

The strongest evidence for a cause-and-effect relationship between circumcision and HIV risk reduction came from three randomized-control trials in sub-Saharan Africa, where the circumcision rate is relatively low and the HIV infection rate is relatively high. All three demonstrated a more than 40 percent reduction in HIV acquisition among circumcised men.

The largest of these three studies - in Rakai, Uganda - was led by Dr. Ronald H. Gray, a renowned epidemiologist at Johns Hopkins and the scientific paper's senior author. Dr. Gray's group collected penile swabs from all of the circumcision trial study participants, which provided the data for the new TGen-Johns Hopkins study.

The new study found that circumcision - the removal of the foreskin, or prepuce, from the penis - eliminates an area of mucous membrane and dramatically changes the penile bacterial ecosystem. Significantly, TGen's analysis of more than 40 types of bacteria, using a 16S rRNA gene-based pyrosequencing approach, suggests that the introduction of more oxygen following circumcision decreases the presence of anaerobic (non-oxygen) bacteria and increases the amount of aerobic (oxygen-required) bacteria.

"This study clearly shows that male circumcision markedly reduces genital colonization with anaerobic bacteria in men," said Dr. Gray, the William G. Robertson Jr. Professor in Population and Family Planning at the Johns Hopkins Bloomberg School of Public Health.

"These bacteria, which cannot grow in the presence of oxygen, have been implicated in inflammation and a number of infections affecting both men and women. Our randomized trials have shown that male circumcision prevents HIV infection in men and protects their female partners from vaginal infections, especially bacterial vaginosis. It is possible that the virtual elimination of anaerobic bacteria by circumcision contributes to these benefits of the procedure," Dr. Gray said.

Several mechanisms have been proposed for how circumcision reduces HIV acquisition in men:

* Circumcision reduces the amount of mucosal tissue exposed to vaginal secretions during heterosexual intercourse and thus may reduce the potential interactions between the virus and its target immune cells.

* Circumcision results in a process called keratinization, whereby the top layer of the inner foreskin becomes thicker, which may provide additional protection for the underlying target immune cells.

* Circumcision-associated physiological changes of the penis - including lower moisture and oxygen availability around the head of the penis - may reduce the number of pro-inflammatory anaerobic bacteria that could make the target immune cells more vulnerable to HIV infection.

"These potential explanations are not mutually exclusive and may work in concert to reduce HIV risk," said Dr. Price, an Associate Investigator in TGen's Pathogen Genomics Division.

The new study found that specific bacteria taxonomically defined as anaerobic dominated the microbiota of the penile coronal sulcus before circumcision. However, after circumcision, these bacteria decreased dramatically.

"Thus, the reduction in the putative anaerobic bacteria after circumcision may play a role in protection from HIV and other sexually transmitted diseases," the study concluded.

Bacteria that form in the absence of, or lower levels of, oxygen may be associated with inflammation and the activation of Langerhans cells. These cells, which are part of the body's normal immune system, work to capture and degrade the virus when they are in an inactivated state. But once activated, the Langerhans cells become re-directed to assisting HIV infection by presenting the virus to CD4+ cells.

Circumcision remains a controversial procedure that has ardent proponents and opponents. Those who favor circumcision point to many studies demonstrating lower risk for sexually transmitted diseases associated with circumcision. Those who oppose circumcision point to the potential dangers of the procedure itself as well as cultural concerns.

This new study shows that circumcision significantly changed the penile bacterial ecology.

"The concept that there are good and harmful bacteria is essential to studying the human microbiome. Our work showed that the profile of the penile bacterial communities changed significantly after circumcision," said Dr. Cindy M. Liu, a medical doctor and researcher at both TGen and Northern Arizona University. She is the paper's other co-lead author.

"With the decrease in putative anaerobic bacteria, we saw a correlated increase in the proportion of other specific facultative anaerobic and aerobic bacteria. This suggests that eliminating harmful bacteria may be only half of the needed action. Ensuring that the niche left by pre-circumcision anaerobic bacteria are filled with "good" bacteria will also be critical," Dr. Liu said.

TGen and Johns Hopkins researchers plan to conduct more studies to determine whether specific bacteria are associated with increased HIV risk and if such bacteria can be eliminated using non-surgical strategies.

Also involved in the study published today were: the University of Maryland School of Medicine; and Makerere University's School of Public Health, Kampala, Uganda.

Planet-hunter spots five worlds

By Jonathan Amos Science correspondent, BBC News

Nasa's Kepler Space Telescope has detected its first five exoplanets, or planets beyond our Solar System.

The observatory, which was launched last year to find other Earths, made the discoveries in its first few weeks of science operations.

Although the new worlds are all bigger than our Neptune, the US space agency says the haul shows the telescope is working well and is very sensitive.

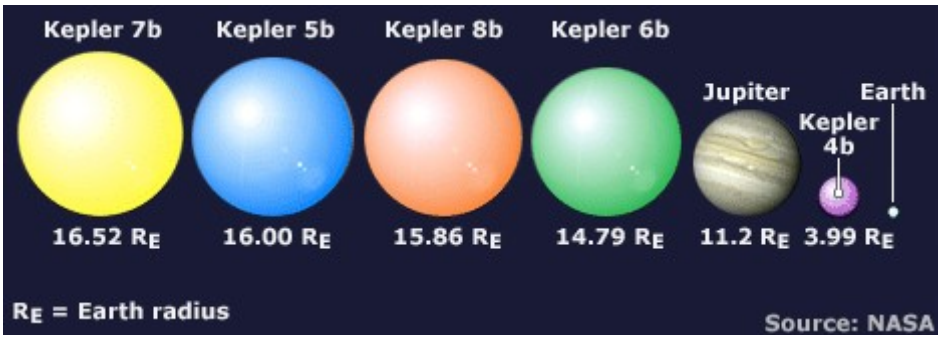
The exoplanets have been given the names Kepler 4b, 5b, 6b, 7b and 8b.

They were announced at an American Astronomical Society meeting in Washington DC.

The planets range in size from an object that has a radius four times that of Earth, to worlds much bigger than even our Jupiter.

And they all circle very close to their parent stars, following orbits that range from about 3.2 to 4.9 days.

This proximity and the fact that the host stars are themselves much hotter than our Sun means Kepler's new exoplanets experience an intense roasting.



Intriguing density

Estimated temperatures go from about 1,200C to 1,650C (2,200F to 3,000F).

"The planets we found are all hotter than molten lava; they all simply glow with their temperatures," said Bill Borucki, Kepler's lead scientist from Nasa's Ames Research Center in Moffett Field, California. In fact the upper two are hotter than molten iron and looking at them might be like looking at a blast furnace. They are very bright in their own right and certainly no place to look for life."

Kepler 7b will intrigue many scientists. It is one of the lowest-density exoplanets (about 0.17 grams per cubic centimetre) yet discovered.

"The average density of this planet with its core is about the same as Styrofoam," explained Dr Borucki. "So it's an amazingly light planet, something I'm sure theoreticians will be delighted to look at in terms of trying to understand [its] structure."

Kepler blasted into space atop a Delta II rocket from Cape Canaveral Air Force Station on 6 March, 2009. It is equipped with the largest camera ever launched into space. The telescope's mission is to continuously and simultaneously observe more than 100,000 stars.

It senses the presence of planets by looking for a tiny "shadowing" effect when one of them passes in front of its parent star.

THE KEPLER SPACE TELESCOPE
Will study more than 100,000 suns
Continuously for 4 to 6+ years
Tuned to see Earth-size planets
Will target the habitable zone
Will also see Mars to Jupiter sizes

'Water worlds'

Kepler's detectors, built by UK firm e2v, have extraordinary sensitivity.

Nasa says that if the observatory were to look down at a small town on Earth at night from space, it would be able to detect the dimming of a porch light as somebody passed in front of it.

The space agency hopes this sensitivity will lead it to planets that are not only Earth-size but which orbit their stars at distances more favourable to life, where liquid water might potentially reside on their surfaces.

The mission's scientists told the AAS meeting that Kepler had measured hundreds of possible planet signatures but that these needed further investigation to establish their true nature.

To confirm the existence of the most ideal Earth-like planets would take a few years, they warned.

In the meantime, all detections will help scientists improve their statistics on the distributions of planet size and orbital period.

The follow-up observations needed to confirm the new exoplanets' existence used a suite of ground-based facilities including the Keck I telescope in Hawaii.

MIT neuroengineers silence brain cells with multiple colors of light

New tools show potential for treating brain disorders

CAMBRIDGE, Mass. - Neuroscientists at MIT have developed a powerful new class of tools to reversibly shut down brain activity using different colors of light. When targeted to specific neurons, these tools could potentially lead to new treatments for the abnormal brain activity associated with disorders such as chronic pain, epilepsy, brain injury, and Parkinson's disease.

The tools work on the principle that such disorders might be best treated by silencing, rather than stimulating, brain activity. These "super silencers" exert exquisite control over the timing of the shutdown of overactive neural circuits – an effect that's impossible with existing drugs or other conventional therapies.

"Silencing different sets of neurons with different colors of light allows us to understand how they work together to implement brain functions," explains Ed Boyden, senior author of the study, to be published in the Jan. 7 issue of Nature. "Using these new tools, we can look at two neural pathways and study how they compute together. These tools will help us understand how to control neural circuits, leading to new understandings and treatments for brain disorders – some of the biggest unmet medical needs in the world."

Boyden is the Benesse Career Development Professor in the MIT Media Lab and an associate member of the McGovern Institute for Brain Research at MIT.

Boyden's super silencers are developed from two genes found in different natural organisms such as bacteria and fungi. These genes, called Arch and Mac, encode for light-activated proteins that help the organisms make energy. When neurons are engineered to express Arch and Mac, researchers can inhibit their activity by shining light on them. Light activates the proteins, which lowers the voltage in the neurons and safely and effectively prevents them from firing. In this way, light can bathe the entire brain and selectively affect only those neurons sensitized to specific colors of light. Neurons engineered to express Arch are specifically silenced by yellow light, while those expressing Mac are silenced by blue light.

"In this way the brain can be programmed with different colors of light to identify and possibly correct the corrupted neural computations that lead to disease," explains co-author Brian Chow, postdoctoral associate in Boyden's lab.

In 2005, Boyden, in collaboration with investigators at Stanford University and the Max Planck Institute, introduced the first such "optogenetic" technique, so called because it combines the use of optics with gene delivery. The 2005 tool, now widely used, involves a light-activated ion channel, ChR2, which allows light to selectively turn on neurons in the brain.

Two years later, Boyden demonstrated that halorhodopsin, another light-sensitive protein, could inhibit the activity of neurons when illuminated. "But the genomic diversity of the world suggested that more powerful tools were out there waiting to be discovered," Boyden says. His group accordingly screened a diverse set of microbial light-sensitive proteins, and found the new multicolor silencers. The newly discovered tools are much better than the old. Arch-expressing neurons were switched off with greater precision and recovered faster than halorhodopsin-expressing neurons, allowing researchers to manipulate different neurons with different colors of light.

"Multicolor silencing dramatically increases the complexity with which you can study neural circuits," says co-author Xue Han, postdoctoral researcher in Boyden's lab. "We will use these tools to parse out the neural mechanisms of cognition."

How they did it: MIT researchers loaded the Arch and Mac genes into viruses that inserted their genetic cargo into mouse neurons. Optical fibers attached to lasers flashed light onto the neurons, and electrodes measured the resulting neural activity. [See graphic]

Next steps: Boyden's team recently demonstrated the efficacy of ChR2 in monkeys with no apparent side effects. Determining whether Arch and Mac are safe and effective in monkeys will be a critical next step toward the potential use of these optical silencing tools in humans. Boyden plans to use these super silencers to examine the neural circuits of cognition and emotion and to find targets in the brain that, when shut down, could relieve pain and treat epilepsy. His group continues to mine the natural world for new and even more powerful tools to manipulate brain cell activity – tools that, he hopes, will empower scientists to explore neural circuits in ways never before possible.

***Source**: "High-Performance Genetically-Targetable Optical Neural Silencing by Light-Driven Proton Pumps," Chow BY, Han X, Dobry AS, Qian X, Chuong AS, Li M, Henninger MA, Belfort GM, Lin Y, Monahan PE, Boyden ES. Nature Jan 7 2010.*

Cell phone exposure may protect against and reverse Alzheimer's disease

Florida Alzheimer's Disease Research Center study in mice indicates long-term exposure to cell phone signals may even boost normal memory

Tampa, FL – The millions of people who spend hours every day on a cell phone may have a new excuse for yakking. A surprising new study in mice provides the first evidence that long-term exposure to electromagnetic waves associated with cell phone use may actually protect against, and even reverse, Alzheimer's disease. The study, led by University of South Florida researchers at the Florida Alzheimer's Disease Research Center (ADRC), was published today in the Journal of Alzheimer's Disease.

"It surprised us to find that cell phone exposure, begun in early adulthood, protects the memory of mice otherwise destined to develop Alzheimer's symptoms," said lead author Gary Arendash, PhD, USF Research Professor at the Florida ADRC. "It was even more astonishing that the electromagnetic waves generated by cell phones actually reversed memory impairment in old Alzheimer's mice."

The researchers showed that exposing old Alzheimer's mice to electromagnetic waves generated by cell phones erased brain deposits of the harmful protein beta-amyloid, in addition to preventing the protein's build-up in younger Alzheimer's mice. The sticky brain plaques formed by the abnormal accumulation of beta amyloid are a hallmark of Alzheimer's disease. Most treatments against Alzheimer's try to target beta-amyloid.

The highly-controlled study allowed researchers to isolate the effects of cell phone exposure on memory from other lifestyle factors such as diet and exercise. It involved 96 mice, most of which were genetically

altered to develop beta-amyloid plaques and memory problems mimicking Alzheimer's disease as they aged. Some mice were non-demented, without any genetic predisposition for Alzheimer's, so researchers could test the effects of electromagnetic waves on normal memory as well.

Both the Alzheimer's and normal mice were exposed to the electromagnetic field generated by standard cell phone use for two 1-hour periods each day for seven to nine months. The mice didn't wear tiny headsets or have scientists holding cell phones up to their ears; instead, their cages were arranged around a centrally-located antenna generating the cell phone signal. Each animal was housed the same distance from the antenna and exposed to electromagnetic waves typically emitted by a cell phone pressed up against a human head.

If cell phone exposure was started when the genetically-programmed mice were young adults -- before signs of memory impairment were apparent -- their cognitive ability was protected. In fact, the Alzheimer's mice performed as well on tests measuring memory and thinking skills as aged mice without dementia. If older Alzheimer's mice already exhibiting memory problems were exposed to the electromagnetic waves, their memory impairment disappeared. Months of cell phone exposure even boosted the memories of normal mice to above-normal levels. The memory benefits of cell phone exposure took months to show up, suggesting that a similar effect in humans would take years if cell phone-level electromagnetic exposure was provided.

Based on their promising and unexpected findings in mice, the researchers concluded that electromagnetic field exposure could be an effective, non-invasive and drug-free way to prevent and treat Alzheimer's disease in humans. They are currently evaluating whether different sets of electromagnetic frequencies and strengths will produce more rapid and even greater cognitive benefits than those found in their current study.

"If we can determine the best set of electromagnetic parameters to effectively prevent beta-amyloid aggregation and remove pre-existing beta amyloid deposits from the brain, this technology could be quickly translated to human benefit against AD" said USF's Chuanhai Cao, PhD, the other major study author. "Since production and aggregation of β-amyloid occurs in traumatic brain injury, particularly in soldiers during war, the therapeutic impact of our findings may extend beyond Alzheimer's disease."

The memory test used to evaluate the effects of cell phone exposure in mice was closely designed from a sensitive test used to determine if Alzheimer's disease, or its very early signs (mild cognitive impairment), are present in humans. "Since we selected electromagnetic parameters that were identical to human cell phone use and tested mice in a task closely analogous to a human memory test, we believe our findings could have considerable relevance to humans," Arendash said.

The researchers found a slight increase in brain temperature during the two one-hour periods when mice were exposed to electromagnetic waves each day. This increase in brain temperature was seen only in the Alzheimer's mice, and only after months of exposure. The researchers suggest the increase in brain temperature helped the Alzheimer's brain to remove newly-formed beta-amyloid by causing brain cells to release it.

The researchers were particularly surprised to discover that months of cell phone exposure actually boosted the memory of non-demented (normal mice) to above-normal levels. They suspect that the main reason for this improvement involves the ability of electromagnetic exposure to increase brain activity, promoting greater blood flow and increased energy metabolism in the brain. "Our study provides evidence that long-term cell phone use is not harmful to brain," Dr. Cao said. "To the contrary, the electromagnetic waves emitted by cell phones could actually improve normal memory and be an effective therapy against memory impairment"

"It will take some time to determine the exact mechanisms involved in these beneficial memory effects," Arendash said. "One thing is clear, however - the cognitive benefits of long-term electromagnetic exposure are real, because we saw them in both protection- and treatment-based experiments involving Alzheimer's mice, as well as in normal mice."

Previous human studies of electromagnetic waves from cell phones involved only brief exposures given to normal humans. While some studies reported small improvements in attention or memory (not enough to impact daily life), others reported no memory effects from short-term exposure. The new study by Arendash, Cao, and their colleagues is the first to investigate the effects of long-term electromagnetic exposure over many months on memory function in either humans or animals. The findings indicate that "long-term" exposure to cell phone level electromagnetic waves is needed to observe enhanced memory in normal or memory-impaired mice.

The USF researchers began investigating the effects of cell phone use on Alzheimer's disease several years ago, after several observational studies in humans linked a possible increased risk of Alzheimer's with "low-frequency" electromagnetic exposure -- like the energy waves generated by power and telephone lines. However, cell phones emit "high-frequency" electromagnetic waves, which are very different because they can have beneficial effects on brain cell function, such as increasing brain cell activity, Arendash said.

There has been recent controversy about whether electromagnetic waves from cell phones cause brain cancer. Some researchers argue that the risk of glioma (40 percent of all brain tumors) doubles after 10 or more years of cell phone use. However, others argue that since the overall lifetime risk of developing a brain tumor of any type is less than 1 percent, any doubling of this risk would still be very low. Groups such as the World Health Organization, the American Cancer Society, and the National Institutes of Health, have all concluded that scientific evidence to date does not support any adverse health effects associated with the use of cell phones. Consistent with the view of these organizations, the researchers found no autopsy evidence of abnormal growth in brains of the Alzheimer's mice following many months of exposure to cell phone-level electromagnetic waves. They also found all major peripheral organs, such as the liver and lungs, to be normal.

The research was conducted by an interdisciplinary group of neuroscientists, electrical engineers, and neurologists from universities in Japan and China as well as from the Florida ADRC at the University of South Florida. The study was supported by funds from the Florida ADRC, a statewide project sponsored by the National Institute on Aging, and the USF Health Byrd Alzheimer's Institute.

Journal citation: *Electromagnetic Field Treatment Protects Against and Reverses Cognitive Impairment in Alzheimer's Disease Mice. Gary W. Arendash, Juan Sanchez-Ramos, Takashi Mori, Malgorzata Mamcarz, Xiaoyang Lin, Melissa Runfeldt, Li Want, Guixin Zhang, Vasyl Sava, Juan Tan and Chuanhai Cao. Journal of Alzheimer's Disease, Volume 19:1 (January 2010).*

'Junk' DNA linked to aggressive cancers

* 20:11 06 January 2010 **by Linda Geddes**

Rogue genetic elements previously dismissed as "junk" DNA may play a role in the development of some cancers, or at least act as a marker of the disease's progression.

That's the conclusion of a study that found that some recurrent DNA sequences previously thought to be nothing more than molecular parasites appear to be active, but only in breast and colon cancer cells.

"If this 'junk' DNA does turn out to play a role in cancer then we could be at the tip of the iceberg in understanding a completely new mechanism behind the disease," says Cristina Tufarelli at the University of Nottingham in the UK.

Hidden function

Only about 3 per cent of the human genome actually encodes instructions into RNA for making proteins. Much of the rest has no apparent role and is often dismissed as junk. Sometimes, however, what seems like junk later turns out to have a function after all.

About 17 per cent of our DNA is made up of recurrent sequences called L1 elements that have colonised the genome by making copies of themselves and inserting these into new locations. Many geneticists had dismissed L1 elements as molecular parasites that do nothing but further their own survival, but recent studies have hinted that they are sometimes transcribed into RNA too.

To investigate if there might be differences in the transcription of L1 elements in cancerous cells, Tufarelli and her colleagues compared RNA transcripts in human breast cancer cell lines with those found in normal breast cells.

They found two L1 RNA transcripts that were present in both cell lines and five that were present only in the breast cancer cells.

Invasion implication

A similar analysis on colon cancer cell lines and normal colon cells also revealed some L1 elements that were only transcribed in the cancerous cells.

What's more, three of the L1 RNA transcripts found in the colon cancer cells were only found in the most aggressive cancers, suggesting that they may be linked to the progression to a more invasive type of tumour.

Since L1 elements have previously been found on DNA next to or even within some tumour-suppressor genes, Tufarelli suggests that they might influence the progression of cancer by reducing, or down-regulating, the expression of these genes.

Driver or by-product?

The next step is to confirm whether L1 elements are driving cancer, or whether the L1 transcripts found in tumours are simply the result of the cancer itself.

If they are driving it, drugs could be developed that target specific L1 elements, potentially slowing cancer progression. Even if they are innocent by-products, they might be useful in diagnosing or monitoring the disease.

"We are learning more about the genes involved in cancer but these so-called 'junk' regions receive relatively little attention," says Lesley Walker, director of cancer information at Cancer Research UK, which funded the research. "We are beginning to see that they could play a really important role."

Journal reference: Genomics, DOI: 10.1016/j.ygeno.2009.08.013

Nitric oxide-releasing wrap for donor organs and cloth for therapeutic socks

Scientists in Texas are reporting development of a first-of-its-kind cloth that releases nitric oxide gas - an advance toward making therapeutic socks for people with diabetes and a wrap to help preserve organs harvested for transplantation. The study is in ACS' Chemistry of Materials, a bi-weekly journal.

Kenneth Balkus and Harvey Liu note in the new study that nitric oxide (NO) helps increase blood flow and regulates a range of other body functions. Scientists have tried for years to find practical ways to store and deliver NO for use in medicine. However, they have had difficulty finding a suitable material that allows controlled delivery of NO. Recent studies suggested that zeolites could work. These porous materials soak up and store large amounts of gases like NO.

The scientists describe development of a new bandage composed of nitric oxide-absorbing zeolites embedded in a special water-repellant polymer. In experiments with laboratory rats, the bandage slowly released nitric oxide and increased blood flow. "The bandage could be used to wrap a donor organ ensuring intimate contact and direct delivery of nitric oxide," the report states. "Additionally, these interwoven fabrics could also find applications in smart textiles such as NO-releasing socks for diabetic patients, who have been shown to produce less nitric oxide than healthy patients."

"Novel Delivery System for the Bioregulatory Agent Nitric Oxide"

Fake Pharmaceuticals

Those fighting against counterfeit medicines face increasingly sophisticated adversaries

Sarah Everts

Of the chemicals he uncovered in various counterfeit malaria pills, Facundo M. Fernandez did not expect to find sildenafil, the active ingredient in the drug Viagra. He also didn't expect to find the antibiotic erythromycin; one of the building blocks for making the street drug ecstasy; or metamizole, a powerful analgesic that is banned in the U.S. because it is suspected of causing serious bone marrow disorders. Yet the Georgia Institute of Technology chemist, who provides scientific support to international anticounterfeiting operations, has recently found all these chemicals and more in counterfeit malaria pills. "It's shocking," he says. "Sick children take these drugs. It's terrible that they don't receive the correct treatment. But worse, the chemicals in these counterfeits could make them sicker."

Putting false active ingredients in fake drugs is just one trend in medicine counterfeiting. Bogus pills used to consist primarily of blanks because counterfeiters focused mostly on making the pills look like the originals. But these days, counterfeiters are increasingly adding all sorts of active ingredients to phony tablets. They slip mild pain relievers such as acetaminophen into pills just to make patients feel like they might be getting better, as was the case in fake Tamiflu seized from U.K. pharmacies in 2007. Sometimes, they add small amounts of the correct active ingredient to dupe testers who may not have equipment to accurately quantitate ingredient levels. More worrisome, some counterfeiters substitute life-threatening chemicals for the real McCoy, such as the antifreeze component diethylene glycol to replace glycerine. The toxic substitute ended up in cough medicines that killed hundreds in Nigeria, Panama, and Bangladesh in recent years.

While international police, pharmaceutical companies, customs officials, scientists, and health and regulatory agencies collaborate more closely to track down fake medicines and those who profit from them, counterfeiters are developing more sophisticated knockoffs and putting them in packaging that possesses anticounterfeiting security features, such as holograms. Science and technology are playing an important role in the anticounterfeiting fight—from the analytical techniques used to quantify fakes to the tracking strategies used to catch perpetrators—but the battle against fake drugs is, by all accounts, far from being won.

Fake pharmaceuticals are incredibly lucrative. In 2010, an estimated $75 billion will find its way into the pockets of those making or distributing counterfeit medicines, an oft-quoted statistic from the Center for Medicines in the Public Interest that many say is probably an underestimation. "Counterfeiters can make more money than hard-drug traffickers, and they have less of a chance to go to prison," says Aline Plançon, an Interpol policewoman who leads an anticounterfeiting task force associated with the World Health Organization (WHO) initiative called IMPACT (International Medical Products Anti-Counterfeiting Taskforce). For example, the profit margin from counterfeit Viagra is some 10 times higher than for the street drug heroin, notes David Shore, associate director of global security for Europe at Pfizer, the company that produces Viagra. The attractive revenues don't come with heavy enough consequences, Plançon adds.

In general, hard-drug traffickers are charged under specific hard-drug laws, whereas pharmaceutical counterfeiters typically face a variety of trademark, fraud, or money-laundering legislation, says Thomas T. Kubic, a former Federal Bureau of Investigation agent who now heads the Washington, D.C.-based Pharmaceutical Security Institute, which tracks medicine counterfeiting. "Instead of punching out ecstasy tablets, counterfeiters can reload pill-producing machinery and make Lipitor," Kubic says. Indeed, those

working on the ground are finding an increasing cross-over between hard-drug and pharmaceutical trafficking. For example, at a recent seizure in Istanbul, investigators nabbed 700,000 fake Viagra pills alongside 51 kg of heroin, Shore says.

High profits with comparatively low risks may be a major motivation, but many other factors also enable counterfeiting. Globalization of manufacturing has created more steps between drug production and patient consumption. Counterfeiters have capitalized on "fragmented" supply chains to penetrate markets "with counterfeits that look identical to the original," says James Thomson, chair of the European Alliance for Fake Medicines. The rise of Internet pharmacies has also permitted anonymous individuals to sell medicines directly to consumers; WHO estimates that half of all drugs sold on the Internet are fakes.

A precise count of just how many fakes currently sit in the world's medicine cabinets does not exist. The best "guesstimate" is that 1% of drugs in the developed world, including the U.S. and Europe, are counterfeit, says Paul Newton, a doctor at the University of Oxford's Center for Tropical Medicine, in Laos. In developing nations, between 10 and 50% of drugs are thought to be fake. "But we really have no idea of the full extent of the problem."

Instead, isolated snapshot statistics provide a sobering, if incomplete, picture. In 2008, the European Union launched a two-month operation called Medi-fake, which tracked and seized more than 34 million illegal pills. That same year, the pharmaceutical company GlaxoSmithKline reported 289 counterfeit cases of its drugs globally, with the fakes valued at about $11 million. These figures may seem high, but they are actually the company's lowest in five years.

NOT QUITE GMP A counterfeit lab in China.

Other companies are in the same boat. Pfizer's Shore notes that in the first nine months of 2009, 8.5 million fake Pfizer pills were seized. He adds that counterfeiters have copied 14 of the company's medicines, which have subsequently infiltrated the legitimate supply chain of at least 36 countries, including the U.S., Canada, and the U.K. Marcy Forman, who leads the U.S. Immigration & Customs Enforcement team responsible for counterfeits, tells C&EN that seizures of suspected fake drugs at the U.S. border occur at least weekly. When U.S. officials caught the fake-drug distributor Kevin Xu in 2007, they found that U.S. citizens had bought $232,568 of his counterfeits over the Internet.

Counterfeiters try to squeeze into European and North American markets, but they have a smoother ride into the markets of many developing nations, which have fewer resources to fight the problem.

One of the few programs that aims to acquire accurate statistics of drug counterfeiting, at least in developing nations, is a Bill & Melinda Gates Foundation-funded project called the ACT consortium. Newton and Fernandez are part of the group, which is currently tracking the malaria drug counterfeiting problem across the African continent.

On an international level, Interpol teamed up with WHO in 2006 to create IMPACT. The task force, led by Plançon, has only a handful of staff who coordinate intelligence received by pharmaceutical companies, local police, national customs officials, and regulatory agencies around the world. Because counterfeiting rings involve nodes in multiple continents, breaking up these rings requires getting all the anticounterfeiting players "ready on time and at the same time" to haul in players simultaneously, Plançon says. This past fall, the team completed an operation called Mamba II that raided 270 buildings in Kenya, Tanzania, and Uganda. They've also brought down counterfeiters in Southeast Asia.

In addition to local, national, and international law enforcement, pharmaceutical companies hire former police officers to investigate counterfeiting cases. Pfizer, for example, has former Scotland Yard and FBI agents, and even a former Turkish general, as counterfeit investigators. "When we have built up a case, then we pass the information on to local authorities to follow up on," Shore says.

The first step to tracking down counterfeiters is figuring out whether a pill is a real or fake. In North America and Europe, myriad labs at regulatory agencies, border control, academia, and pharmaceutical companies use a battery of analytical tools to check suspected pills for authenticity. Wet chemistry, thin-layer chromatography, X-ray fluorescence, high-performance liquid chromatography, and mass spectrometry are all commonly used to find fakes. But the situation is radically different in developing countries. For example, in the entire continent of Africa, only two labs, one in Kenya and one in South Africa, are equipped to check for counterfeits at WHO standards. International labs, such as Fernandez', provide additional scientific support.

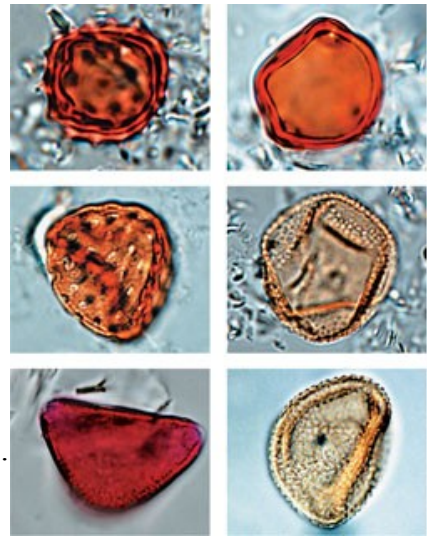
When Michael Green, a chemist at the U.S. Centers for Disease Control & Prevention, travels to Africa to check for fake malaria pills, he opts for basic wet chemistry color tests to verify medicine authenticity. He uses solvents he brings from the U.S., because "you can't count on the fact that solvents we use regularly at home

will be available," he says. Green has developed simple color tests that can assess whether specific active ingredients can be found in artesunate malaria tablets and Tamiflu influenza medication.

Giving pills a basic physical exam can also highlight fakes. For example, the weight of pills made in current Good Manufacturing Practices-certified labs won't vary by more than about 1%, whereas fakes can sometimes fluctuate by as much as 10% or even 50%. Calcite (calcium carbonate) is also often used instead of starch as an excipient—the bulk material in tablets. If a pill that normally uses starch as the excipient fizzes when dropped in vinegar—a common reaction with calcite—then "you can be pretty sure it's a fake," Green says. Counterfeiters also use talc, dolomite, anhydrite, and gypsum as excipients, says Dallas Mildenhall, a forensic scientist at GNS Science, a government research organization in New Zealand. Some of these materials do not dissolve in water, which every pill should because the contents must be absorbed by the body. If a pill doesn't dissolve in water at body temperature, then it is likely bogus.

Handheld analytical devices based on Raman and near-infrared spectroscopy are ideal for field situations because they are noninvasive: Pill pouches don't even need to be opened to be assessed for authenticity. These tools are not without challenges, however. Identifying chemical components in samples requires comparing the acquired spectra with reference spectra from a database. However, reference spectra of the same drug from different, legitimate manufacturers may vary. One solution researchers are pursuing is to use sophisticated statistical algorithms for comparing spectra.

If a comprehensive ingredient list of a tablet is required, then the tool of choice is mass spectrometry, Fernandez says. Checking pill authenticity of a large batch of pills using mass spec would take hours, and sometimes days, because of the extensive sample prep required - grinding up pills, for example. Fernandez has spearheaded the use of new mass spectrometry techniques that can take mass spectra directly from the surface of a pill. That strategy has sped up analysis by a factor of 60, Fernandez says.



***TINY EVIDENCE** The type of pollen found in counterfeit and genuine drugs can be used to identify where the drugs were manufactured. Each pollen grain is about 20 µm wide.*

As counterfeiters put increasingly good fakes on the market, some companies are investigating the possibility of putting special chemical tags in the coating of pills that could distinguish the originals. The U.S. Food & Drug Administration has given a preliminary go-ahead to try out this strategy, but European regulators have kiboshed the idea of allowing "anything in tablets unless it needs to be," Pfizer's Shore says.

Aside from exploring the idea of adding security features to a pill, companies around the world have primarily considered adding authenticity features to pill boxes and packaging. Yet any new security features for packaging last only about 18 months before counterfeiters can produce mimics, Shore says. Holograms were one of the first security features pharmaceutical companies added to packaging. But counterfeiters have been able to hire reputable hologram-making companies who don't even realize they are supplying to counterfeiters, Shore notes. He says drug counterfeiters have purchased from a company that also supplied holograms for Euro bank notes. In fact, counterfeiters' ability to add holograms to packaging is so common that "one pharmaceutical company reported a counterfeit product that had a hologram on the packaging, but in their genuine product, they had never actually put one," Kubic says.

Another security feature that has come and gone are so-called color-shift logos, which change color as the label twists in the light, Shore says. Only three companies in the world could make the ink for these logos, he says. "Then we found a pack in Hong Kong earlier this year that was such good quality it was almost impossible for the laboratory to tell whether it was a real product or not." Pfizer has stopped using this technology, Shore says. He did not divulge what the company is now using as security feature, but he says that Pfizer maintains a queue of new technologies to replace whatever counterfeiters can adeptly mimic.

Those wanting to prevent counterfeiting are trying out bar codes or RFID tags on packaging so that pharmacists can check the pedigree of a package before dispensing the drug. If the package has been dispensed elsewhere, then it's a likely sign that a counterfeiter has reused security tags for fakes. Yet as much as holograms, color-shift logos, bar codes, or RFIDs might be appropriate security measures in industrialized societies, "in tropical Asia, Africa, and South America, it's going to be very difficult for them to be used," because they require sophisticated detection technology, Newton says.

Despite the challenges of identifying counterfeits, finding the counterfeiters can be even more difficult. Those involved are increasingly using forensic science to track down perpetrators. One strategy is to take a closer look at the isotopes of elements that form the pill's excipient. These isotopes can give geographical clues

about where the pill was manufactured. For example, isotope analysis of a calcite excipient found in a counterfeit malaria drug called artesunate helped GNS Science's Mildenhall figure out that the fake pills were probably made at the border between China and Vietnam. In particular, the unusual isotope ratios of calcium, hydrogen, and oxygen suggested that the calcite had not come from the typical ocean source but instead from a hydrothermal mine. Because there is only one hydrothermal mine in the world—in southern China—the calcite helped narrow down where the manufacturing was being done.

The calcite data supported other evidence Mildenhall had that pointed to the region. He had also been scrutinizing pollen found in the fakes. Pollen "is found in all pills—real or fake," he says. But the pollen found on the counterfeit malaria drugs also came from plants native to the China-Vietnam border.

Mildenhall's pollen and calcite analyses, in combination with analyses from Fernandez, Green, and Newton, eventually allowed the IMPACT team to orchestrate the arrest of a Xu Qiang, a counterfeit trader in southern China. The team published a rare article about the case (PLOS, DOI: 10.1371/journal.pmed.0050032). Details of many other cases in the fight against counterfeits have not been released.

Even though "we are seeing some successes, fighting counterfeits has a long road ahead," Thomson says. "The fact is, these people can make fakes look perfect and they can get them into the distribution system. Is it possible to stop medicines counterfeiting altogether? I doubt very much whether it is. All we can do is to try our best to secure the supply chain."

Old antidepressant offers promise in treating heart failure

Monoamine oxidase-A inhibitor drug blocks buildup of toxic free radicals in animal hearts

A team of Johns Hopkins and other researchers have found in animal experiments that an antidepressant developed over 40 years ago can blunt and even reverse the muscle enlargement and weakened pumping function associated with heart failure.

In a report to be published in the Jan. 8 edition of the journal Circulation Research, the international team of U.S. and Italian heart experts describes in a dozen key laboratory experiments in rodents how the antidepressant clorgyline, which is no longer in use in humans, blocks the action of enzyme monoamine oxidase-A (MAO-A) and stops its breakdown of a key neurohormone. Norepinephrine, as it is called, controls the pace of blood pumping and makes the heart pump harder and faster in response to stress.

The latest study results, they say, are believed to be the first evidence showing how elevated MAO-A activity biochemically drives heart failure and that its dangerous downstream effects can be stalled by drug therapy.

"Our study helps describe heart failure as a vicious chemical circle of stimulant norepinephrine overload and breakdown, and it offers a disease blueprint with monoamine oxidase-A as the target for drugs similar to clorgyline to rein in the disease," says senior study investigator and cardiologist Nazareno Paolocci, M.D.

"When norepinephrine is not properly stored and released from the nerves directed to the heart, monoamine oxidase-A breaks it down, generating dangerous chemical species in the nerves and the heart muscle.

"These toxic free radicals produce the same deleterious effects on heart muscle size and pumping function long observed in heart failure," says Paolocci, an assistant professor at the Johns Hopkins University School of Medicine and its Heart and Vascular Institute, and at the University of Perugia in Italy.

Paolocci cautions that their studies with clorgyline are initial proof of an important principle, but far from any current use of the drug to treat heart disease in humans. He says newer drugs in the same class, such as moclobemide (sold as Aurorix or Manerix, and already approved by the U.S. Food and Drug Administration), will have to be tested first, citing numerous and potentially lethal drug effects with clorgyline that prevent it from being prescribed.

Notable side effects from clorgyline, Paolocci says, include insomnia and agitation, or high blood pressure after ingestion of foods containing the amino acid tyramine, a protein building block that stimulates a surge of stored stimulatory hormones, specifically, norepinephrine. Patients who have taken clorgyline, whose chemical binding to MAO-A is irreversible, had to carefully avoid such tyramine-rich foods as red wine, chocolate, certain beans, meat and especially aged cheeses. The phenomenon was sometimes dubbed the cheese effect.

It was previous observations of this norepinephrine surge and accelerated breakdown that led logically, the team reports, to see if inhibitor drugs – preferably those already on the shelf – could stop or reverse the damage.

Among the study's first findings was that after six weeks, mice with failing hearts responded to concurrent low-dose clorgyline treatment, with restoration of normal heart function and only half the harmful changes seen in untreated mice over the same time period.

Heart muscle cell death rates were normal in clorgyline-treated mice, but three and a half times higher in untreated mice. Heart muscle chamber expansion also slowed in the clorgyline-treated group, returning to an average chamber dimension of 1.2 millimeters, when the heart was contracting. Hearts in the untreated group

expanded to an average of 3 millimeters. In addition, depleted stores of the hormone norepinephrine were replenished in treated mice, but not at all in untreated mice.

The team believes that when norepinephrine is not properly stored in the nerves, it overflows into the heart, accelerating the hormone's breakdown by MAO-A. This in turn leads to the buildup inside the heart of harmful reactive oxygen species, such as hydrogen peroxide, that strain normal muscle cell contraction.

"Now that we know clorgyline works, we can focus future drug testing on newer, safer MAO-A inhibitors, such as moclobemide, whose chemical bindings are reversible, unlike those of clorgyline," says Paolocci.

Lead study investigator Nina Kaludercic, Ph.D., a postdoctoral fellow at Johns Hopkins and the University of Padova in Italy, says that researchers had long known that the buildup of hydrogen peroxide was dangerous, but no one knew that MAO-A was a major source due to the elevated breakdown of norepinephrine and how MAO-A's action spurred heart failure.

In other experiments in live heart cells taken from mice and rats, Kaludercic and her colleagues clarified MAO-A's connection to the muscle-enlarging effects of catecholamines, of which norepinephrine is one. They found that incubating the cells with norepinephrine for a day triggered increased MAO-A enzyme activity, generating hydrogen peroxide and muscle cell expansion, much like what happens in humans with failing hearts. Again, subsequent clorgyline treatment, at a single low dose of 2 micromoles per liter, reversed the damage.

Another key finding was that the overflow of norepinephrine did not just lead to raised activity of the muscle's alpha and beta receptors, which trigger the heart to beat harder and faster, but also led to upped activity of MAO-A.

Kaludercic says these experiments "deepen our understanding" of the close ties between the brain and the heart, and how problems with nerve-muscle interaction can influence key organ failure.

Researchers next plan to analyze medical records from people who have already taken MAO-A inhibitors to determine if their drug therapy offered any protection or lower risk of developing heart failure or other kinds of cardiovascular disease. They also plan experiments in animals to assess if clorgyline therapy can reverse heart failure at later stages of the disease, and at which dose. In addition, the team has proposed studies to evaluate other MAO-A inhibitors, including moclobemide, and what effects, if any, they have on failing hearts.

Some 5.7 million American men and women suffer from chronic heart failure, which caused an estimated 290,000 deaths in 2005. A majority of sufferers have high blood pressure, the leading risk factor for the disease.

Funding for the reported study, which took three years to complete, was provided by the American Heart Association and the National Institutes of Health (NIH). Clorgyline remains in use for scientific research and is sold by many different suppliers. The clorgyline used in this study was manufactured by Sigma-Aldrich, based in St. Louis, Mo. Moclobemide is manufactured by Roche, based in Basel, Switzerland.

Besides Paolocci and Kaludercic, other Hopkins researchers involved in this study were Eiki Takimoto, M.D., Ph.D.; Ning Feng, M.D., Ph.D.; Takahiro Nagayama, Ph.D.; Djahida Bedja, Ph.D.; Kathleen Gabrielson, D.V.M., Ph.D.; and David Kass, M.D. Kass is the Abraham and Virginia Weiss Professor of Cardiology at Johns Hopkins. Additional members of the research team were Edwin Lai, Ph.D., and Karel Pacak, M.D., Ph.D., at the NIH's National Institute on Chemical Dependency; Randy Blakely, Ph.D., at Vanderbilt University, in Nashville, Tenn.; Kevin Chen, Ph.D., and Jean C. Shih, Ph.D., at the University of Southern California, Los Angeles; and Fabio Di Lisa, M.D, at the University of Padova.

Johns Hopkins researchers say vaccine appears to 'mop up' leukemia cells Gleevec leaves behind

Team cautions that results are very preliminary and they cannot yet rule out other reasons for success

Johns Hopkins Kimmel Cancer Center researchers say preliminary studies show that a vaccine made with leukemia cells may be able to reduce or eliminate the last remaining cancer cells in some chronic myeloid leukemia (CML) patients taking the drug Imatinib mesylate (Gleevec).

Gleevec, one of the first targeted cancer therapies with wide success in CML patients, destroys most leukemic cells in the body, but in most patients, some cancerous cells remain and are measurable with sensitive molecular tests. These remaining cells are a source of relapse, according to the investigators, especially if Gleevec therapy is stopped.

In a pilot study published in Clinical Cancer Research, the Johns Hopkins investigators used a vaccine made from CML cells irradiated to halt their cancerous potential and genetically altered to produce an immune system stimulator called GM-CSF. The treated cells also carry molecules, called antigens, specific to CML cells, which prime the immune system to recognize and kill circulating CML cells.

The study vaccine was given to 19 CML patients with measurable cancer cells, despite taking Gleevec for at least one year. A series of 10 skin injections were given every three weeks for a total of four times. After a median of 72 months of follow-up, the number of remaining cancer cells declined in 13 patients, 12 of whom

reached their lowest levels of residual cancer cells. In seven patients, CML became completely undetectable. Because the study was conducted in a limited number of patients and not compared with other therapies, the researchers warn they cannot be sure that the responses were a result of the vaccine.

"We want to get rid of every last cancer cell in the body, and using cancer vaccines may be a good way to mop up residual disease," says Hyam Levitsky, M.D., professor of oncology, medicine and urology at the Johns Hopkins Kimmel Cancer Center. More research to confirm and expand the results is needed, Levitsky said.

The investigators will be testing blood samples taken from the study patients to identify the precise antigens that the immune system is recognizing. With this information, they will tailor their vaccine for additional studies that monitor immune response more precisely.

Patients receiving the trial vaccine experienced relatively few side effects that included injection site pain and swelling, occasional muscle aches and mild fevers.

According to the investigators, most patients with CML will need to remain on Gleevec therapy for the rest of their lives. More than 90 percent of them will achieve remission, but about 10 to 15 percent of patients cannot tolerate the drug long term. "Often patients have low blood cell counts, fluid retention, significant nausea and other gastrointestinal problems," says B. Douglas Smith, M.D., associate professor of oncology at the Johns Hopkins Kimmel Cancer Center. Secondary therapies, including dasatinib and nilotinib, also have many side effects.

Another common side effect of Gleevec, says Smith, is fatigue. "Patients often tell me that they feel about 80 to 90 percent of what they should, and over time, this may have a big impact on their quality of life," he says.

Gleevec also cannot be taken during pregnancy, and since one-third of CML patients are in their 20s and 30s, many patients hoping to start families would like to discontinue taking it.

"Ultimately, should this vaccine approach prove to be successful, the ability to get patients off lifelong Gleevec therapy would be a significant advance," says Levitsky.

The research was funded by the National Institutes of Health. Study contributors include Yvette Kasamon, Jeanne Kowalski, Christopher Gocke, Kathleen Murphy, Hua-Ling Tsai, Lu Qin, Christina Chia, Barbara Biedrzycki, and Richard Jones from Johns Hopkins; Carole Miller from St. Agnes Hospital; Elizabeth Garrett-Mayer from the Medical University of South Carolina; and Thomas Harding and Guang Haun Tu from Cell Genesys, Inc.

Under a licensing agreement between BioSante Pharmaceuticals Inc. and the Johns Hopkins University, Dr. Levitsky is entitled to a share of milestone payments and a share of royalty received by the University on sales of GVAX. Dr. Levitsky previously served as a paid consultant to Cell Genesys, which has since been acquired by BioSante Pharmaceuticals Inc. The terms of this arrangement are being managed by the Johns Hopkins University in accordance with its conflict-of-interest policies.

New approach precisely tracks evolution's footprints in the human genome

Researchers devise method to pinpoint key genetic variations under positive natural selection that may impact human health

Fossils may provide tantalizing clues to human history but they also lack some vital information, such as revealing which pieces of human DNA have been favored by evolution because they confer beneficial traits — resistance to infection or the ability to digest milk, for example. These signs can only be revealed through genetic studies of modern humans and other related species, though the task has proven difficult. Now, in a paper appearing in the January 7 edition of Science Express, researchers describe a method for pinpointing these preferred regions within the human genome that offers greater precision and resolution than ever before, and the possibility of deeply understanding both our genetic past and present.

"It's clear that positive natural selection has been a critical force in shaping the human genome, but there are remarkably few examples that have been clearly identified," said senior author Pardis Sabeti, an associate member of the Broad Institute of Harvard and MIT and an assistant professor of organismic and evolutionary biology at Harvard University. "The method we've developed makes it possible to zero in on individual genes as well as the specific changes within them that are driving important evolutionary changes."

Positive natural selection is a process in which advantageous traits become more common in a population. That is because these traits boost an individual's chances of survival and reproduction, so they are readily passed on to future generations. Identifying such traits — and the genes underlying them — is a cornerstone of current efforts to dissect the biological history of the human species as well as the diseases that threaten human health today.

"In the human genome, positive natural selection leaves behind very distinctive signals," said co-first author Sharon Grossman, a research assistant at Harvard University and the Broad Institute. Yet earlier methods for detecting these signals are limited, highlighting relatively large chunks of the genome that are hundreds of thousands to millions of genetic letters or "bases" in length, and that can contain many genes.

Of the hundreds of these large genomic regions thought to be under positive natural selection in humans, only a handful have so far been winnowed to a precise genetic change. "Finding the specific genetic changes that are under selection can be like looking for a needle in a haystack," said Grossman.

Sabeti, Grossman and their colleagues wondered if there might be a way to enhance this genomic search. Because existing methods for detecting natural selection each measure distinct genomic features, the researchers predicted that an approach that combines them together could yield even better results.

After some initial simulations to test their new method, the research team applied it to more than 180 regions of the human genome that are thought to be under recent positive selection, yet in most cases, the specific gene or genetic variant under selection is unknown.

The researchers' method, called "Composite of Multiple Signals" or CMS, enabled them to dramatically narrow the size of the candidate regions, reducing them from an average of eight genes per region to one. Moreover the number of candidate genetic changes was reduced from thousands to just a handful, helping the researchers tease out the needles from the haystack.

"The list of genes and genetic loci we identified includes many intriguing candidates to follow up," said co-first author Ilya Shylakhter, a computational biologist at the Broad Institute and Harvard University. "For example, a number of genes identified are involved in metabolism, skin pigmentation and the immune system."

In some cases, the researchers were able to identify a specific genetic change that is the likely focal point of natural selection. For example, a variation in a gene called protocadherin 15, which functions in sensory perception, including hearing and vision, appears to be under selection in some East Asian populations. Several other genes involved in sensory perception also appear to be under selection in Asia. In addition, the team uncovered strong evidence of selection in East Asians at a specific point within the leptin receptor gene, which is linked to blood pressure, body mass index and other important metabolic functions.

Interestingly, the researchers also localized signals to regions outside of genes, suggesting that they function not by altering gene structure per se, but by changing how certain genes are turned on and off.

While the findings in the Science paper offer a deep glimpse of evolution's handiwork, the researchers emphasize that further studies of individual genetic variations, involving experiments that explore how certain genetic changes influence biological function, are necessary to fully dissect the role of natural selection and its impact on human biology.

"This method allows us to trace evolution's footprints with a much finer level of granularity than before, but it's one piece of a much larger puzzle," said Sabeti. "As more data on human genetic variation becomes available in the coming years, an even more detailed evolutionary picture should emerge."

Paper cited: *Grossman et al. A composite of multiple signals distinguishes causal variants in regions of positive selection. Science DOI: 10.1126/science.1183863*

Blood glucose self-monitoring: No benefit for noninsulin-dependent patients with type 2 diabetes

Insufficient trials - no conclusions possible on diabetes-related diseases

Contrary to the widely-held belief, there is no proof that non-insulin-dependent patients with type 2 diabetes benefit from glucose self-monitoring. Moreover, it remains unclear whether an additional benefit is displayed by the blood test compared to the urine test or vice versa, in other words, whether one or other of the tests might offer an advantage to patients. The current data are quantitatively and qualitatively inadequate: the few trials that are suitable for investigating these questions have not included or have insufficiently reported many outcomes important to patients. Owing to their short duration, it is also not possible to draw any conclusions on the long-term benefit of glucose self-monitoring. This is the conclusion of the final report of the Institute for Quality and Efficiency in Health Care (IQWiG), published on 14 December 2009.

Self-monitoring is well established in insulin-dependent patients

Anyone who injects insulin should check their blood glucose level regularly, so that they can regulate the insulin dose according to need - this is an established procedure for patients with type 1 or type 2 diabetes. However, it is unclear whether people with type 2 diabetes, who manage without insulin, also benefit from blood glucose self-monitoring. The Federal Joint Committee (G-BA) therefore commissioned IQWiG to assess the patient-relevant benefit of urine glucose and blood glucose self-monitoring when treating diabetes type 2 without insulin.

Self-monitoring should also contribute towards changes in lifestyle

Besides drug therapy, lifestyle, especially diet and exercise, also plays an important role in the treatment of type 2 diabetes. Many experts assume that blood glucose self-monitoring helps patients in adapting their lifestyle, because the measured values enable them to see the direct effect of diet and physical activity and then

to take suitable measures. The result should be that their blood glucose is better controlled and acute and long-term complications are reduced - at least this is the assumption.

Currently, there are two options for self-monitoring blood glucose. The kidneys excrete glucose via urine when the glucose level in the blood is too high. Patients can test for hyperglycaemia by carrying out a urine dipstick test. However, hypoglycaemia cannot be detected in this way. It can only be reliably detected by blood glucose monitoring: a small sample of blood is taken and placed on a test strip. In each case patients require thorough instruction in handling the test strips correctly and in being able to interpret the blood and urine test results and take appropriate action.

6 trials included in the assessment

In order to examine whether the above-mentioned assumptions can be scientifically proven, IQWiG searched for comparative trials with and without self-monitoring. Self-monitoring could also be a component of a complex education and treatment programme, such as are often offered to patients with diabetes mellitus. These trials were included if the participants in the treatment and control groups received the same treatment regimen - the only difference being that one group was with self-monitoring and the other without.

Overall, IQWiG and its external experts found 6 randomized controlled trials that were suitable for investigating the impact of medical interventions on the course of the disease. In all the included trials, education was a component in the therapy strategy. All 6 trials investigated the benefit of blood glucose self-monitoring; no suitable clinical comparisons were identified on urine glucose self-monitoring. The duration of the included trials was between 6 and 12 months, in other words, none of them were designed to investigate the long-term benefit of self-monitoring.

Not possible to draw conclusions on important outcomes

However, data on criteria that were important for the patient-relevant benefit were not even collected in these trials. This applies in particular to concomitant and late complications caused by diabetes, such as sight loss or cardiac disease. Other outcomes, such as quality of life and patient satisfaction, were in fact investigated in a few trials but inadequately reported, so that the results cannot be accepted as reliable. Yet even the few available data did not display any advantage for self-monitoring.

According to IQWiG and its external experts, therefore, the quality of trials on glucose self-monitoring is still inadequate overall. What is lacking are trials of longer duration that enable the long-term effects of glucose self-monitoring to be evaluated. Even the Canadian Agency for Drugs and Technologies in Health (CADTH) has complained in its most recent assessment of blood glucose self-monitoring that there is a lack of long-term trials.

No evidence of better results in blood glucose control

Blood glucose self-monitoring provides a snapshot of the blood glucose level. Depending on the measured value, patients can then take appropriate measures, for example, by eating something. However, blood glucose self-monitoring is not suitable for determining the quality of metabolic control. The HbA1c value is used for this. It is an indicator for long-term blood glucose control and serves as the "memory" for the blood glucose level. High HbA1c values in diabetes indicate poor metabolic control.

All trials included in the assessment additionally investigated the impact of blood glucose self-monitoring on the HbA1c value. The joint analysis revealed that blood glucose self-monitoring actually does assist in lowering blood glucose. However, the difference was marginal compared to the group that did not carry out self-monitoring. It was inside the range that is acceptable within the context of drug approval for describing a new drug as "not inferior" compared to existing drugs. No health advantage from this difference can therefore be anticipated.

Advantage for hypoglycaemia not proven

Furthermore, the HbA1c value alone has no validity in assessing the benefit of glucose self-monitoring, since the more the blood glucose level drops, the greater the risk of hypoglycaemia. In this case, hypoglycaemia is not merely unpleasant, but can also represent a serious complication in individual cases. For this reason, it is always necessary to assess changes in the HbA1c value in relation to the occurrence of hypoglycaemia. The available trials on blood glucose self-monitoring were inappropriate for this, however. Thus, an advantage of hypoglycaemia is not proven. In addition, it remains unclear whether glucose self-monitoring has contributed towards patients being able to make changes to their lifestyle.

Overall, IQWiG and its external experts come to the conclusion, therefore, that a benefit of blood glucose self-monitoring cannot be proven from the available trials. Due to a lack of trials on urine glucose self-monitoring, no conclusions can be drawn from a comparison of urine and blood tests, either.

Commenting procedure: *IQWiG published the preliminary results in the form of the preliminary report in June 2009 and interested parties were invited to submit comments. When the comments stage ended, the preliminary report was revised and*

sent as a final report to the contracting agency, the Federal Joint Committee, in October 2009. Documentation of the written comments and minutes of the oral debate are published in a separate document simultaneously with the final report. The report was produced in collaboration with external experts.

Tracks record oldest land-walkers

By Jonathan Amos Science correspondent, BBC News

The oldest evidence of four-legged animals walking on land has been discovered in southeast Poland.

Rocks from a disused quarry record the "footprints" of unknown creatures that lived about 397 million years ago. Scientists tell the journal Nature that the fossil trackways even retain the impressions left by the "toes" on the animals' feet. The team says the find means that land vertebrates appeared millions of years earlier than previously supposed.

"This place has yielded what I consider to be some of the most exciting fossils I've ever encountered in my career as a palaeontologist," said team member Per Ahlberg from Uppsala University, Sweden. "[They are] fossil of footprints that give us the earliest record of how our very distant ancestors moved out of the water and moved on to the land and took their first steps."

Numerous trackways have been identified in the Zachelmie Quarry in the Holy Cross Mountains. They represent the movements of many animals as they scurried around what would have been a tropical muddy shoreline in the Middle Devonian Period of Earth history.

Slabs of carbonate rock are dappled with prints that range in size and detail. Some indentations are obscured where successive animals have trampled over the same patch of ground; but others retain exquisite features of the pads and digits that made them.

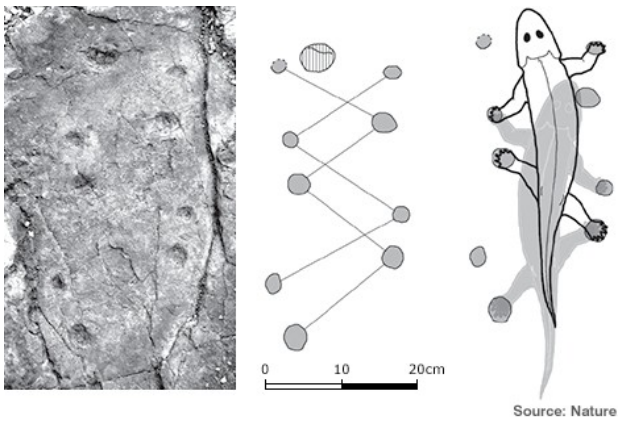
The animals were probably crocodile-like in appearance and lived an amphibian-like existence (although those specific animal forms did not appear until many millions of years later). The dimensions of the prints suggest some individuals were more than two metres long.

The Polish and Swedish scientific team analysed the trackway patterns to reconstruct how the ancient creatures would have moved their "hips", "elbows" and "knees". This confirms that only true four-legged animals, or tetrapods, could have left the marks.

Theory holds that the first land creatures evolved from fish that had pairs of lobed fins. The precise timing of this transition has been a dynamic field of study in recent years. The assumption of palaeontologists had been that there was a swift but stepwise transition between water and land.

Perhaps the most notable fossil in this story is an organism called Tiktaalik roseae , an animal that had features intermediate between fish and tetrapods. But Tiktaalik lived about 375 million years ago; and although there are slightly older transition fossils, the Zachelmie Quarry tetrapods break the neat and simple timeline.

"The discovery of undoubted trackways from the earliest period of the Eifelian - that is 397 million years ago - pushes back the divergence between fishes and the four-legged vertebrates by about 18 million years, if not probably more," commented Dr Philippe Janvier from the National Museum of Natural History, Paris, France.



How one of the Devonian animals might have made the tracks

"I suspect that now we can push the divergence back to the Emsian stage, maybe 400 million years ago. That's surprising, but this is what the fossil evidence tells us," the independent researcher told BBC News.

Another key surprise from the research is the recognition that these tetrapods lived in a marine environment, perhaps a coral lagoon. The favoured origin before now for the emergence of tetrapods had been marshy environments, such as deltas or lakes where freshwater dominated. The team behind the latest research said the new explanation made sense because it would have allowed marine ancestors of tetrapods gradually to acquire terrestrial competence while accessing a new and essentially untouched resource of food washed up with the tides.

"In the intertidal setting, you've got a smorgasbord laid out twice a day," said Dr Ahlberg. "Every time the tide goes out, it leaves behind this drift-line of dead and moribund animals. All this was just left there for vertebrates - our ancestors - to emerge on to land and pick them off."

Egg white provides a puncture repair kit for fetuses

BETTER known for giving meringues and soufflés their texture, egg white is being tested as a sealant for the amnion, a membrane that surrounds developing fetuses.

The amnion can rupture spontaneously, but can also tear after amniocentesis - in which a needle is used to extract amniotic fluid to test for genetic diseases - or fetal surgery. Such a breach can cause the mother's waters to break prematurely, resulting in miscarriage.

Noting its stickiness and its role in protecting a developing chick, Ken Moise and his colleagues at the Baylor College of Medicine in Houston, Texas, turned to purified, treated white from chicken eggs, which they had already used to repair holes in balloons and condoms.

They took discarded human amnions and stretched each across the bottom of an open-ended glass tube, which they then filled with human amniotic fluid. Next they ruptured the membrane with a needle, and after 30 seconds applied purified egg white. Of 21 tubes, 19 stopped leaking immediately. The others stopped after a second application (American Journal of Obstetrics & Gynecology, DOI: 10.1016/j.ajog.2009.10.862).

Moise had to use antibiotics to quell microbial infections caused by the procedure, which would complicate using it in the body. But as other attempts to seal or patch amnions have been disappointing, the development is a positive step, he says.

Liver donations from living donors increase 42 percent after educational intervention

Living liver donors share their stories -- more step forward to donate

A recent study found that living donation increased 42% and the number of individuals who presented for donation evaluation increased 74% at centers in New York. The surge in live donation and donor evaluation occurred after additional education was provided to liver transplant candidates. Those candidates exposed to the peer-based intervention (education) reported significantly greater knowledge, greater likelihood to discuss donation and increased self-efficacy compared to those not exposed to the intervention. Details of the study are reported in the January 2010 issue of Liver Transplantation, a journal of the American Association for the Study of Liver Diseases, published by Wiley-Blackwell.

According to the United Network for Organ Sharing (UNOS) as of January 30, 2009 there were 100,539 candidates on the waiting list in the U.S., with over 15,000 individuals in need of a liver transplant. UNOS also reported the number of deceased donors is decreasing from 6,650 donors in 2006 to 6,494 donors in 2007—a concerning fact for liver transplant candidates. Past studies have shown that the median wait time for a liver was 296 and 306 days (2005 and 2006, respectively). In New York State in 2008, there were 133 deaths on the liver waitlist, an increase of 16% over 2007. The critical shortage of deceased liver donors, a lack of broader national sharing, increased wait times and deaths on the wait list, all incentivize transplant programs to look to alternative ways to expand the pool of livers available for transplant.

At the time of the study and based on UNOS data, New York had 1,947 individuals on the liver wait list which represents 12% of candidates nationally. In 2006-2007, random samples of waitlisted candidates at five transplant centers in New York were selected to complete (pre-intervention) surveys. A second sample of waitlisted candidates completed post-intervention surveys in 2008. These surveys included questions about: length of time on waiting list, education level, ethnicity, age, if they received educational materials (and helpfulness of materials), if they had discussed living liver donation with loved ones and if they had any plans to do so and where else they may have learned about liver transplantation.

"Past studies have show waitlisted candidates concerns over donor safety coupled with their general lack of knowledge about organ donation created a reluctance on the part of candidates to discuss living donor liver transplantation (LDLT) with family and friends," said Samantha DeLair, Director, New York Center for Liver Transplantation and lead author of this study. "The intervention material we used included testimonials and self-report data from living donors to educate liver candidates about the impacts, both the positives and the challenges of living liver donation," added Ms. DeLair.

In New York all living liver donors are periodically surveyed to assess the individuals' health and quality of life post-donation. Educational material used in the study to educate liver candidates was derived from 44 survey respondents in 2004-2005. The content of the booklet and DVD focuses on donor responses regarding: the surgery, recovery after donation, costs of donation, employment issues, and life after donation. The educational material used in this study, ***"In Their Own Words – The Experiences of Living Liver Donors,"***.

Of the donors whose self-reports were used to create the educational material, 87% recommend seeking input of a former donor prior to donating. One anonymous donor gives this advice to individuals considering the option of LDLT, "Every decision is personal…get as much information as possible and speak to other donors."

There were 437 waitlisted candidates at pre-test who completed surveys and 338 individuals at post-test. Participants had a median age of 55 years with 63% male and 56% of the total sample was White, non-

Hispanic. Most surveyed were either newly listed (26%) or had been on the list for greater than 1 year (50%). For those participants exposed to the educational intervention, 91% reported having a "fair amount" or "a lot" of knowledge regarding LDTL compared to 70% of the unexposed group.

This study also tracked the number of friends and family members who presented to the five transplant centers for further information, discussion, and if appropriate, comprehensive evaluation for LDLT. Results indicate there was a 74% increase in LDLT evaluations from 2006 to 2008 at the intervention sites. After the educational intervention, there was a 42% increase in the number of individuals who completed an evaluation and donated a liver graft.

"Our data is compelling given the gains in waitlist candidates' knowledge of LDLT and the increases in the number of individuals interested in using this transplantation procedure," concluded Ms. DeLair. "It is important to follow live donors post-donation both for the donors themselves and to provide waitlist patients and their loved ones with as much information as possible as they consider live donation for themselves."

Article: *"A Peer-Based Intervention to Educate Liver Transplant Candidates about Living Liver Donation." Samantha DeLair, Thomas Hugh Feeley, Hyunjung Kim, Juan del Rio Martin, Leona Kim-Schluger, Dianne LaPointe Rudow, Mark Orloff, Patricia A. Sheiner, Lewis Teperman. Liver Transplantation; Published Online: December 30, 2009 (DOI10.1002/lt.21937); Print Issue Date: January 2010 http://www3.interscience.wiley.com/journal/123226251/abstract*

Viral phenomenon: Ancient microbe invaded human DNA

PARIS (AFP) – Humans carry in their genome the relics of an animal virus that infected their forerunners at least 40 million years ago, according to research published Wednesday by the British science journal Nature.

The invader is called bornavirus, a brain-infecting pathogen that was first identified in 1970s.

Scientists led by Keizo Tomonaga of Japan's Osaka University compared the DNA of a range of mammals, including humans, apes, elephants, marsupials and rodents, to look for tell-tale signatures of bornavirus code.

In the human genome, the team found several bornavirus fragments but also in the form of two genes that may be functional, although what they do is unclear. Until now, the only viruses known to have been handed on in vertebrates were retroviruses, which work by hijacking cellular machinery in order to reproduce.

Retroviruses are effective in infiltrating the germline - the DNA of reproductive cells, which means their sequence, or part of it, is handed on to ensuing generations.

By some estimates, retroviruses account for as much as eight percent of the human code for life.

Bornavirus has a different stealth tactic, replicating in the nucleus of infected cells. The disease owes its name to the German town of Borna, where a regiment of cavalry horses was wiped out in 1885 by a mysterious "heated head" disease. Later research also found the disease among sheep, llamas, ostriches, cats and cattle, although how it spreads is poorly understood.

The impact of bornavirus on the human genetic odyssey is likely to trigger fierce debate.

The big questions are whether it provided a potential cause of genetic mutation or innovation in our species, or whether it provided a source for inherited illness - or, conversely, protection.

Bornavirus has not been clearly linked to diseases in humans, although some researchers speculate there could be a link with schizophrenia and other mental disorders.

Did We Mate Or Murder Neanderthals?

Scientists Say Modern Humans' More Varied Lifestyle May Have Been Key To Survival

(CBS) This article was written **by Jane Bosveld** of Discover.

Aiming his crossbow, Steven Churchill leaves no more than a two-inch gap between the freshly killed pig and the tip of his spear. His weapon of choice is a bamboo rod attached to a sharpened stone, modeled after the killing tools wielded by early modern humans some 50,000 years ago, when they cohabited in Eurasia with their large-boned relatives, the Neanderthals. Churchill, an evolutionary anthropologist at Duke University, is doing an experiment to see if a spear thrown by an early modern human might have killed Shanidar 3, a roughly 40-year-old Neanderthal male whose remains were uncovered in the 1950s in Shanidar Cave in northeastern Iraq. Anthropologists have long debated about a penetrating wound seen in Shanidar 3's rib cage: Was he injured by another Neanderthal in a fight-or was it an early modern human who went after him?

"Anyone who works on the ribs of Shanidar 3 wonders about this," Churchill says.

The possibility that early humans attacked, killed, and drove small bands of Neanderthals to extinction has intrigued anthropologists and fascinated the public ever since Neanderthal bones were first studied in the mid-19th century. At first naturalists were not sure what to make of the funny-looking humanlike bones. But with publication of Darwin's On the Origin of Species, the idea that the bones were from a species closely related to us began to make sense. Eventually scientists recognized that Neanderthals were an extinct species that shared a common ancestor (probably Homo heidelbergensis) with Homo sapiens. For thousands of years, Neanderthals were the only hominids living in Europe and parts of Asia.

Then, around 50,000 years ago, early modern humans migrated into Europe from Africa. By 28,000 to 30,000 years ago, the Neanderthals had disappeared.

For more than a century after their discovery, our robust relatives were depicted as dumb brutes, but the Neanderthals have had something of a face-lift in recent years. They are now considered to have been intelligent (as smart as early modern humans, some anthropologists think), perhaps red-haired and pale-skinned, and capable of speech. They might even have created their own language. The more we learn about Neanderthals, the more familiar they seem. But one deep mystery remains: Whatever happened to them, and why did they disappear?

There are many theories but not a lot of proof. That is why Churchill's study of Shanidar 3 and another study published this year about humans cannibalizing Neanderthals are essential. They add a few details to the shadowy picture we have of our long-lost cousins. Anthropologists have many interpretations. Maybe our direct ancestors and Neanderthals largely coexisted (as did many other overlapping hominid species before them), with occasional bouts of quasi-tribal warfare that ebbed and flowed. Then again, maybe humans relentlessly drove Neanderthals into extinction. Right now these are just possibilities. Only the bones and artifacts can tell what really happened.

The Killing of Shanidar 3

Churchill's curiosity about the fate of Shanidar 3 led him to try re-creating the sharp, deep scratch in the left ninth rib of this hapless Neanderthal. This strategy actually came from Churchill's colleague John Shea, a paleoanthropologist at Stony Brook University in New York who reconstructs the behavior of prehistoric peoples by analyzing their stone tools. To understand how stone points are worn down when piercing flesh and bone, Shea had run a set of experiments, stabbing goat carcasses and then noting the damage to the tools.

Churchill hoped to compare the cuts on Shea's goat bones to the mark on Shanidar 3's rib. Unfortunately, the goat bones were so damaged by the blows that "it was impossible to analyze them," he says.

He concluded that he would have to do his own experiments to replicate the physics of Shanidar 3's prehistoric wound. Neanderthals were the power-thrusters of the Paleolithic world, driving their heavy spears with great kinetic energy and momentum into bison, boar, and deer. If Shanidar 3 had been injured by such a thrust, it would suggest that he had gotten into a fight with another Neanderthal, or perhaps that he had been hurt in a hunting accident. But if the wound had resulted from a lighter spear-from a projectile deftly thrown at a distance, with less momentum and energy-the attacker was most likely human. There is no evidence whatsoever that Neanderthals ever used throwing spears, Churchill says.

After inflicting a set of sample wounds on pig bones, which are close in terms of size and shape to those of Neanderthals (and which were easily obtained from a nearby slaughterhouse), Churchill and his team of students spent an evening cleaning the bones by boiling them in hot water and Biz, a laundry detergent containing enzymes that are, Churchill says, "really good at breaking down proteins."

The process revealed signs of damage to the pig bones similar to those seen in Shanidar 3. "We cannot definitively rule out accidental wounding, attack with a knife, or attack with a hand-delivered, heavy Neanderthal spear," Churchill says. "But Shanidar 3's wound is most consistent with injury from a lightweight, long-range projectile weapon."

In other words, a human probably did it.

Eating the Neanderthal of Les Rois

The spearing of Shanidar 3 documents only the act of one individual against another. Paleontologist Fernando Ramirez Rossi discovered something far more nefarious while comparing the jawbones of a Neanderthal child and an early modern human last year at the Institute of Human Paleontology in Paris. Both mandibles, dating from about 30,000 years ago, had been excavated from a cave called Les Rois in southwestern France. Finding Neanderthal bones mixed in with human bones is in itself significant because it shows that early humans and Neanderthals truly did meet face-to-face.

Ramirez Rozzi thinks that some of the encounters may have been peaceful, but this one apparently was not. The Neanderthal jawbone exhibits cut marks made by a stone tool that mirrors those seen on a number of reindeer jawbones found nearby. The marks are distinctive indicators of slaughtering, including repeated indentations in the bone where the tongues were cut out. "It is clear that early humans were eating Neanderthals," Ramirez Rozzi says. The cut marks are also similar to ones noted a decade earlier on deer and Neanderthal bones found at Moula-Guercy, a Paleolithic site in southeastern France near the Rhone River. The cannibals in that instance, though, were other Neanderthals, not early humans.

Anthropologists suspect that there was never a huge population of Neanderthals, although we do not have enough evidence yet to know how many lived at any given time. That is why some scientists doubt there were frequent run-ins between Neanderthals and humans. But Ramirez Rozzi disagrees. He thinks that Neanderthals

and early humans met "on many occasions" and that some of those meetings were violent. "We can also say that, as with violent encounters between different peoples, on one of those violent meetings the loser-the Neanderthal-was eaten by the winner," he says.

The proven proximity has fostered a debate over whether humans and Neanderthals might have mated with each other as well. Ramirez Rozzi classifies Neanderthals as a separate species, Homo neanderthalensis, and therefore suspects that close relationships with early humans were rare. "I think early modern humans viewed Neanderthals as a different group, as 'the other,'" he says.

But Erik Trinkhaus, a physical anthropologist at Washington University in St. Louis, thinks the two hominids had a much stronger connection. In fact, he controversially argues that Neanderthals did not really go extinct. Rather, he claims, they were absorbed into the larger, rapidly growing population of early humans migrating into Eurasia from Africa. "We will never know to what extent they were absorbed. The bottom line is that they were humans, and sex happens," he says.

Many of Trinkaus's colleagues dispute that idea. Svante Pääbo who leads the Neanderthal Genome Project at the Max Planck Institute in Germany, painstakingly sequenced samples of Neanderthal DNA and found little evidence of their genes in us. His result implies that there was minimal interbreeding. "But so far we have only been able to see if humans have any genes from Neanderthals," he says. "We are now starting to look to see if there are genes in Neanderthals that came from modern humans."

Most anthropologists interpret the disappearance of the Neanderthals some 30,000 years ago as a true extinction. They are just not sure why it occurred. "My gut feeling," says Neanderthal expert Francesco d'Errico, director of the National Center for Scientific Research in France, "is that the Neanderthal extinction went on for several millennia and was modulated, but not determined, by climatic changes."

Indeed, the era between 65,000 and 25,000 years ago, toward the end of the Paleolithic, was a time of major volcanic eruptions, along with extremes of climate that included rapid shifts in temperature accompanied by alternately creeping and contracting glaciers across many regions of Eurasia. "This put a lot of stress on plant and animal life," says archaeologist Steve Kuhn, of the University of Arizona. "Habitats were shrinking. Some researchers believe that everything was changing faster than the Neanderthals' capacity to adjust to them."

There also probably were not very many Neanderthals, and their small population may have played a role in their extinction. "Rare animals can be wiped out by climatic stress and competition more easily than animals that are common," Kuhn says.

Kuhn and his colleague and spouse, archaeologist Mary Stiner, also suggest that the Neanderthals' social structure put them at risk. Unlike early human hunter-gatherer groups, Neanderthals concentrated almost entirely on hunting big game, as evidenced by the abundance of large animal bones in Neanderthal archaeological sites. At these sites there is also an absence of technology for grinding or crushing plant foods to extract their nutrients, which is essential to the lifestyle of foragers. "They engaged their entire group-men, women and children-in hunting big game," Kuhn says. Involving the whole tribe in hunting worked well until the climate changed and competition showed up in the form of early humans. Homo sapiens's division of labor allowed women and children to focus on small game and gathering while men went after the larger prey. In tough times, Kuhn argues, this diversified diet gave early humans a survival edge.

It is impossible to know exactly how major a role human aggression played in the Neanderthals' disappearance. The groups undoubtedly competed for resources, though, and evidently humans sometimes attacked or even ate Neanderthals. The death of Shanidar 3 may thus have foreshadowed the fate of his entire species.

After a human threw a spear into his chest, Shanidar 3 lived at least another two weeks with the spearhead (if not the whole spear) stuck in his ribs. At the time of his death, the gouge in his bone had started to heal. He was one tough guy.

Archaeologists found him some 50,000 years later in the cave in Iraq's Zagros Mountains, buried under the rubble of a collapsed ceiling. There is no way to tell whether he died from his wound or from being trapped under the rock. Like so much else about our wayward cousins, the final cause of Shanidar 3's death remains a mystery.

Sleeping Beauty Hooks Up with Herpes to Fight Brain Disease

Tag-team Approach Breaks the Size Barrier for Gene Therapy

William Bowers, Ph.D.

Neuroscientists have forged an unlikely molecular union as part of their fight against diseases of the brain and nervous system. The team has brought together the herpes virus and a molecule known as Sleeping Beauty to improve a technology known as gene therapy, which aims to manipulate genes to correct for molecular flaws that cause disease.

The work, detailed in a paper published online in Gene Therapy, has allowed scientists at the University of Rochester Medical Center to reach a long-sought goal: Shuttling into brain cells a relatively large gene that can remain on for an extended period of time.

"We've broken what is in effect a size barrier – a limit to how much genetic material we can put into the nucleus of a cell and keep functioning for a long period of time," said neuroscientist William Bowers, Ph.D., a scientist in the Center for Neural Development and Disease and the leader of the team. "That opens up more diseases to possible treatment with gene therapy."

The molecular rendezvous of Sleeping Beauty and herpes in human brain cells could spell good news in the search for treatments for horrific brain diseases known as pediatric leukodystrophies, or a group of diseases known as lysosomal storage disorders. In many of these diseases, even though just a single gene or protein is defective, the effects are devastating – the diseases slowly rob children of their brain cells and are often fatal after years of severe symptoms.

The findings bolster the tools that researchers have when approaching certain diseases, said Bowers, including Usher syndrome, which results in deafness and vision loss; Niemann-Pick disease Type C, a fatal childhood lysosomal storage disorder; and von Willebrand disease, an inherited disease that causes extensive, chronic bleeding.

"The field of gene therapy is just beginning to yield some successes for patients. Improvements like this are crucial for increasing the number of patients who might benefit from such an approach," said Bowers, who is an associate professor of Neurology, Microbiology and Immunology, and of Pharmacology and Physiology.

The research is part of a decades-long endeavor by scientists trying to get the right genes into the right cells at the right time to improve human health.

In the new work, scientists dramatically increased the size of the "genetic payload" they can deliver to brain cells compared to some conventional techniques, nearly tripling the amount of genetic material by some measures. They hope to deliver even bigger genes in the future. The team did this by bringing together in a new way two molecular players, herpes and Sleeping Beauty, which are commonly used in molecular technology.

For years Bowers' team has been using the herpes virus – HSV-1, the type that causes cold sores – to shuttle genes into cells. Viruses like herpes are adept at infecting human cells, and scientists like Bowers use such viruses to carry into cells genes that would help people who are sick. Bowers and colleagues modify the viruses extensively, removing the portions that could make a person sick and using the portions that the virus uses to gain access to human cells.

Many scientists use other viruses, such as lentiviruses or a cold-related virus known as adeno-associated virus (AAV), to do a similar job. Each virus has its strengths and weaknesses when it comes to gene therapy. Herpes, for instance, readily infects cells, and it can carry a huge amount of genetic material, typically 15 to 30 times the amount of DNA that other viruses can carry into a cell.

But herpes as a genetic tool has a couple of big weaknesses. While the virus can deliver DNA into the nucleus of a cell, the genetic payload it carries does not become part of the package of genes that cells pass from one to another. Simply put, herpes cannot integrate the new DNA into the host genome. Instead, the DNA is adrift in the nucleus, where it's silenced within a few weeks. The short time span spells trouble when scientists are trying to treat a disease that requires the genes to be active for months or years.

That's where Sleeping Beauty comes in.

In molecular biology, Sleeping Beauty is a mobile genetic element that jumps into and out of longer segments of DNA. It's normally silent, but years ago a team of scientists was able to activate or "awaken" the snippet – hence, Sleeping Beauty. Since Sleeping Beauty actually integrates segments of DNA into mammalian genomes, it sidesteps the main difficulties that herpes encounters inside a cell: Genes integrated within the cell's chromosomes by Sleeping Beauty operate for much longer periods of time. The drawback: The molecule can insert only small snippets of DNA.

So the Rochester team brought herpes and Sleeping Beauty together in an attempt to get the best of both worlds: Delivery of the bigger genetic package made possible by herpes, and the integration of the DNA into the host genome made possible by Sleeping Beauty.

And that's exactly what happened. In the tag-team approach funded by the National Institute of Neurological Disorders and Stroke, herpes gets the genetic package into the right neighborhood, the cell's nucleus, and then Sleeping Beauty delivers the package precisely where it needs to go to be most effective – into the cellular genome.

In the current experiments, the herpes virus carried into cell nuclei the gene for green fluorescent protein, which allows scientists to track where the gene is active. The team also outfitted the herpes package with special molecular signals that Sleeping Beauty would recognize. Separately, the team introduced Sleeping

Beauty into the cells. When the two met, Sleeping Beauty transferred the gene for GFP from the herpes package to the genome of the human cells, where the gene was stably expressed.

The team has previously shown that the Sleeping Beauty/herpes combination works efficiently in brain cells known as neural progenitor cells, which go on to form brain cells known as neurons. Modifying these cells – perhaps by adding a gene that creates a protein crucial for health – is one technique scientists are experimenting with to try to treat several brain diseases that are currently untreatable.

The gene segment used in the experiment described in Gene Therapy was about 12 kilobases long, which is larger than the limit of either AAV (4.5 kb) or lentiviruses (9 kb). Those few kilobases matter, a lot. The ability to transfer bigger genes gives scientists room to try to address more diseases with a gene therapy approach. The added space also makes it possible to include more regulatory elements – instructions that help determine how and when genes are turned on or off. This allows scientists to package additional safety directives, in the form of more DNA, along with the gene designed to treat the disease.

In addition to de Silva and Bowers, authors include technical associates Michael Mastrangelo, Louis T. Lotta Jr., and Clark Burris, as well as Howard J. Federoff, M.D., Ph.D., a former Rochester faculty member who is now executive vice president for health sciences at Georgetown University.

Egyptian Eyeliner May Have Warded Off Disease

By Katie Cottingham ScienceNOW Daily News

Clearly, ancient Egyptians didn't get the memo about lead poisoning. Their eye makeup was full of the stuff. Although today we know that lead can cause brain damage and miscarriages, the Egyptians believed that lead-based cosmetics protected against eye diseases. Now, new research suggests that they may have been on to something.

Previous work indicates that the Egyptians added lead to their cosmetics on purpose. When analytical chemist Philippe Walter and colleagues at CNRS and the Louvre Museum in Paris analyzed the composition of several samples of the Egyptians' famous bold, black eyeliner in the Louvre's collection, they identified two types of lead salt not found in nature. That means that ancient Egyptians must have synthesized them. But making lead salt is a tricky, delicate process that requires tending for weeks--and unlike other common makeup components, the salts are not glossy. So why did they bother?

Ancient manuscripts gave the scientists a clue. It turns out that in those days, people made lead salts and used them as treatments for eye ailments, scars, and discolorations. When Walter told analytical chemist Christian Amatore of the Ecole Normale Supérieure in Paris about the findings, Amatore says he was intrigued because lead is now known to have so many toxic effects.

To see if the lead might confer any health benefits, Amatore, Walter, and colleagues added lead salts to human skin cells called keratinocytes, which were grown in the lab. The researchers hypothesized that the lead would stress the cells and cause them to make hydrogen peroxide, nitric oxide, and other compounds involved in the body's immune response. And indeed, cells treated with lead began pumping out more nitric oxide than did control cells, the team reports online in Analytical Chemistry.

Amatore says that nitric oxide sets off a series of biochemical processes in the body that ultimately send immune cells called macrophages to the site of infection, where they engulf invading organisms. That's probably not what's happening in keratinocytes, says immunologist Martin Olivier of McGill University in Montreal, Canada, who was not involved in the study. It's unlikely that macrophages or other immune cells would exit the body and burst through the skin to fight off infectious agents at the surface, he notes. Instead, nitric oxide released by keratinocytes could directly kill eye-disease-causing bacteria on the skin or near the eye by breaking down a bacterium's structure or DNA. Another plausible scenario, says Olivier, is that lead itself could directly stimulate immune cells already present in the eyelid.

This potential benefit of lead is contrary to everything we know about the substance, but it could fit the model of hormesis, says epidemiologist Jennifer Weuve of Rush University Medical Center in Chicago, Illinois. "The premise behind hormesis is that, for certain exposures, there might be a window where the exposure is harmful but also one where it's helpful," she explains.

Still, Weuve cautions against adding lead to the eyeliner in your makeup case. Modern people live a lot longer than did the ancient Egyptians--many of whom died in their 30s--and the dangers of prolonged lead exposure outweigh any antimicrobial benefit, she says. Indeed, the Egyptians' eyeliner strategy would have backfired on them if they had lived long enough, she notes, as long-term exposure to lead may increase the risk of developing cataracts.

Heavy Brows, High Art?: Newly Unearthed Painted Shells Show Neandertals Were Homo sapiens's Mental Equals

A discovery of painted shells shows that Neandertals were capable of symbolism, sweeping away age-old thinking that they were stupid

By Charles Q. Choi

Newly discovered painted scallops and cockleshells in Spain are the first hard evidence that Neandertals made jewelry. These findings suggest humanity's closest extinct relatives might have been capable of symbolism, after all.

Body ornaments made of painted and pierced seashells dating back 70,000 to 120,000 years have been found in Africa and the Near East for years, and serve as evidence of symbolic thought among the earliest modern humans (Homo sapiens).

SHELL GAME: The two sides of a perforated upper half-valve of Pecten maximus from Middle Paleolithic level I-k of Cueva Anton (height: 120 mm). The external side (right, in the picture) was painted with an orange mix of goethite and hematite, either to regain the original appearance or to make it the same color as the internal side, which remained its natural red **Joao Zilhao**

The absence of similar finds in Europe at that time, when it was Neandertal territory, has supported the notion that they lacked symbolism, a potential sign of mental inferiority that might help explain why modern humans eventually replaced them.

Although hints of Neandertal art and jewelry have cropped up in recent years, such as pierced and grooved animal-tooth pendants or a decorated limestone slab on the grave of a child, these have often been shrugged off as artifacts mixed in from modern humans, imitation without understanding, or ambiguous in nature. Now archaeologist João Zilhão at the University of Bristol in England and his colleagues have found 50,000-year-old jewelry at two caves in southeastern Spain, art dating back 10,000 years before the fossil record reveals evidence of modern humans entering Europe.

At the Cueva (Cave) Antón, the scientists unearthed a pierced king scallop shell (Pecten maximus) painted with orange pigment made of yellow goethite and red hematite collected some five kilometers from that site. In material collected from the Cueva de los Aviones, alongside quartz and flint artifacts were bones from horses, deer, ibex, rabbits and tortoises as well as seashells from edible cockles (Glycymeris insubrica), mussels, limpets and snails; the researchers also discovered two pierced dog-cockleshells painted with traces of red hematite pigment. No dyes were found on the food shells or stone tools, suggesting the jewelry was not just painted at random.

In addition, Zilhão and his colleagues saw an orange pigment–coated horse bone at Aviones that might have served as a pin to prepare or apply mineral dyes or to pierce painted hides as well as three thorny oyster (Spondylus gaederopus) shells that might have served as paint cups, holding as they did residues of hematite, charcoal, dolomite and pyrite. The researchers also came across lumps of red and yellow pigments there that had to have come from afield, such as the area of La Unión three to five kilometers to the northwest, which has served as a gold and silver mining district since antiquity.

These discoveries, in combination with earlier findings hinting at Neandertal ornaments and funerary practices, suggest "Neandertals had the same capabilities for symbolism, imagination and creativity as modern humans," Zilhão says. Anthropologist Erik Trinkaus at Washington University in Saint Louis, who did not take part in this study, notes, "I'm hoping that this will start to bury the idea that's been around for 100 years—that Neandertals died out because they were stupid."

The rarity of such finds, however, thus far might still suggest to some that Neandertals were not great minds, "the number of sites that have these pigmented shells from either Neandertals or modern humans is something that you can count on the fingers of one hand," Trinkaus says. "These finds are very thin on the landscape."

Instead of Neandertals and modern humans developing jewelry independently, two intriguing possibilities this discovery raises are that Neandertals taught our ancestors art - or vice versa.

"I have argued that the archaeological culture associated with Europe's earliest modern humans, the Proto-Aurignacian, features a mix of ornaments of different traditions: small, basket-shaped beads similar to those known from South Africa since about 75,000 years ago, likely to have been used as parts of composite beadworks, and pierced animal teeth, likely to have been used as isolated pendants," Zilhão says.

Although tooth pendants are entirely unknown in the modern humans of Africa and the Near East prior to their dispersal into Europe, Zilhão adds they are precisely the kinds of ornaments linked with the Châtelperronian industry in France during the upper Paleolithic period of the Stone Age, which is linked with the Neandertals. "This mix indicates a significant level of cultural exchange at the time of contact, and the persistence in early modern human cultures of Europe of items and traditions of Neandertal origin," he says.

The scientists are set to detail their findings online January 11 in the Proceedings of the National Academy of Sciences.

Suzaku finds 'fossil' fireballs from supernovae

Studies of two supernova remnants using the Japan-U.S. Suzaku observatory have revealed never-before-seen embers of the high-temperature fireballs that immediately followed the explosions. Even after thousands of years, gas within these stellar wrecks retain the imprint of temperatures 10,000 times hotter than the sun's surface.

"This is the first evidence of a new type of supernova remnant -- one that was heated right after the explosion," said Hiroya Yamaguchi at the Institute of Physical and Chemical Research in Japan.

A supernova remnant usually cools quickly due to rapid expansion following the explosion. Then, as it sweeps up tenuous interstellar gas over thousands of years, the remnant gradually heats up again.

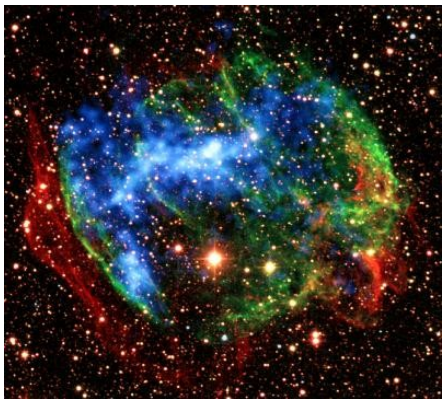
Capitalizing on the sensitivity of the Suzaku satellite, a team led by Yamaguchi and Midori Ozawa, a graduate student at Kyoto University, detected unusual features in the X-ray spectrum of IC 443, better known to amateur astronomers as the Jellyfish Nebula.

The remnant, which lies some 5,000 light-years away in the constellation Gemini, formed about 4,000 years ago. The X-ray emission forms a roughly circular patch in the northern part of the visible nebulosity.

Suzaku's X-ray Imaging Spectrometers (XISs) separate X-rays by energy in much the same way as a prism separates light into a rainbow of colors. This allows astronomers to tease out the types of processes responsible for the radiation.

Some of the X-ray emission in the Jellyfish Nebula arises as fast-moving free electrons sweep near the nuclei of atoms. Their mutual attraction deflects the electrons, which then emit X-rays as they change course. The electrons have energies corresponding to a temperature of about 12 million degrees Fahrenheit (7 million degrees Celsius).

Several bumps in the Suzaku spectrum were more puzzling. "These structures indicate the presence of a large amount of silicon and sulfur atoms from which all electrons have been stripped away," Yamaguchi said. These "naked" nuclei produce X-rays as they recapture their lost electrons.



But removing all electrons from a silicon atom requires temperatures higher than about 30 million degrees F (17 million C); hotter still for sulfur atoms. "These ions cannot form in the present-day remnant," Yamaguchi explained. "Instead, we're seeing ions created by the enormous temperatures that immediately followed the supernova."

The team suggests that the supernova occurred in a relatively dense environment, perhaps in a cocoon of the star's own making. As a massive star ages, it sheds material in the form of an outflow called a stellar wind and creates a cocoon of gas and dust. When the star explodes, the blast wave traverses the dense cocoon and heats it to temperatures as high as 100 million degrees F (55 million C), or 10,000 times hotter than the sun's surface.

In the supernova remnant W49B, Suzaku found another fossil fireball. It detected X-rays produced when heavily ionized iron atoms recapture an electron. This view combines infrared images from the ground (red, green) with X-ray data from NASA's Chandra X-Ray Observatory (blue). Credit: JAXA/NASA/Suzaku, Tom Bash and John Fox/Adam Block/NOAO/AURA/NSF

Eventually, the shock wave breaks out into true interstellar space, where the gas density can be as low as a single atom per cubic centimeter -- about the volume of a sugar cube. Once in this low-density environment, the young supernova remnant rapidly expands.

The expansion cools the electrons, but it also thins the remnant's gas so much that collisions between particles become rare events. Because an atom may take thousands of years to recapture an electron, the Jellyfish Nebula's hottest ions remain even today, the astronomers reported in the Nov. 1 issue of The Astrophysical Journal. "Suzaku sees the Jellyfish's hot heart," Ozawa said.

The team has already identified another fossil fireball in the supernova remnant known as W49B, which lies 35,000 light-years away in the constellation Aquila. In the Nov. 20 edition of The Astrophysical Journal, Ozawa, Yamaguchi and colleagues report X-ray emission from iron atoms that are almost completely stripped of electrons. Forming these ions requires temperatures in excess of 55 million degrees F (30 million C)-- nearly twice the observed temperature of the remnant's electrons.

Launched on July 10, 2005, Suzaku was developed at the Japanese Institute of Space and Astronautical Science (ISAS), which is part of the Japan Aerospace Exploration Agency (JAXA), in collaboration with NASA and other Japanese and U.S. institutions.

Ancient hominids may have been seafarers

Hand axes excavated on Crete suggest hominids made sea crossings to go 'out of Africa'

By Bruce Bower

ANAHEIM, Calif. — Human ancestors that left Africa hundreds of thousands of years ago to see the rest of the world were no landlubbers. Stone hand axes unearthed on the Mediterranean island of Crete indicate that an ancient Homo species - perhaps Homo erectus - had used rafts or other seagoing vessels to cross from northern Africa to Europe via at least some of the larger islands in between, says archaeologist Thomas Strasser of Providence College in Rhode Island.

Several hundred double-edged cutting implements discovered at nine sites in southwestern Crete date to at least 130,000 years ago and probably much earlier, Strasser reported January 7 at the annual meeting of the American Institute of Archaeology. Many of these finds closely resemble hand axes fashioned in Africa about 800,000 years ago by H. erectus, he says. It was around that time that H. erectus spread from Africa to parts of Asia and Europe.

Until now, the oldest known human settlements on Crete dated to around 9,000 years ago. Traditional theories hold that early farming groups in southern Europe and the Middle East first navigated vessels to Crete and other Mediterranean islands at that time.

“We’re just going to have to accept that, as soon as hominids left Africa, they were long-distance seafarers and rapidly spread all over the place,” Strasser says. Other researchers have controversially suggested that H. erectus navigated rafts across short stretches of sea in Indonesia around 800,000 years ago and that Neandertals crossed the Strait of Gibraltar perhaps 60,000 years ago.

Questions remain about whether African hominids used Crete as a stepping stone to reach Europe or, in a Stone Age Gilligan’s Island scenario, accidentally ended up on Crete from time to time when close-to-shore rafts were blown out to sea, remarks archaeologist Robert Tykot of the University of South Florida in Tampa. Only in the past decade have researchers established that people reached Crete before 6,000 years ago, Tykot says.

Strasser’s team cannot yet say precisely when or for what reason hominids traveled to Crete. Large sets of hand axes found on the island suggest a fairly substantial population size, downplaying the possibility of a Gilligan Island’s scenario, in Strasser’s view.

In excavations conducted near Crete’s southwestern coast during 2008 and 2009, Strasser’s team unearthed hand axes at caves and rock shelters. Most of these sites were situated in an area called Preveli Gorge, where a river has gouged through many layers of rocky sediment.

At Preveli Gorge, Stone Age artifacts were excavated from four terraces along a rocky outcrop that overlooks the Mediterranean Sea. Tectonic activity has pushed older sediment above younger sediment on Crete, so 130,000-year-old artifacts emerged from the uppermost terrace. Other terraces received age estimates of 110,000 years, 80,000 years and 45,000 years.

These minimum age estimates relied on comparisons of artifact-bearing sediment to sediment from sea cores with known ages. Geologists are now assessing whether absolute dating techniques can be applied to Crete’s Stone Age sites, Strasser says.

Intriguingly, he notes, hand axes found on Crete were made from local quartz but display a style typical of ancient African artifacts.

“Hominids adapted to whatever material was available on the island for tool making,” Strasser proposes. “There could be tools made from different types of stone in other parts of Crete.”

Strasser has conducted excavations on Crete for the past 20 years. He had been searching for relatively small implements that would have been made from chunks of chert no more than 11,000 years ago. But a current team member, archaeologist Curtis Runnels of Boston University, pointed out that Stone Age folk would likely have favored quartz for their larger implements. “Once we started looking for quartz tools, everything changed,” Strasser says.