

## History in the Remaking

***A temple complex in Turkey that predates even the pyramids is rewriting the story of human evolution.***

**By Patrick Symmes** NEWSWEEK

They call it potbelly hill, after the soft, round contour of this final lookout in southeastern Turkey. To the north are forested mountains. East of the hill lies the biblical plain of Harran, and to the south is the Syrian border, visible 20 miles away, pointing toward the ancient lands of Mesopotamia and the Fertile Crescent, the region that gave rise to human civilization. And under our feet, according to archeologist Klaus Schmidt, are the stones that mark the spot - the exact spot - where humans began that ascent.



***A pillar at the Göbekli Tepe temple near Sanliurfa, Turkey, the oldest known temple in the world*** Berthold Steinhilber / Laif-Redux

Standing on the hill at dawn, overseeing a team of 40 Kurdish diggers, the German-born archeologist waves a hand over his discovery here, a revolution in the story of human origins. Schmidt has uncovered a vast and beautiful temple complex, a structure so ancient that it may be the very first thing human beings ever built. The site isn't just old, it redefines old: the temple was built 11,500 years ago - a staggering 7,000 years before the Great Pyramid, and more than 6,000 years before Stonehenge first took shape. The ruins are so early that they predate villages, pottery, domesticated animals, and even agriculture - the first embers of civilization. In fact, Schmidt thinks the temple itself, built after the end of the last Ice Age by hunter-gatherers, became that ember - the spark that launched mankind toward farming, urban life, and all that followed.

Göbekli Tepe - the name in Turkish for "potbelly hill" - lays art and religion squarely at the start of that journey. After a dozen years of patient work, Schmidt has uncovered what he thinks is definitive proof that a huge ceremonial site flourished here, a "Rome of the Ice Age," as he puts it, where hunter-gatherers met to build a complex religious community. Across the hill, he has found carved and polished circles of stone, with terrazzo flooring and double benches. All the circles feature massive T-shaped pillars that evoke the monoliths of Easter Island.

Though not as large as Stonehenge - the biggest circle is 30 yards across, the tallest pillars 17 feet high - the ruins are astonishing in number. Last year Schmidt found his third and fourth examples of the temples. Ground-penetrating radar indicates that another 15 to 20 such monumental ruins lie under the surface. Schmidt's German-Turkish team has also uncovered some 50 of the huge pillars, including two found in his most recent dig season that are not just the biggest yet, but, according to carbon dating, are the oldest monumental artworks in the world.

The new discoveries are finally beginning to reshape the slow-moving consensus of archeology. Göbekli Tepe is "unbelievably big and amazing, at a ridiculously early date," according to Ian Hodder, director of Stanford's archeology program. Enthusing over the "huge great stones and fantastic, highly refined art" at Göbekli, Hodder - who has spent decades on rival Neolithic sites - says: "Many people think that it changes everything...It overturns the whole apple cart. All our theories were wrong."

Schmidt's thesis is simple and bold: it was the urge to worship that brought mankind together in the very first urban conglomerations. The need to build and maintain this temple, he says, drove the builders to seek stable food sources, like grains and animals that could be domesticated, and then to settle down to guard their new way of life. The temple begat the city.

This theory reverses a standard chronology of human origins, in which primitive man went through a "Neolithic revolution" 10,000 to 12,000 years ago. In the old model, shepherds and farmers appeared first, and then created pottery, villages, cities, specialized labor, kings, writing, art, and - somewhere on the way to the airplane - organized religion. As far back as Jean-Jacques Rousseau, thinkers have argued that the social compact of cities came first, and only then the "high" religions with their great temples, a paradigm still taught in American high schools.

Religion now appears so early in civilized life - earlier than civilized life, if Schmidt is correct - that some think it may be less a product of culture than a cause of it, less a revelation than a genetic inheritance. The archeologist Jacques Cauvin once posited that "the beginning of the gods was the beginning of agriculture," and Göbekli may prove his case.

The builders of Göbekli Tepe could not write or leave other explanations of their work. Schmidt speculates that nomadic bands from hundreds of miles in every direction were already gathering here for rituals, feasting, and initiation rites before the first stones were cut. The religious purpose of the site is implicit in its size and location. "You don't move 10-ton stones for no reason," Schmidt observes. "Temples like to be on high sites," he adds, waving an arm over the stony, round hilltop. "Sanctuaries like to be away from the mundane world." Unlike most discoveries from the ancient world, Göbekli Tepe was found intact, the stones upright, the order and artistry of the work plain even to the un-trained eye. Most startling is the elaborate carving found on about half of the 50 pillars Schmidt has unearthed. There are a few abstract symbols, but the site is almost covered in graceful, naturalistic sculptures and bas-reliefs of the animals that were central to the imagination of hunter-gatherers. Wild boar and cattle are depicted, along with totems of power and intelligence, like lions, foxes, and leopards. Many of the biggest pillars are carved with arms, including shoulders, elbows, and jointed fingers. The T shapes appear to be towering humanoids but have no faces, hinting at the worship of ancestors or humanlike deities. "In the Bible it talks about how God created man in his image," says Johns Hopkins archeologist Glenn Schwartz. Göbekli Tepe "is the first time you can see humans with that idea, that they resemble gods."

The temples thus offer unexpected proof that mankind emerged from the 140,000-year reign of hunter-gatherers with a ready vocabulary of spiritual imagery, and capable of huge logistical, economic, and political efforts. A Catholic born in Franconia, Germany, Schmidt wanders the site in a white turban, pointing out the evidence of that transition. "The people here invented agriculture. They were the inventors of cultivated plants, of domestic architecture," he says.

Göbekli sits at the Fertile Crescent's northernmost tip, a productive borderland on the shoulder of forests and within sight of plains. The hill was ideally situated for ancient hunters. Wild gazelles still migrate past twice a year as they did 11 millennia ago, and birds fly overhead in long skeins. Genetic mapping shows that the first domestication of wheat was in this immediate area - perhaps at a mountain visible in the distance - a few centuries after Göbekli's founding. Animal husbandry also began near here - the first domesticated pigs came from the surrounding area in about 8000 B.C., and cattle were domesticated in Turkey before 6500 B.C. Pottery followed. Those discoveries then flowed out to places like Çatalhöyük, the oldest-known Neolithic village, which is 300 miles to the west.

The artists of Göbekli Tepe depicted swarms of what Schmidt calls "scary, nasty" creatures: spiders, scorpions, snakes, triple-fanged monsters, and, most common of all, carrion birds. The single largest carving shows a vulture poised over a headless human. Schmidt theorizes that human corpses were ex-posed here on the hilltop for consumption by birds - what a Tibetan would call a sky burial. Sifting the tons of dirt removed from the site has produced very few human bones, however, perhaps because they were removed to distant homes for ancestor worship. Absence is the source of Schmidt's great theoretical claim. "There are no traces of daily life," he explains. "No fire pits. No trash heaps. There is no water here." Everything from food to flint had to be imported, so the site "was not a village," Schmidt says. Since the temples predate any known settlement anywhere, Schmidt concludes that man's first house was a house of worship: "First the temple, then the city," he insists.

Some archeologists, like Hodder, the Neolithic specialist, wonder if Schmidt has simply missed evidence of a village or if his dating of the site is too precise. But the real reason the ruins at Göbekli remain almost unknown, not yet incorporated in textbooks, is that the evidence is too strong, not too weak. "The problem with this discovery," as Schwartz of Johns Hopkins puts it, "is that it is unique." No other monumental sites from the era have been found. Before Göbekli, humans drew stick figures on cave walls, shaped clay into tiny dolls, and perhaps piled up small stones for shelter or worship. Even after Göbekli, there is little evidence of sophisticated building. Dating of ancient sites is highly contested, but Çatalhöyük is probably about 1,500 years younger than Göbekli, and features no carvings or grand constructions. The walls of Jericho, thought until now to be the oldest monumental construction by man, were probably started more than a thousand years after Göbekli. Huge temples did emerge again - but the next unambiguous example dates from 5,000 years later, in southern Iraq.

The site is such an outlier that an American archeologist who stumbled on it in the 1960s simply walked away, unable to interpret what he saw. On a hunch, Schmidt followed the American's notes to the hilltop 15 years ago, a day he still recalls with a huge grin. He saw carved flint everywhere, and recognized a Neolithic quarry on an adjacent hill, with unfinished slabs of limestone hinting at some monument buried nearby. "In one minute - in one second - it was clear," the bearded, sun-browned archeologist recalls. He too considered walking away, he says, knowing that if he stayed, he would have to spend the rest of his life digging on the hill.

Now 55 and a staff member at the German Archaeological Institute, Schmidt has joined a long line of his countrymen here, reaching back to Heinrich Schliemann, the discoverer of Troy. He has settled in, marrying a

Turkish woman and making a home in a modest "dig house" in the narrow streets of old Urfa. Decades of work lie ahead.

Disputes are normal at the site - the workers, Schmidt laments, are divided into three separate clans who feud constantly. ("Three groups," the archeologist says, exasperated. "Not two. Three!") So far Schmidt has uncovered less than 5 percent of the site, and he plans to leave some temples untouched so that future researchers can examine them with more sophisticated tools.

Whatever mysterious rituals were conducted in the temples, they ended abruptly before 8000 B.C., when the entire site was buried, deliberately and all at once, Schmidt believes. The temples had been in decline for a thousand years - later circles are less than half the size of the early ones, indicating a lack of resources or motivation among the worshippers. This "clear digression" followed by a sudden burial marks "the end of a very strange culture," Schmidt says. But it was also the birth of a new, settled civilization, humanity having now exchanged the hilltops of hunters for the valleys of farmers and shepherds. New ways of life demand new religious practices, Schmidt suggests, and "when you have new gods, you have to get rid of the old ones."

### **AAN guideline evaluates treatments for muscle cramps**

ST. PAUL, Minn. – A new guideline from the American Academy of Neurology recommends that the drug quinine, although effective, should be avoided for treatment of routine muscle cramps due to uncommon but serious side effects. The guideline is published in the February 23, 2010, issue of *Neurology*®, the medical journal of the American Academy of Neurology.

"It's important for people to know that quinine should be avoided since the drug is still available in some countries," said lead guideline author Hans D. Katzberg, MD, of Stanford University and a member of the American Academy of Neurology. "Quinine should be considered only when cramps are very disabling, when no other drugs relieve the symptoms, and when side effects are carefully monitored. It should also be used only after the affected person is informed about the potentially serious side effects."

The guideline found that naftidrofuryl, diltiazem and vitamin B complex may be considered for use in the treatment of muscle cramps, but more research is needed on their safety and effectiveness.

The guideline authors also reviewed studies on the use of calf stretching to treat muscle cramps, but there was not enough evidence to determine whether it is an effective therapy.

Muscle cramps are involuntary contractions, or tightening, of a muscle or muscle group. They are usually painful. Muscle cramps occur with neurologic disorders such as amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and peripheral neuropathy. They also occur with other conditions, such as hypothyroidism and low calcium levels in the blood.

The guideline did not evaluate treatments for muscle cramps due to muscle diseases, kidney diseases, menstruation, pregnancy, or excessive exercise, heat or dehydration.

"If you have muscle cramps, you should see your doctor to determine the cause," Katzberg said. "Sometimes the cramps are due to a serious underlying medical condition that needs treatment."

### **Dry winters linked to seasonal outbreaks of influenza**

The seasonal increase of influenza has long baffled scientists, but a new study published this week in *PLoS Biology* has found that seasonal changes of absolute humidity are the apparent underlying cause of these wintertime peaks. The study also found that the onset of outbreaks might be encouraged by anomalously dry weather conditions, at least in temperate regions.

Scientists have long suspected a link between humidity and seasonal (epidemic) flu outbreaks, but most of the research has focused on relative humidity – the ratio of water vapor content in the air to the saturating level, which varies with temperature. Absolute humidity quantifies the actual amount of water in the air, irrespective of temperature. Though somewhat counter-intuitive, absolute humidity is much higher in the summer. "In some areas of the country, a typical summer day can have four times as much water vapor as a typical winter day – a difference that exists both indoors and outdoors," said Jeffrey Shaman, an Oregon State University atmospheric scientist and lead author.

The researchers used 31 years of observed absolute humidity conditions to drive a mathematical model of influenza and found that the model simulations reproduced the observed seasonal cycle of influenza throughout the United States. They first examined influenza in New York, Washington, Illinois, Arizona and Florida, and found that the absolute humidity conditions in those states all produced model-simulated seasonal outbreaks of influenza that correlated well with the observed seasonal cycle of influenza within each state. Shaman and colleagues then extended their model to the rest of the continental U.S. and were able to reproduce the seasonal cycle of influenza elsewhere. They also discovered that the start of many influenza outbreaks during the winter was directly preceded by a period of weather that was drier than usual.

"This dry period is not a requirement for triggering an influenza outbreak, but it was present in 55 to 60 percent of the outbreaks we analyzed so it appears to increase the likelihood of an outbreak," said Shaman. "The virus response is almost immediate; transmission and survival rates increase and about 10 days later, the observed influenza mortality rates follow."

Though the findings by Shaman and his colleagues build a strong case for absolute humidity's role in influenza outbreaks, it does not mean you can predict where influenza will strike next. As Shaman emphasized, "Certainly absolute humidity may affect the survival of the influenza virus, but the severity of outbreaks is also dependent upon other variables, including the type of virus and its virulence, as well as host-mediated factors such as the susceptibility of a population and rates of population mixing and person-to-person interactions."

Marc Lipsitch, a professor of epidemiology at the Harvard School of Public Health and senior author on the new study, said the new analysis may have implications for other diseases. "Seasonality of infectious diseases is one of the oldest observations in human health, but the mechanisms – especially for respiratory diseases like flu – have been unclear," Lipsitch said. "This study, in combination with Shaman and (Melvin) Kohn's earlier analysis of laboratory experiments on flu transmission, points to variation in humidity as a major cause of seasonal cycles in flu."

"Seasonal variation in flu, in turn, helps to explain variation in other infectious diseases – such as pneumococcal and meningococcal disease – as well as seasonal variation in heart attacks, strokes and other important health outcomes."

Lipsitch directs the Center for Communicable Disease Dynamics, of which Shaman is a member. This study and the center are supported by the Models of Infectious Disease Agent Study, or "MIDAS Program," of the U.S. National Institute of General Medical Sciences.

"The discovery of a link between influenza outbreaks and absolute humidity could have a major impact on the development of strategies for limiting the spread of infection," said Irene Eckstrand, who oversees the MIDAS program. "Understanding why outbreaks arise is an important first step toward containing or even preventing them, so it is essential for scientists to follow up on this intriguing connection."

*Additional collaborators on the study published in PLoS Biology were Virginia Pitzer and Bryan Grenfell, Princeton University; and Cecile Viboud, National Institutes of Health, Fogarty International Center. The study builds on previous laboratory research that found influenza virus survival rates increased greatly as absolute humidity decreased.*

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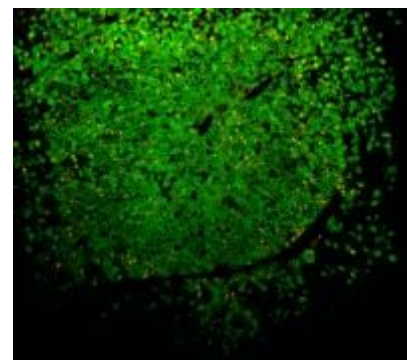
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<http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.1000316>

### **The mouse with a human liver: A new model for the treatment of liver disease**

LA JOLLA, CA-How do you study-and try to cure in the laboratory-an infection that only humans can get? A team led by Salk Institute researchers does it by generating a mouse with an almost completely human liver. This "humanized" mouse is susceptible to human liver infections and responds to human drug treatments, providing a new way to test novel therapies for debilitating human liver diseases and other diseases with liver involvement such as malaria.

"We found that, not only can we infect our humanized mouse with Hepatitis B and Hepatitis C, but we can then successfully treat this infection using typical drugs," explains first author Karl-Dimiter Bissig, M.D. Ph.D, an internist and post-doctoral researcher in the Laboratory of Genetics. "As a physician, I understand the importance of this type of bench-to-bedside research. This study shows a real application for our mouse model, making it relevant from both an academic and a clinical perspective." The Salk researchers' findings will be published in the Feb. 22, 2010 online edition of the *Journal of Clinical Investigation*.



***Mice whose own liver cells have been replaced with human hepatocytes (shown in green) can be successfully infected with hepatitis B virus (shown in red) providing a new way to test novel therapies for debilitating human liver diseases.***

Courtesy of Dr. Karl-Dimiter Bissig, Salk Institute for Biological Studies

Host-pathogen specificity is both a blessing and a curse-preventing widespread infection but making successful treatments harder to find. For example, Hepatitis B and Hepatitis C can only infect humans and

chimpanzees, and although this species barrier prevents us from being susceptible to every infection out there, the flipside is that finding treatments for human infections can be extremely difficult.

This is particularly true when it comes to liver infections. The usual approach is to grow human cells in a dish, to infect and try to treat them there, but this is not possible with liver cells or hepatocytes. "Human hepatocytes are almost impossible to work with as they don't grow and are hard to maintain in culture," explains senior author Inder Verma, Ph.D., a professor in the Laboratory of Genetics and holder of the Irwin and Joan Jacobs Chair in Exemplary Life Science.

And since small animals cannot be infected with Hepatitis C, they cannot be used to test drugs that may cure this disease. What's more, species differences mean that drugs that appear to be effective and non-toxic in animal models sometimes prove to be toxic to humans, and vice versa. Mice whose own hepatocytes have been replaced with human liver cells provide a solution to all these hurdles.

Explains Verma, "This robust model system opens the door to utilize human hepatocytes for purposes that were previously impossible. This chimeric mouse can be used for drug testing and gene therapy purposes, and in the future, may also be used to study liver cancers."

The Salk team had previously generated a mouse with a partially "humanized" liver, but wanted to improve their method to achieve almost complete transformation. They use a special mouse that has liver problems of its own, but whose problems can be kept in check with a drug called NBTC. Taking away NBTC allows human hepatocytes to take hold and populate the mouse liver with human cells.

The team perfected this system so that nearly 95% of the liver cells are of human origin, but the important question was whether they would behave like a human livers. To test this, the researchers exposed the mice to Hepatitis B and Hepatitis C and found that, unlike normal mice, which are resistant to these viruses, the chimeric animals developed the disease.

More importantly, using pegylated interferon alpha 2a-the standard treatment for Hepatitis C-the researchers showed that the "humanized" liver inside the mouse responds just like a normal human liver. The team also tested additional experimental drugs and found that they too behaved as they did in humans.

"This shows that our chimeric mouse model is medically relevant and can be used to validate novel drugs in a pre-clinical setting," says Bissig. "This is great news as it provides us with a tool with which we can examine many human hepatotropic pathogens, including malaria. In the future, it also has potential applications for regenerative medicine; allowing confirmation of the true hepatocyte nature of cells prior to human transplantation."

The methodology of generating these mice is freely available to the research community.

*The work was funded in part by the National Institutes of Health, the American Cancer Society, the Leducq Foundation, the Ellison Medical Foundation, the Frances C Berger Foundation, Ipsen Biomeasure and Sanofi-Aventis.*

*Other than Bissig and Verma, contributors to this work were Phu Tran and Tam T. Le from the Laboratory of Genetics at the Salk Institute, and Stefan F. Wieland, Masanori Isogawa, and Francis V. Chisari from The Scripps Research Institute, San Diego.*

## **Is an animal's agility affected by the position of its eyes?**

### ***Does the need for speed shape the arrangement of the eyes and inner ear?***

New research from scientists in Liverpool has revealed the relationship between agility and vision in mammals. The study, published today in the Journal of Anatomy, sampled 51 species to compare the relationship between agility and vision between frontal eyed species, such as cats, to lateral-eyed mammals such as rabbits, to establish if the positioning of the eyes resulted in limitations to speed and agility.

"Footballers do it, cheetahs do it, and even sedentary academics can do it. We all have the ability to visually track an object whilst on the move and you don't give a second thought to the effort involved," explained co-author Dr Nathan Jeffery from the University of Liverpool. "As you walk or run your head swings up and down, tilts from side to side and rotates. Three semicircular canals of fluid found on each side of the skull sense these movements, one for each direction. These then send signals via the brain to three pairs of muscles that move the eyeball in the opposite direction and ensure that you can keep your eye on the ball, gazelle or the beer in your hand."

This process, known as the vestibulo-ocular reflex, is affected by the directions sensed by the canals and the pull directions of the eye muscles. In mammals, the eyes can be on the side of the head, as with rabbits, or at the front of the head like in cats, however the position of the canals is basically the same. In some mammals the brain must do extra calculations to adjust the signal from the canals to match the different pull directions of the eye muscles.

"In our study we wanted to find out if these extra calculations placed any limitations on how fast an animal could move," said co-author Phillip Cox. "We asked if there could be a point whereby, if an animal moves too

quickly it could result in the brain being unable to adjust the signals from canal to muscle planes, which in turn would result in blurred vision." The work was funded by the Biotechnology and Biological Sciences Research Council.

The team used MRI scanners to analyse the arrangement of canals and eye muscles in 51 species of mammal including giraffes, camels and zebra, tree shrews, bats and sloths. Astonishingly, the team found that the position of canals and eye muscles had no effect on the ability to see clearly at speed. In theory, a Sloth could travel as fast as a Cheetah without blurring its vision.

The team also found evidence suggesting that the role of the extraocular muscles switches with changes of eye position. For instance, muscles that make up-down compensatory movements in frontal-eyed species appear aligned for torsional movements in lateral-eyed species. Before this, scientists had assumed that major rewiring of the connections was essential to adapt the reflex to changes of eye position.

"Switching between muscles offers an economical way of adapting the vestibulo-ocular reflex to changes of eye position without major rewiring of the connections or changes of canal orientations," concluded Dr Jeffery. "The mammalian brain can apparently cope with the extra demands placed on it whether the eyes are at the front, side or almost at the back of the head."

### **Killer ants with taste for cat food attack toads**

**Wendy Zukerman**, Australasia reporter

The war against Australia's cane toad has a new tool: cat food. Using cat food to lure meat ants makes the insects more likely to attack large baby cane toads, according to researchers at the University of Sydney. Cane toads were introduced to Australia in 1935 to control beetles destroying sugar cane crops. But they've since spread and become an invasive menace by eating and poisoning native species.

Unlike many native Australian animals, meat ants can eat toads because they can tolerate the toxic chemicals found within them.

Lead researcher Rick Shine told the Australian Broadcasting Corporation: "It's not exactly rocket science. We went out and put out a little bit of cat food right beside the area where the baby toads were coming out of the ponds. The ants rapidly discovered the cat food and thought it tasted great."

But the cat food was just the appetiser. "When the young toads left the water, they were a perfectly-sized snack for the hungry ants," writes BigPond News.

"Meat ants are already killing millions of cane toads," Shine told Queensland's Cairns Post. "We're just looking to make it a bit easier for them."

By attracting many ants to one location, the researchers found that the ants are more likely to attack larger baby toads (*Journal of Applied Ecology*, DOI: 10.1111/j.1365-2664.2010.01773). 98 per cent of the baby toads were attacked by the ants within 2 minutes, and about 70 per cent of those cane toads were killed. "Even the ones that don't die immediately die within a day or so of being attacked," Shine told ABC.

Shine and colleagues have previously demonstrated that luring meat ants wouldn't affect native wildlife because native frogs have evolved with meat ants and so know how to avoid them.

### **New study shows sepsis and pneumonia caused by hospital-acquired infections kill 48,000 patients Cost \$8.1 billion to treat**

Washington D.C. – Two common conditions caused by hospital-acquired infections (HAIs) killed 48,000 people and ramped up health care costs by \$8.1 billion in 2006 alone, according to a study released today in the *Archives of Internal Medicine*. This is the largest nationally representative study to date of the toll taken by sepsis and pneumonia, two conditions often caused by deadly microbes, including the antibiotic-resistant bacteria MRSA. Such infections can lead to longer hospital stays, serious complications and even death.

"In many cases, these conditions could have been avoided with better infection control in hospitals," said Ramanan Laxminarayan, Ph.D., principal investigator for Extending the Cure, a project examining antibiotic resistance based at the Washington, D.C. think-tank Resources for the Future.

"Infections that are acquired during the course of a hospital stay cost the United States a staggering amount in terms of lives lost and health care costs," he said. "Hospitals and other health care providers must act now to protect patients from this growing menace."

Laxminarayan and his colleagues analyzed 69 million discharge records from hospitals in 40 states and identified two conditions caused by health care-associated infections: sepsis, a potentially lethal systemic response to infection and pneumonia, an infection of the lungs and respiratory tract.

The researchers looked at infections that developed after hospitalization. They zeroed in on infections that are often preventable, like a serious bloodstream infection that occurs because of a lapse in sterile technique during surgery, and discovered that the cost of such infections can be quite high: For example, people who

developed sepsis after surgery stayed in the hospital 11 days longer and the infections cost an extra \$33,000 to treat per person.

Even worse, the team found that nearly 20 percent of people who developed sepsis after surgery died as a result of the infection. "That's the tragedy of such cases," said Anup Malani, a study co-author, investigator at Extending the Cure, and professor at the University of Chicago. "In some cases, relatively healthy people check into the hospital for routine surgery. They develop sepsis because of a lapse in infection control - and they can die."

The team also looked at pneumonia, an infection that can set in if a disease-causing microbe gets into the lungs - in some cases when a dirty ventilator tube is used. They found that people who developed pneumonia after surgery, which is also thought to be preventable, stayed in the hospital an extra 14 days. Such cases cost an extra \$46,000 per person to treat. In 11 percent of the cases, the patient died as a result of the pneumonia infection.

According to the authors, HAIs frequently are caused by microbes that defy treatment with common antibiotics. "These superbugs are increasingly difficult to treat and, in some cases, trigger infections that ultimately cause the body's organs to shut down," said Malani.

In 2002, the Centers for Disease Control and Prevention estimated that all hospital-acquired infections were associated with 99,000 deaths per year. While the Extending the Cure study looked at only two of the most common and serious conditions caused by these infections, it also calculated deaths actually caused by, rather than just associated with, infections patients get in the hospital.

Based on their research, study authors were able to estimate the annual number of deaths and health care costs due to sepsis and pneumonia that is actually preventable. "The nation urgently needs a comprehensive approach to reduce the risk posed by these deadly infections," he added. "Improving infection control is a clear way to both improve patient outcomes and lower health care costs."

*This study was supported by the Robert Wood Johnson Foundation's Pioneer Portfolio, which funds innovative ideas that may lead to breakthroughs in the future of health and health care.*

### **Few professionals keep current**

Researchers at the University of Gothenburg and the University of Borås in Sweden have looked at how professionals in different occupational groups seek and use information and keep updated after finishing their education. The results show that teachers seek information they can use in their own teaching and that librarians focus on helping library users find information, while nurses just don't have the time.

The high degree of specialisation in today's work life demands that many occupational groups stay updated on new developments in their fields. In the research project Information seeking in the transition from educational to occupational practice, which is part of the larger research programme LearnIT, researchers interviewed professionals in different sectors to find out how different occupational groups seek information.

#### **Use of information sources**

One thing the researchers looked at was which information sources the studied occupational groups use in work life compared to the groups' information practices during education.

The findings of the study are presented in the writing series Lärande och IT (Learning and IT), which comprises the final reports of the major research programme LearnIT at the University of Gothenburg.

Teachers, nurses and librarians are all part of knowledge-intensive professions that require scientifically based higher education and their occupational practices are partly based on research. Yet, being information literate as a student does not automatically transfer to being information literate in work life.

#### **Teachers looking for teaching material**

When a student graduates and starts teaching professionally, he or she starts seeking for information for different purposes than before. The focus changes from finding research based information to finding information that can be used as teaching material in the daily work with students. Teachers also spend time teaching students how to seek and use information. The interviewed teachers also said that they, as students, did not learn how to remain updated with the latest research as practicing teachers.

#### **Difficult to live up to**

While the interviewed nurses were in fact told that they should keep up with current research as professionals, they said that this is easier said than done. Nursing education is about producing texts while the nursing profession is about attending to patients. The time it takes to keep updated on nursing science research is simply not available, making such practice uncommon.

#### **Part of the job**

Librarians differ from teachers and nurses in that information seeking is essential to the profession. However, similar to the teachers, the interviewed librarians were never trained to stay current. Time at work

earmarked for activities such as literature studies is scarce in all three occupational groups, although the librarians benefit from their extensive access to information resources at work.

### **Culture**

## **Hourglass Figures Affect Men's Brains Like a Drug**

**By Charles Q. Choi**, LiveScience Contributor

Watching a curvaceous woman can feel like a reward in the brain of men, much as drinking alcohol or taking drugs might, research now reveals.

These new findings might help explain the preoccupation men can have toward pornography, scientists added.

Shapely hips in women are linked with fertility and overall health. As such, it makes sense evolutionarily speaking that studies across cultures have shown men typically find hourglass figures sexy.

To explore the roots of this behavior, researchers had 14 men, average age 25, rate how attractive they found pictures of the naked derrieres of seven women before and after cosmetic surgery that gave them more shapely hips. These operations did not reduce weight but just redistributed it, by implanting fat harvested from the waists into the buttocks.

Brain scans of the men revealed that seeing post-surgery women activated parts of the brain linked with rewards, including regions associated with responses to drugs and alcohol.

It might not be especially surprising that evolution wired the male brain to find attractive bodies rewarding. "Hugh Hefner could have told us that by showing us how many zeroes are in his bank account," said researcher Steven Platek, an evolutionary cognitive neuroscientist at Georgia Gwinnett College in Lawrenceville, Georgia. "But there's more to it than buying Playboy, Maxim, or FHM."

For instance, "these findings could help further our understanding pornography addiction and related disorders, such as erectile dysfunction in the absence of pornography," he explained. "These findings could also lend to the scientific inquiry about sexual infidelity."

The scientists also found that changes in a woman's body-mass index or BMI - a common measure of body fat - only really affected brain areas linked to simple visual evaluations of size and shape. This may be evidence that body fat influences judgments of female beauty due more to societal norms than brain wiring. "The media portrays women as wholly too skinny," Platek said. "It's not just about body fat, or body mass index."

### **What do women think?**

Future research could also investigate the effects that attractive figures have on the female brain.

"It turns out women find similar optimally attractive female bodies as attention-grabbing, albeit for different reasons," Platek said. "Women size up other women in an effort to determine their own relative attractiveness and to maintain mate guarding - or, in other words, keep their mate away from optimally designed females."

These findings should not be construed as saying that men are solely programmed by their biology, nor that "women without optimal design should just hang up their mating towel," Platek added.

*Platek and his colleague Devendra Singh detailed their findings online Feb. 5 in the journal PLoS ONE.*

## **The secret of long life is up in the trees**

\* 19:00 22 February 2010 **by Bob Holmes**

Living in the trees may be the secret to longevity – in the evolutionary long run, at least. Tree-dwelling mammals live nearly twice as long as their ground-bound cousins.

Evolutionary biologists have long predicted that natural selection should favour extending the lifespan of animals that live relatively safe lifestyles. And in fact, birds and bats, whose ability to fly helps them escape from predators, do have particularly long lives.

*My fountain of youth? Why, it's up in the trees (Image: Mattias Klum/National Geographic)*

Like fliers, tree-dwelling mammals can easily escape many predators. To see if this might also help them live longer, biological anthropologists Milena Shattuck and Scott Williams at the University of Illinois at Urbana-Champaign gathered data on the lifespans of 776 species representing all the major groups of mammals. They discovered that the maximum lifespans of tree-dwellers were almost twice those of terrestrial species of similar sizes.

It is well established that larger mammals tend to live longer than smaller ones. The kinkajou (pictured), however, is clearly not aware of this: it is a tree-living relative of the racoon and it lives longer than the tiger, even though it is just 1/40th the size.

The team is now setting its sights on burrowing mammals, to see if life underground also reduces risk and so ultimately extends the lifespans of those species. *Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0911439107*





## **Remember Magnesium If You Want to Remember**

### ***TAU finds new synthetic supplement improves memory and staves off age-related memory loss***

Those who live in industrialized countries have easy access to healthy food and nutritional supplements, but magnesium deficiencies are still common. That's a problem because new research from Tel Aviv University suggests that magnesium, a key nutrient for the functioning of memory, may be even more critical than previously thought for the neurons of children and healthy brain cells in adults.

Begun at MIT, the research started as a part of a post-doctoral project by Dr. Inna Slutsky of TAU's Sackler School of Medicine and evolved to become a multi-center experiment focused on a new magnesium supplement, magnesium-L-threonate (MgT), that effectively crosses the blood-brain barrier to inhibit calcium flux in brain neurons.

Published recently in the scientific journal *Neuron*, the new study found that the synthetic magnesium compound works on both young and aging animals to enhance memory or prevent its impairment. The research was carried out over a five-year period and has significant implications for the use of over-the-counter magnesium supplements.

In the study, two groups of rats ate normal diets containing a healthy amount of magnesium from natural sources. The first group was given a supplement of MgT, while the control group had only its regular diet. Behavioral tests showed that cognitive functioning improved in the rats in the first group and also demonstrated an increase of synapses in the brain - connective nerve endings that carry memories in the form of electrical impulses from one part of the brain to the other.

### **Bad news for today's magnesium supplements**

"We are really pleased with the positive results of our studies," says Dr. Slutsky. "But on the negative side, we've also been able to show that today's over-the-counter magnesium supplements don't really work. They do not get into the brain. "We've developed a promising new compound which has now taken the first important step towards clinical trials by Prof. Guosong Liu, Director of the Center for Learning and Memory at Tsinghua University and cofounder of Mageutics company," she says.

While the effects were not immediate, the researchers in the study - from Tel Aviv University, MIT, the University of Toronto, and Tsinghua University in Beijing - were able to assess that the new compound shows improved permeability of the blood-brain barrier. After two weeks of oral administration of the compound in mice, magnesium levels in the cerebral-spinal fluid increased.

### **Toward a more "plastic" brain**

"It seems counterintuitive to use magnesium for memory improvement because magnesium is a natural blocker of the NMDA receptor, a molecule critical for memory function. But our compound blocks the receptor only during background neuronal activity. As a result, it enhances the brain's 'plasticity' and increases the number of brain synapses that can be switched on," says Dr. Slutsky.

"Our results suggest that commercially available magnesium supplements are not effective in boosting magnesium in cerebro-spinal fluid," she says. "Magnesium is the fourth most abundant mineral in the body, but today half of all people in industrialized countries are living with magnesium deficiencies that may generally impair human health, including cognitive functioning."

Before the new compound becomes commercially available, Dr. Slutsky advises people to get their magnesium the old-fashioned way - by eating lots of green leaves, broccoli, almonds, cashews and fruit. The effects on memory won't appear overnight, she cautions, but with this persistent change in diet, memory should improve, and the effects of dementia and other cognitive impairment diseases related to aging may be considerably delayed.

## **Gene mutation is linked to autism-like symptoms in mice, UT Southwestern researchers find**

DALLAS – Feb. 23, 2010 – When a gene implicated in human autism is disabled in mice, the rodents show learning problems and obsessive, repetitive behaviors, researchers at UT Southwestern Medical Center have found.

The researchers also report that a drug affecting a specific type of nerve function reduced the obsessive behavior in the animals, suggesting a potential way to treat repetitive behaviors in humans. The findings appear in the Feb. 24 issue of the *Journal of Neuroscience*.

"Clinically, this study highlights the possibility that some autism-related behaviors can be reversed through drugs targeting specific brain function abnormalities," said Dr. Craig Powell, assistant professor of neurology and psychiatry at UT Southwestern and the study's senior author.

"Understanding one abnormality that can lead to increased, repetitive motor behavior is not only important for autism, but also potentially for obsessive-compulsive disorder, compulsive hair-pulling and other disorders of excessive activity," Dr. Powell said.

The study focused on a protein called neuroligin 1, or NL1, which helps physically hold nerve cells together so they can communicate better with one another. Mutations in proteins related to NL1 have been implicated in previous investigations to human autism and mental retardation.

In the latest study, the UT Southwestern researchers studied mice that had been genetically engineered to lack NL1. These mice were normal in many ways, but they groomed themselves excessively and were not as good at learning a maze as normal mice.

The altered mice showed weakened nerve signaling in a part of the brain called the hippocampus, which is involved in learning and memory, and in another brain region involved in grooming. When treated with a drug called D-cycloserine, which activates nerves in those brain regions, the excessive grooming lessened.

"Our goal was not to make an 'autistic mouse' but rather to understand better how autism-related genes might alter brain function that leads to behavioral abnormalities," Dr. Powell said. "By studying mice that lack neuroligin-1, we hope to understand better how this molecule affects communication between neurons and how that altered communication affects behavior.

"This study is important because we were able to link the altered neuronal communication to behavioral effects using a specific drug to 'treat' the behavioral abnormality."

Future studies, Dr. Powell said, will focus on understanding in more detail how NL1 operates in nerve cells. *Other UT Southwestern researchers participating in the study were co-lead authors Jacqueline Blundell, former postdoctoral researcher in neurology, and Dr. Cory Blaiss, postdoctoral researcher in neurology; Felipe Espinosa, senior research scientist in neurology; and graduate student Christopher Walz. Researchers at Stanford University also contributed to this work. The research was supported by Autism Speaks, the Simons Foundation, the National Institute of Mental Health, BRAINS for Autism, and the Hartwell Foundation.*

### **Really?**

## **The Claim: To Cut Calories, Eat Slowly**

**By ANAHAD O'CONNOR**

**THE FACTS** For ages, mothers have admonished children at the dinner table to slow down and chew their food. Apparently, they're onto something.

Researchers have found evidence over the years that when people wolf their food, they end up consuming more calories than they would at a slower pace. One reason is the effect of quicker ingestion on hormones.

In a study last month, scientists found that when a group of subjects were given an identical serving of ice cream on different occasions, they released more hormones that made them feel full when they ate it in 30 minutes instead of 5 . The scientists took blood samples and measured insulin and gut hormones before, during and after eating. They found that two hormones that signal feelings of satiety, or fullness - glucagon-like peptide-1 and peptide YY - showed a more pronounced response in the slow condition.

Ultimately, that leads to eating less, as another study published in The Journal of the American Dietetic Association suggested in 2008. In that study, subjects reported greater satiety and consumed roughly 10 percent fewer calories when they ate at a slow pace compared with times when they gobbled down their food. In another study of 3,000 people in The British Medical Journal, those who reported eating quickly and eating until full had triple the risk of being overweight compared with others.

In other words, experts say, it can't hurt to slow down and savor your meals.

**THE BOTTOM LINE** Eating at a slower pace may increase fullness and reduce caloric intake.

## **A magnetometer in the upper beak of birds?**

### **How to identify magnetoreceptive systems in various organisms**

FRANKFURT. Iron containing short nerve branches in the upper beak of birds may serve as a magnetometer to measure the vector of the Earth magnetic field (intensity and inclination) and not only as a magnetic compass, which shows the direction of the magnetic field lines. Already several years ago, the Frankfurt neurobiologists Dr. Gerta Fleissner and her husband Prof. Dr. Günther Fleissner have discovered these structures in homing pigeons and have, in close cooperation with the experimental physicist Dr. Gerald Falkenberg (DESY Hamburg), characterized the essential iron oxides. "After we had shown the system of dendrites with distinct subcellular iron-containing compartments in homing pigeons, immediately the question was posed whether similar dendritic systems may be found in other bird species, too", as Gerta Fleissner, the principal investigator, comments. Meanwhile they could describe similar candidate structures in the beaks of various avian species. X-Ray-fluorescence measurements at DESY demonstrated that the iron oxides within these nervous dendrites are identical. These findings were published few days ago in the high-ranking interdisciplinary online journal PlosOne.

More than about 500 dendrites in the periphery encode the magnetic field information, which is composed in the central nervous system to a magnetic map. It obviously does not matter, whether birds use this magnetic

map for their long distance orientation or do not – the equipment can be found in migratory birds, like robin and garden warbler, and well as in domestic chicken. "This finding is astonishing, as the birds studied have a different life styles and must fulfil diverse orientational tasks: Homing pigeons, trained to return from different release sites to their homeloft, short-distance migrants like robins, long-distance migratory birds like garden warblers and also extreme residents like domestic chicken", explains Gerta Fleissner.

In order to provide convincing evidence, several thousand comparative measurements were performed. The beak tissue was studied under the microscope to identify iron-containing hot spots as a basis for consecutive physicochemical analyses. At the Hamburg Synchrotron Strahlungslabor at DESY the distribution and quantity of various elements was topographically mapped by a high resolution X-ray device. "Here, the beak tissue can be investigated without destruction by histological procedures concerning the site and detailed nature of magnetic iron compounds within the dendrites", Gerta Fleissner explains and she emphasizes that the cooperation with the experimental physicist Gerald Falkenberg as project leader at DESY was essential for this scientific breakthrough.

Specialized iron compounds in the dendrites locally amplify the Earth magnetic field and thus induce a primary receptor potential. Most probably each of these more than 500 dendrites encodes only one direction of the magnetic field. These manifold data are processed to the brain of the bird and here – recomposed – serve as a basis for a magnetic map, which facilitates the spatial orientation. Whether this magnetic map is consulted, strongly depends on the avian species and its current motivation to do so: migratory birds, for example, show magnetic orientation only during their migratory restlessness, as could be shown in multiple behavioural experiments by Prof. Wolfgang Wiltschko, who has discovered magnetic field guided navigation in birds. The cooperation with his research team has suggested that magnetic compass and magnetic map sense are based on different mechanisms and are localized at different sites: The magnetic compass resides in the eye, the magnetometer for the magnetic map lies in the beak.

"The now published results clearly help to falsify the old myths concerning iron-based magnetoreception via randomly distributed sites everywhere in the organism, like blood, brain or skull. They rather deliver a sound concept how to identify magnetoreceptive systems in various organisms", Günther Fleissner happily reports. These clear and well-reproducible data may be used as a basis for further experimental projects that might elucidate the manifold unknown steps between magnetic field perception and its use as a navigational cue. *The project was funded by Frankfurt foundations (Stiftung Polytechnische Gesellschaft and Kassel-Stiftung), by the "Freunde und Förderer" of the Goethe University, by the ZEN-program of the Hertie-Stiftung and the Deutsche Forschungsgemeinschaft. The elaborate measurements at the HASYLAB are based on grants of the Helmholtz-Foundation. Reference: Falkenberg G, Fleissner Ge, Schuchardt K, Kuehbacher M, Thalau P, et al. (2010) Avian Magnetoreception: Elaborate Iron Mineral Containing Dendrites in the Upper Beak Seem to Be a Common Feature of Birds. PLoS ONE 5(2): e9231. doi:10.1371/journal.pone.0009231 (plosone@plos.org)*

### **Protecting the brain from a deadly genetic disease**

Huntington's disease (HD) is a cruel, hereditary condition that leads to severe physical and mental deterioration, psychiatric problems and eventually, death. Currently, there are no treatments to slow down or stop it. HD sufferers are born with the disease although they do not show symptoms until late in life. In a new study published in The Journal of Neuroscience, Stephen Ferguson and Fabiola Ribeiro of Robarts Research Institute at The University of Western Ontario identified a protective pathway in the brain that may explain why HD symptoms take so long to appear. The findings could also lead to new treatments for HD.

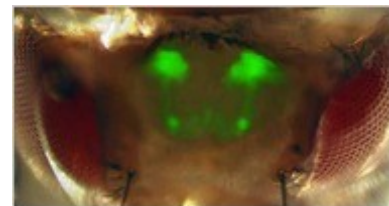
The symptoms of Huntington's disease are caused by cell death in specific regions of the brain. Patients who have HD are born with a mutated version of the protein huntingtin (Htt), which is thought to cause these toxic effects. While researchers know HD results from this single, mutated protein, no one seems to know exactly what it does, why it does not cause symptoms until later in life, or why it kills a specific set of brain cells, even though Htt is found in every single cell in the human body.

Ferguson and Ribeiro used a genetically-modified mouse model of HD to look at the effects of mutated Htt on the brain. "We found there was some kind of compensation going on early in the life of these mice that was helping to protect them from the development of the disease," says Ferguson, director of the Molecular Brain Research Group at Robarts, and a professor in the Department of Physiology & Pharmacology at Western's Schulich School of Medicine and Dentistry. "As they age, they lose this compensation and the associated protective effects, which could explain the late onset of the disease."

Ferguson adds that metabotropic glutamate receptors (mGluRs), which are responsible for communication between brain cells, play an important role in these protective effects. By interacting with the mutant Htt protein, mGluRs change the way the brain signals in the early stages of HD in an attempt to offset the disease, and save the brain from cell death. As a result, mGluRs could offer a drug target for HD treatment.

Because HD is a dominant genetic disease, every child with an affected parent has a 50 per cent chance of inheriting the fatal condition. This research, funded by the Canadian Institutes of Health Research, sheds light on the onset of HD and the potential role of a mutant protein in patients, paving the way for the development of new drug therapies.

**Observatory**  
**Forgetting, With a Purpose**  
By SINDYA N. BHANOO



Just why the brain erases certain memories has long been a topic of interest to scientists.

*Scientists found the brains of fruit flies erased short-term memories.* Glenn Turner/Cold Spring Harbor Laboratory

Now, new research suggests that short-term memory is erased by the brain on purpose, so that new, more relevant memories can be recorded. At least in fruit flies.

Researchers from China and the United States have found that flies have a protein called Rac that does the job of eroding a memory when needed. The researchers experimented with Rac levels in fruit flies and subjected the flies to two circumstances: a foul smelling odor and a foul smelling odor that also came with an electric shock. Under normal circumstances, after being exposed to both situations, flies picked the lesser of the two evils - the foul odor without the shock.

The scientists then changed the shock to be tied with the first odor instead of the second. The flies noted this new information, and erased their original memory. The shock, in their minds, was now correctly tied to the first odor. When exposed to both odors, they again correctly picked the odor without the shock. But when the experiment was repeated after the memory-eroding protein was blocked, there was utter confusion. The flies had not erased their first memory, and had made a second memory. Unable to pick which odor to fly toward, they zigzagged back and forth.

Humans also have the protein Rac, and Yi Zhong, the paper's lead author, believes that further study may reveal how human memories are made.

There is also hope that once they are better understood, Rac levels can be controlled to help people with abnormal memory, said Dr. Zhong of Tsinghua University in China and Cold Spring Harbor Laboratory in New York. The findings were in last week's edition of the journal Cell.

**Prednisolone not beneficial in most cases of community-acquired pneumonia**

Patients hospitalized with mild to moderate community-acquired pneumonia (CAP) should not be routinely prescribed prednisolone, a corticosteroid, as it is associated with a recurrence of symptoms after its withdrawal, according to the first randomized double-blind clinical trial to address the subject.

"Prednisolone therapy next to antibiotic therapy in patients hospitalized with CAP should not be recommended due to lack of clinical benefit and a higher rate of late failures," said Dominic Snijders, M.D., lead author on the study and at the Medical Centre Alkmaar in the Netherlands.

The findings have been published online ahead of print publication in the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

To assess the efficacy of prednisolone therapy along with standard doctor-managed care for patients admitted to the hospital with CAP, Dr. Snijders and colleagues prospectively enrolled 213 patients who had been hospitalized with CAP and randomly assigned them to receive the usual antibiotic therapy as prescribed by their physicians supplemented with either prednisolone (40 mg dose once daily) or placebo for a week.

They found that patients on prednisolone recovered more rapidly from their fevers and had a more rapid decline in their c-reactive protein (CRP) levels than patients on placebo, indicating decreased inflammation. However, after 14 days, the patients in the prednisolone group had higher levels of CRP than the patients in the placebo group. Furthermore, three times as many patients in the prednisolone group had "late failure," defined as the recurrence of symptoms more than 72 hours after initial therapeutic success, and these patients were almost four times as likely to require additional antibiotic treatment than patients with late failure in the placebo group (6.7 percent versus 1.8 percent).

"Our study clearly shows that prednisolone therapy does not have a place in patients with CAP," said Dr. Snijders. However, he pointed out, in some cases such as when CAP is severe or occurs in conjunction with COPD, there is not enough information to draw a conclusion. Previous studies have found benefit of corticosteroid therapy among patients with severe CAP. Studies with patients with CAP and COPD have also indicated the possibility of a protective effect of prednisolone, but there have been no controlled trials.

Dr. Snijders suggested that the association of prednisolone therapy in CAP with late failures may be due to a rebound effect that could be precipitated by the abrupt withdrawal of the therapy. "Non-survivors on

corticosteroid therapy died later than non-survivors without corticosteroids, respectively 13.8 versus 7.1 days," he wrote. "A tapering of the corticosteroids might protect against the rebound of inflammation."

"Further trials are indeed needed in patients with severe CAP," said Dr. Snijders. "Also, more information is needed about COPD patients, corticosteroids and pneumonia. Possible future intervention could be monoclonal TNF-alpha-antibodies or specific antibodies against other key mediators in the inflammation response. We are considering further studies in these directions."

Link to original article: [http://www.thoracic.org/newsroom/press-releases/resources/022610\\_snijders.pdf](http://www.thoracic.org/newsroom/press-releases/resources/022610_snijders.pdf)

## **Transplants That Do Their Job, Then Fade Away**

**By DENISE GRADY**

Jonathan Nuñez was 8 months old when a liver transplant saved his life. Three years later, his body rejected the transplant, attacking it so fiercely that it wasted away and vanished, leaving barely a trace.

That result, seemingly a disaster, was exactly what his doctors had hoped for. They had deliberately withdrawn Jonathan's antirejection medicine because he no longer needed the transplant. His own liver had - as planned - regenerated.

Jonathan, a 4-year-old with a shy smile and a love of dinosaurs, is among a small number of children in the United States who have undergone a highly unusual type of transplant surgery, one that - for the few who are eligible - offers a tremendous advantage: a normal life, free from antirejection drugs, which suppress the immune system and increase the risk of infections, cancer and other problems. Normally, transplant patients must take these powerful drugs for life.

In standard transplants, the diseased organ is completely removed and a new one put in its place. What is different about the operation Jonathan and the other children had is that only part of the recipient's liver is removed, and it is replaced with part of a donor's liver. At first, to prevent rejection, the patient takes the usual drugs.

Then, doctors watch and wait. The liver has an extraordinary ability to regenerate, especially in children, and the hope is that while the transplant is doing its job, what remains of the patient's own liver will regenerate and start working again. The process can take a year or more; in Jonathan's case, it took three.

If the liver does regenerate and grow large enough, doctors begin to withdraw the antirejection medicines. The patient's immune system reactivates and, in most cases, gradually destroys the transplant, which is no longer needed. Life goes back to normal, free from a daily schedule of pills and their risks and expense.

"I think we need to promote this idea," said Dr. Tomoaki Kato, Jonathan's surgeon. He works at NewYork-Presbyterian Hospital/Columbia University Medical Center, but performed Jonathan's transplant in 2006 at the University of Miami/Jackson Memorial Hospital.

"A lot of the transplant community is focused on how to get patients off immunosuppression, and this is one way," he added.

But only a tiny fraction of transplant patients are candidates for the operation: certain children with acute liver failure - probably fewer than 100 a year in the United States, where 525 under 18 had liver transplants last year. The operation is a difficult one. It is longer and more risky than a standard transplant, and surgeons caution that patients have to be selected carefully because not all can withstand the surgery.

The surgery was first tried in Europe in the early 1990s, and later in the United States. But the results were mixed - the liver did not always regenerate - and it never really caught on. (In medical journals, it is called auxiliary partial orthotopic liver transplantation.) Dr. Kato said the results may have been poor because the early attempts included adults.

"I think the key is children," he said.

The best candidates are children with acute hepatic failure, a deadly condition in which the liver suddenly stops working, often for unknown reasons. Although the liver might be able to recover, it cannot do so fast enough to prevent brain damage and death from the toxins that build up. The only way to save the life of someone with this condition is to perform a transplant - or a partial one. Such partial transplants do not work for chronic liver diseases that cause scarring because it prevents the liver from regenerating.

All told, Dr. Kato has performed the surgery on seven children, ranging in age from 8 months (Jonathan) to 8 years, at Jackson Memorial. So far, the patient's own liver has recovered in six of the seven children, and they no longer require antirejection drugs, Dr. Kato said, adding that he expected the need for the drugs to taper off soon for the seventh. In four, he described the transplant as "melting" away completely on its own, but two others, including Jonathan, needed surgery to remove a remnant or clear up an infection.

Dr. Kato's first case was in 1997. That child spent three months in intensive care. "We didn't think it was successful," he said. But after two years, the liver had fully recovered.

“That gave us the idea this was something worth doing,” Dr. Kato said.

Other surgeons have tried the procedure. Dr. Alan Langnas, director of liver transplantation at the Nebraska Medical Center, said he had performed it on about 10 patients, mostly children, in the last 15 years. In some cases, he said, the patient’s liver did not regenerate. At least one required a second transplant.

“I think the success has always been a little mixed,” Dr. Langnas said. “It depends on the patient selection and how well their native liver recovers. But I think it is an important option for some patients.”

Dr. Simon Horslen, the medical director of liver and intestine transplant at Seattle Children’s Hospital, who was at the Nebraska center when the operations were done there, said: “In the right hands it’s a wonderful technique. It is a case of those of us who have experienced it having to convince others.”

Surgeons at Kings College in London have also performed the surgery, on 20 children ranging from 1 to 16 years old, during the last 20 years. Seventeen have survived. One needed a second transplant, but in 14, their own livers regenerated, and, so far, 11 have been able to stop taking antirejection drugs. In a recent article in a medical journal, the medical team from Kings College said the operation should be considered for children who need transplants for acute liver failure.

But Dr. J. Michael Millis, the chief of transplantation at the University of Chicago Medical Center, said, “This has not been particularly successful in most of the hands that have tried it.”

He added, “Even in Kato’s series, the operative time is almost double, so the patients have to spend almost twice as much time in the operating room, and I think that is actually the area that is the Achilles’ heel.” (A liver transplant usually takes about six hours.)

Long operations require that patients be given large amounts of intravenous fluid, something that children with liver failure generally cannot tolerate, Dr. Millis said, explaining that the fluid causes brain swelling that can kill them.

“I’ve been waiting for kids to do this on for a decade,” he said. “But by the time I get a liver that is suitable, they’re too sick. I have to get them in and out of the operating room and back to intensive care as quickly as possible, with minimal fluids.”

Dr. Langnas had similar concerns. “Sometimes these kids are so sick, they literally have hours or a day to live,” he said. “Under those circumstances, we want to not take any chances.”

Jonathan Nuñez, whose family lives in Miami, had a textbook case of acute liver failure. At 8 months, he was perfectly happy and healthy, then he suddenly turned cranky and sleepy. He cried too much, ate too little and began vomiting. He turned yellow, and his stomach and legs swelled. The diagnosis was acute liver failure, cause unknown. The only hope was a transplant.

At Jackson Memorial, Dr. Kato suggested a partial transplant. Jonathan’s mother, Yailin Nuñez, said she and her husband immediately said yes, because it offered at least a chance that Jonathan would be able to live a normal life, without immunosuppressants.

Children with acute liver failure shoot to the top of the list, and Jonathan got a transplant one day after being listed. He had a rocky recovery, more so than most of Dr. Kato’s patients. Severe rejection episodes required high doses of steroids. Other complications took him in and out of the hospital for three months.

He stabilized, but his own liver did not seem to be regenerating; at one point it even shrank. Ms. Nuñez never gave up hope, but after about two years, Dr. Kato started to doubt that Jonathan’s liver would ever recover, and he even contemplated removing it to prevent problems. Then it began to grow.

By last September, Jonathan’s liver was large enough to work on its own. He no longer needed the transplant. Doctors began decreasing antirejection drugs, and Jonathan’s immune system did the rest. In September, the transplant had been plainly visible on his CT scan. By November, it was gone.

But the transplant atrophied so fast that one spot where it had been connected to the small intestine did not have a chance to close properly. An abscess formed, causing fevers and making Jonathan quite sick. He needed antibiotics and a procedure to drain the infection. Two months later, on Jan. 28, at NewYork-Presbyterian Morgan Stanley Children’s Hospital, Dr. Kato operated to remove the abscess completely. A few days later, Jonathan and his family flew home to Miami.

“At the end of the day, I’m so glad,” Ms. Nuñez said. “I feel so fortunate that my son’s liver regenerated. The complications have been a struggle, and not knowing what caused his liver failure haunts me to this day. But he can live a normal life without immunosuppression. That’s what matters. There is hope out there when you’re given devastating news.”

“When it works, it’s cool,” Dr. Langnas said.

“In Seattle, they are considering it,” Dr. Horslen said

## The Science of Hollywood Blockbusters

There is something about the rhythm and texture of early cinema that has a very different “feel” than modern films. But it’s hard to put one’s finger on just what that something is. New research may help explain this elusive quality. Cognitive psychologist (and film buff) James Cutting of Cornell University, along with his students Jordan DeLong and Christine Nothelfer, decided to use the sophisticated tools of modern perception research to deconstruct 70 years of film, shot by shot. They measured the duration of every shot in every scene of 150 of the most popular films released from 1935 to 2005. The films represented five major genres - action, adventure, animation, comedy and drama. Using a complex mathematical formula, they translated these sequences of shot lengths into “waves” for each film.

What these researchers looked for were patterns of attention. Specifically, they looked for a pattern called the  $1/f$  fluctuation. The  $1/f$  fluctuation is a concept from chaos theory, and it means a pattern of attention that occurs naturally in the human mind. Indeed, it’s a rhythm that appears throughout nature, in music, in engineering, economics, and elsewhere. In short, it’s a constant in the universe, though it’s often undetectable in the apparent chaos.

Cutting and his students found that modern films - those made after 1980 - were much more likely than earlier films to approach this universal constant. That is, the sequences of shots selected by director, cinematographer and film editor have gradually merged over the years with the natural pattern of human attention. This may explain the more natural feel of newer films - and the “old” feel of earlier ones. Modern movies may be more engrossing - we get “lost” in them more readily - because the universe’s natural rhythm is driving the mind.

These researchers don’t believe that filmmakers have deliberately crafted their movies to match this pattern in nature. Instead, they believe the relatively young art form has gone through a kind of natural selection, as the edited rhythms of shot sequences were either successful or unsuccessful in producing more coherent and gripping films. The most engaging and successful films were subsequently imitated by other filmmakers, so that over time and through cultural transmission the industry as a whole evolved toward an imitation of this natural cognitive pattern.

Overall, action movies are the genre that most closely approximates the  $1/f$  pattern, followed by adventure, animation, comedy and drama. But as Cutting, DeLong, and Nothelfer report in the study in *Psychological Science*, a journal of the Association for Psychological Science, individual films from every genre have almost perfect  $1/f$  rhythms. *The Perfect Storm*, released in 2000, is one of them, as is *Rebel Without a Cause*, though it was made in 1955. So too is *The 39 Steps*, Hitchcock’s masterpiece from way back in 1935.

### Findings

## When It Comes to Salt, No Rights or Wrongs. Yet.

By JOHN TIERNEY

Suppose, as some experts advise, that the new national dietary guidelines due this spring will lower the recommended level of salt. Suppose further that public health officials in New York and Washington succeed in forcing food companies to use less salt. What would be the effect?

- A) More than 44,000 deaths would be prevented annually (as estimated recently in *The New England Journal of Medicine*).
- B) About 150,000 deaths per year would be prevented annually (as estimated by the New York City Department of Health and Mental Hygiene).
- C) Hundreds of millions of people would be subjected to an experiment with unpredictable and possibly adverse effects (as argued recently in *The Journal of the American Medical Association*).
- D) Not much one way or the other.
- E) Americans would get even fatter than they are today.

Don’t worry, there’s no wrong answer, at least not yet. That’s the beauty of the salt debate: there’s so little reliable evidence that you can imagine just about any outcome. For all the talk about the growing menace of sodium in packaged foods, experts aren’t even sure that Americans today are eating more salt than they used to.



Viktor Koen

When you don’t know past trends, predicting the future is a wide-open game.

My personal favorite prediction is E, the further fattening of America, but I’m just guided by a personal rule: Never bet against the expansion of Americans’ waistlines, especially not when public health experts get involved.

The harder the experts try to save Americans, the fatter we get. We followed their admirable advice to quit smoking, and by some estimates we gained 15 pounds apiece afterward. The extra weight was certainly a worthwhile trade-off for longer life and better health, but with success came a new challenge.

Officials responded by advising Americans to shun fat, which became the official villain of the national dietary guidelines during the 1980s and 1990s. The anti-fat campaign definitely made an impact on the marketing of food, but as we gobbled up all the new low-fat products, we kept getting fatter. Eventually, in 2000, the experts revised the dietary guidelines and conceded that their anti-fat advice may have contributed to diabetes and obesity by unintentionally encouraging Americans to eat more calories.

That fiasco hasn't dampened the reformers' enthusiasm, to judge from the growing campaign to impose salt restrictions. Pointing to evidence that a salt-restricted diet causes some people's blood pressure to drop, the reformers extrapolate that tens of thousands of lives would be saved if there were less salt in everybody's food.

But is it even possible to get the public to permanently reduce salt consumption? Researchers have had a hard enough time getting people to cut back during short-term supervised experiments.

The salt reformers say change is possible if the food industry cuts back on all the hidden salt in its products. They want the United States to emulate Britain, where there has been an intensive campaign to pressure industry as well as consumers to use less salt. As a result, British authorities say, from 2000 to 2008 there was about a 10 percent reduction in daily salt consumption, which was measured by surveys that analyzed the amount of salt excreted in urine collected over 24 hours.

But the British report was challenged in a recent article in *The Clinical Journal of the American Society of Nephrology* by researchers at the University of California, Davis, and Washington University in St. Louis. The team, led by Dr. David A. McCarron, a nephrologist at Davis, criticized the British authorities for singling out surveys in 2008 and 2000 while ignoring nearly a dozen similar surveys conducted in the past two decades.

When all the surveys in Britain are considered, there has been no consistent downward trend in salt consumption in recent years, said Dr. McCarron, who has been a longtime critic of the salt reformers. (For more on him and his foes, go to [nytimes.com/tierneylab](http://nytimes.com/tierneylab).) He said that the most notable feature of the data is how little variation there has been in salt consumption in Britain - and just about everywhere else, too.

Dr. McCarron and his colleagues analyzed surveys from 33 countries around the world and reported that, despite wide differences in diet and culture, people generally consumed about the same amount of salt. There were a few exceptions, like tribes isolated in the Amazon and Africa, but the vast majority of people ate more salt than recommended in the current American dietary guidelines.

The results were so similar in so many places that Dr. McCarron hypothesized that networks in the brain regulate sodium appetite so that people consume a set daily level of salt. If so, that might help explain one apparent paradox related to reports that Americans are consuming more daily calories than they used to. Extra food would be expected to come with additional salt, yet there has not been a clear upward trend in daily salt consumption evident over the years in urinalysis studies, which are considered the best gauge because they directly measure salt levels instead of relying on estimates based on people's recollections of what they ate. Why no extra salt? One prominent advocate of salt reduction, Dr. Lawrence Appel of Johns Hopkins University, said that inconsistent techniques in conducting the urinalysis surveys may be masking a real upward trend in salt consumption.

But Dr. McCarron called the measurements reliable and said they could be explained by the set-point theory:

As Americans ate more calories, they could have eased up on some of the saltier choices so that their overall sodium consumption remained constant. By that same logic, he speculated, if future policies reduce the average amount of salt in food, people might compensate by seeking out saltier foods - or by simply eating still more of everything.

The salt reformers dismiss these speculations, arguing that with the right help, people can maintain low-salt diets without gaining weight or suffering other problems. But even if people could be induced to eat less salt, would they end up better off? The estimates about all the lives to be saved are just extrapolations based on the presumed benefits of lower blood pressure.

If you track how many strokes and heart attacks are suffered by people on low-salt diets, the results aren't nearly as neat or encouraging, as noted recently in *JAMA* by Michael H. Alderman, a hypertension expert at Albert Einstein College of Medicine. A low-salt diet was associated with better clinical outcomes in only 5 of the 11 studies he considered; in the rest, the people on the low-salt diet fared either the same or worse.

"When you reduce salt," Dr. Alderman said, "you reduce blood pressure, but there can also be other adverse and unintended consequences. As more data have accumulated, it's less and less supportive of the case for salt reduction, but the advocates seem more determined than ever to change policy."



Before changing public policy, Dr. Alderman and Dr. McCarron suggest trying something new: a rigorous test of the low-salt diet in a randomized clinical trial. That proposal is rejected by the salt reformers as too time-consuming and expensive. But when you contemplate the potential costs of another public health debacle like the anti-fat campaign, a clinical trial can start to look cheap.

### **Stress hormone, depression trigger obesity in girls**

Depression raises stress hormone levels in adolescent boys and girls but may lead to obesity only in girls, according to researchers. Early treatment of depression could help reduce stress and control obesity -- a major health issue.

"This is the first time cortisol reactivity has been identified as a mediator between depressed mood and obesity in girls," said Elizabeth J. Susman, the Jean Phillips Shibley professor of biobehavioral health at Penn State.

"We really haven't seen this connection in kids before, but it tells us that there are biological risk factors that are similar for obesity and depression."

Cortisol, a hormone, regulates various metabolic functions in the body and is released as a reaction to stress. Researchers have long known that depression and cortisol are related to obesity, but they had not figured out the exact biological mechanism.

Although it is not clear why high cortisol reactions translate into obesity only for girls, scientists believe it may be due to physiological and behavioral differences - estrogen release and stress eating in girls - in the way the two genders cope with anxiety. "The implications are to start treating depression early because we know that depression, cortisol and obesity are related in adults," said Susman.

If depression were to be treated earlier, she noted, it could help reduce the level of cortisol, and thereby help reduce obesity. "We know stress is a critical factor in many mental and physical health problems," said Susman. "We are putting together the biology of stress, emotions and a clinical disorder to better understand a major public health problem."

Susman and her colleagues Lorah D. Dorn, professor of pediatrics, Cincinnati Children's Hospital Medical Center, and Samantha Dockray, postdoctoral fellow, University College London, used a child behavior checklist to assess 111 boys and girls ages 8 to 13 for symptoms of depression. Next they measured the children's obesity and the level of cortisol in their saliva before and after various stress tests.

"We had the children tell a story, make up a story, and do a mental arithmetic test," said Susman. "The children were also told that judges would evaluate the test results with those of other children."

Statistical analyses of the data suggest that depression is associated with spikes in cortisol levels for boys and girls after the stress tests, but higher cortisol reactions to stress are associated with obesity only in girls. The team reported its findings in a recent issue of the *Journal of Adolescent Health*.

"In these children, it was mainly the peak in cortisol that was related to obesity," Susman explained. "It was how they reacted to an immediate stress." *The National Institutes of Health supported this work.*

### **DNA sequencing unlocks relationships among flowering plants**

GAINESVILLE, Fla. - The origins of flowering plants from peas to oak trees are now in clearer focus thanks to the efforts of University of Florida researchers.

A study appearing online this week in the *Proceedings of the National Academy of Sciences* unravels 100 million years of evolution through an extensive analysis of plant genomes. It targets one of the major moments in plant evolution, when the ancestors of most of the world's flowering plants split into two major groups.

Together the two groups make up nearly 70 percent of all flowering plants and are part of a larger clade known as Pentapetalae, which means five petals. Understanding how these plants are related is a large undertaking that could help ecologists better understand which species are more vulnerable to environmental factors such as climate change.

Shortly after the two groups split apart, they simultaneously embarked upon a rapid burst of new species that lasted 5 million years. This study shows how those species are related and sheds further light on the emergence of flowering plants, an evolutionary phenomenon described by Charles Darwin as an abominable mystery.

"This paper and others show flowering plants as layer after layer of bursts of evolution," said Doug Soltis, study co-author and UF distinguished professor of biology. "Now it's falling together into two big groups." Pentapetalae has enormous diversity and contains nearly all flowering plants. Its two major groups, superrosids and superasterids, split apart between 111 million and 98 million years ago and now account for more than 200,000 species. The superrosids include such familiar plants as hibiscus, oaks, cotton and roses. The superasterids include mint, azaleas, dogwoods and sunflowers.

Earlier studies were limited by technology and involved only four or five genes. Those studies hinted at the results found in the new study but lacked statistical support, said study co-author Pam Soltis, distinguished professor and Florida Museum of Natural History curator of molecular systematics and evolutionary genetics.

The new study at UF's Florida Museum of Natural History analyzed 86 complete plastid genome sequences from a wide range of plant species. Plastids are the plant cell component responsible for photosynthesis.

Previous genetic analyses of Pentapetalae failed to untangle the relationships among living species, suggesting that the plants diverged rapidly over 5 million years. Researchers selected genomes to sequence based on their best guess of genetic relationships from the previous sequencing work.

Genome sequencing is more time-consuming for plants than animals because plastid DNA is about 10 times larger than the mitochondrial DNA used in studying animal genomes. But continual improvements in DNA sequencing technology are now allowing researchers to analyze those larger amounts of data more quickly.

The study provides an important framework for further investigating evolutionary relationships by providing a much clearer picture of the deep divergence that led to the split within flowering plants, which then led to speciation in the two separate branches.

Eventually, researchers hope to match these evolutionary bursts with geological and climatic events in the earth's history. "I think we're starting to get to a point with a dated tree where we could start looking at what was happening at some of those time frames," Pam Soltis said.

### **Damaged protein identified as early diagnostic biomarker for Alzheimer's disease in healthy adults**

Researchers at NYU School of Medicine have found that elevated cerebrospinal fluid levels of phosphorylated tau231 (P-tau231), a damaged tau protein found in patients with Alzheimer's disease, may be an early diagnostic biomarker for Alzheimer's disease in healthy adults.

The study published this month online by Neurobiology of Aging shows that high levels of P-tau231 predict future memory decline and loss of brain gray matter in the medial temporal lobe- a key memory center. Prior studies found the medial temporal lobe to be the most vulnerable brain region in the early stages of Alzheimer's disease accumulating damaged tau proteins in the form of neurofibrillary tangles. Tangles are one of the signature indicators of Alzheimer's disease, in addition to beta amyloid plaques.

"Our research results show for the first time that elevated levels of P-tau 231 in normal individuals can predict memory decline and accompanying brain atrophy," said lead author Lidia Glodzik MD, PhD, assistant research professor, Department of Psychiatry at the Center for Brain Health and Center of Excellence on Brain Aging at NYU School of Medicine. "Our findings suggest that P-tau231 has the potential to be an important diagnostic tool in the pre-symptomatic stages of Alzheimer's disease."

Researchers evaluated 57 cognitively healthy older adults and studied the relationships between baseline cerebrospinal fluid biomarkers, longitudinal memory performance and longitudinal measures of the medial temporal lobe gray matter using Magnetic Resonance Imaging, or MRI. Two years later, researchers found that 20 out of 57 healthy adults showed decreased memory performance. The group with worsened memory had higher baseline levels of P-tau231 and more atrophy in the medial temporal lobe. The higher P-tau231 levels were associated with reductions in medial temporal lobe gray matter. Authors concluded that elevated P-tau231 predicts both memory decline and medial temporal lobe atrophy.

"Identifying people at risk for Alzheimer's disease is the necessary first step in developing preventive therapies," said co-author Mony de Leon, EdD, professor, Department of Psychiatry and director of the Center for Brain Health at the Center of Excellence on Brain Aging at NYU School of Medicine and Research Scientist at the Nathan S. Kline Institute for Psychiatric Research. "This study shows that Alzheimer's disease pathology may be recognized in the normal stages of cognition. This observation may be of value in future studies investigating mechanisms that cause or accelerate dementia".

*This study was done in collaboration with the Nathan S. Kline Institute for Psychiatric Research (NY), Applied NeuroSolutions, Inc. (IL), QiLu Hospital of Shandong University (China), The Sahlgrenska Academy at University of Gothenburg and Sahlgrenska University Hospital (Sweden) and the Institute for Basic Research (NY).*

*Funding for this study was provided by the National Institutes of Health (NIH) in Bethesda, Maryland.*

### **Bitter Melon Extract Decreased Breast Cancer Cell Growth**

Bitter melon extract, a common dietary supplement, exerts a significant effect against breast cancer cell growth and may eventually become a chemopreventive agent against this form of cancer, according to results of a recent study. "Our findings suggest that bitter melon extract modulates several signal transduction pathways, which induces breast cancer cell death," said lead researcher Ratna B. Ray, Ph.D., professor in the Department of Pathology at Saint Louis University. "This extract can be utilized as a dietary supplement for the prevention of breast cancer."

Results of this study are published in *Cancer Research*, a journal of the American Association for Cancer Research. Previous research has shown *Momordica charantia*, also known as bitter melon, to have hypoglycemic and hypolipidemic effects, according to Ray. Because of these effects, the extract is commonly used in folk medicines as a remedy for diabetes in locales such as India, China and Central America, according to the researchers.

Using human breast cancer cells and primary human mammary epithelial cells in vitro, Ray and colleagues found the mechanism of bitter melon extract significantly decreased proliferation, that is, cell growth and division, and induced death in breast cancer cells. These early results offer an encouraging path for research into breast cancer.

"Breast cancer is a major killer among women around the world, and in that perspective, results from this study are quite significant," said Rajesh Agarwal, Ph.D., professor in the Department of Pharmaceutical Sciences at the University of Colorado, Denver School of Pharmacy. "This study may provide us with one more agent as an extract that could be used against breast cancer if additional studies hold true."

According to Agarwal, the *Cancer Research* associate editor for this study, the simple study design, clear-cut results and the overall importance of these findings in breast cancer prevention makes this research different from previous research.

However, he stressed that "this study is only a step towards establishing the cancer preventive efficacy of bitter melon against breast cancer." Additional studies are needed to further understand the molecular targets of bitter melon extract in cancer cells, as well as for establishing its in vivo efficacy. Agarwal gave a note of caution, stating that while these results do provide hope as an anti-cancer agent, it is important to establish the validity of these results in animal models before adding them to one's diet to inhibit breast cancer cell growth.

Ray and colleagues are currently conducting follow-up studies using a number of cancer cell lines to examine the anti-proliferative effect of the extract. They are also planning a preclinical trial to evaluate its chemopreventive efficacy by oral administration.

Bitter melon extract is cultivated in Asia, Africa and South America. Extract of this vegetable is being popularized as a dietary supplement in Western Countries, since it is known to contain additional glycosides such as mormordin, vitamin C, carotenoids, flavanoids and polyphenols.

### **Study shows that suffocating head lice works in new treatment**

#### ***New FDA approved treatment is safe and effective in children as young as 6 months old***

A new non-neurotoxic treatment for head lice has been found to have an average of 91.2% treatment success rate after one week, and to be safe in humans from six months of age and up. This is the finding of a study published today in *Pediatric Dermatology*.

Benzyl Alcohol Lotion 5% (known as Ulesfia™) works by suffocating lice, a method which has been attempted by treating with household items such as mayonnaise, olive oil and petroleum jelly. Studies have shown that overnight treatments with these home remedies may initially appear to kill lice, but later a "resurrection effect" occurs after rinsing, because lice can resist asphyxiation. This is accomplished by the louse's ability to presumably close its spiracles, the external entry points to the breathing apparatus, when submerged. Unlike commonly used asphyxiant remedies, scanning electron microscopy appears to indicate that benzyl alcohol lotion effectively asphyxiates lice by "stunning" the spiracles open, allowing the lotion, comprised of mineral oil and other inactive ingredients, to infiltrate the "honeycomb" respiratory apparatus and kill lice.

The phase III trials were comprised of two multicenter, randomized, double-blind, placebo-controlled trials, conducted among ten geographically diverse sites which assessed the clinical effectiveness and safety of benzyl alcohol lotion. 250 participants took part in the trials and were randomised to treatment or vehicle (lotion but with no active ingredient) groups, treatment was given at day one and day seven, and participants were checked for success at day eight and day 14. On day eight the treatment group had a success rate of 91.2% as an average of both trials, and a 75.6% success rate on day 14; in the vehicle group the success rates were 27.9% and 15.5% respectively.

"Existing over-the-counter head lice treatments contain neurotoxic pesticides as active ingredients, resulting in potential toxicity and other problems, including lengthy applications, odor, ineffective treatment. Resistance has also become a problem now that lice have had such prolonged exposure to these products," said study author Terri L Meinking, PhD, of Global Health Associates of Miami, USA. "This leaves practitioners, parents and patients hoping for a safe, non-neurotoxic cure."

"Since the most popular products have been made readily available, their overuse has caused lice to become resistant just as bacteria have become resistant to many antibiotics," added Meinking. "Because benzyl alcohol lotion kills by suffocation, resistance should not be an issue."

## Drug laws are painful for cancer patients

\* 11:46 24 February 2010 by Ewen Callaway

Overzealous regulation of opioids is having a painful knock-on effect on eastern Europeans with cancer. "There are literally tens of thousands of people who are suffering unnecessarily," says lead author Nathan Cherny of Shaare Zedek Medical Center in Jerusalem, Israel.

Opioid-type drugs are potent painkillers. In fact, the World Health Organization lists two of them, codeine and morphine, as "essential medicines" that should be available worldwide.

Cherny and his colleagues asked cancer pain specialists, including doctors, nurses and social workers from 40 European countries plus Israel, to review access to opioids in their countries.

They found that tens of thousands of cancer patients in several former Soviet bloc countries can't easily get the drugs because of laws aimed at preventing a black market in opioids. In Ukraine, for example, patients are only allowed a day's supply of medicine at a time, while in Georgia they must get a stamp from a police station to obtain painkillers.

### Loosened restrictions

James Cleary at the Pain and Policy Studies Group in Madison, Wisconsin, is hopeful that laws will soon be relaxed in some eastern European countries.

Romania loosened restrictions on opioid painkillers in 2005 after doctors, pharmacists and patient advocates banded together to press the country's government for changes. Similar efforts are under way in Moldavia, Georgia, Armenia and other countries where access to opioids is restricted.

Cherny's team found fewer restrictions on opioid painkillers in western Europe. But outside the US, Canada and Australia, the situation in the rest of the world is similar to eastern Europe's or worse, Cleary says. "Ten countries consume 80 per cent of the world's opioids."

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## Chemical Element 112 is named "Copernicium"

### **The name proposed by GSI for the heaviest chemical element has been officially endorsed**

The heaviest recognized chemical element with the atomic number 112 was discovered at the GSI Helmholtzzentrum für Schwerionenforschung and – since February 19, 2010 – officially carries the name copernicium and the chemical symbol "Cn". The name was approved and officially announced today by the international union for chemistry IUPAC\*. The name "Copernicium" honors scientist and astronomer Nicolaus Copernicus (1473-1543).

IUPAC accepted the name proposed by the international discovering team around Sigurd Hofmann at the GSI Helmholtzzentrum. The team had suggested "Cp" as the chemical symbol for the new element. However, since the chemical symbol "Cp" gave cause for concerns, as this abbreviation also has other scientific meanings, the discoverers and IUPAC agreed to change the symbol to "Cn". Copernicium is 277 times heavier than hydrogen, making it the heaviest element officially recognized by IUPAC.

The suggested name "Copernicium" in honor of Nicolaus Copernicus follows the tradition of naming chemical elements after merited scientists. IUPAC officially announced the endorsement of the new element's name on February 19th, Nicolaus Copernicus' birthday. Copernicus was born on February 19, 1473 in Toruń, Poland. His work in the field of astronomy is the basis for our modern, heliocentric world view, which states that the Sun is the center of our solar system with the Earth and all the other planets circling around it.

An international team of scientists headed by Sigurd Hofmann was able to produce the element copernicium at GSI for the first time already on February 9, 1996. Using the 100 meter long GSI accelerator, they fired zinc ions onto a lead foil. The fusion of the atomic nuclei of the two elements produced an atom of the new element 112. This atom was only stable for the fraction of a second. The scientists were able to identify the new element by measuring the alpha particles emitted during the radioactive decay of the atom with the help of highly sensitive analytical procedures.

Further independent experiments confirmed the discovery of the element. Last year, IUPAC officially recognized the existence of element 112, acknowledged the GSI team's discovery and invited them to propose a name.

Copernicium is the sixth chemical element GSI scientist named. The other elements carry the names Bohrium (element 107), Hassium (element 108), Meitnerium (element 109), Darmstadtium (element 110), and Roentgenium (element 111).

*21 scientists from Germany, Finland, Russia, and Slovakia collaborated in the GSI experiments that lead to the discovery of element 112.*

*\*IUPAC - International Union of Pure and Applied Chemistry*

## **Dementia in extreme elderly population expected to become epidemic according to the 90+ study**

### ***Oldest men and women experience 18 percent annual dementia incidence that increases with age***

University of California researchers found that the incidence rate for all causes of dementia in people age 90 and older is 18.2% annually and significantly increases with age in both men and women. This research, called "The 90+ Study," is one of only a few to examine dementia in this age group, and the first to have sufficient participation of centenarians. Findings of the study appear in the February issue of *Annals of Neurology*, a journal published by Wiley-Blackwell on behalf of the American Neurological Association.

Dementia (senility) is a progressive, degenerative disorder that affects memory, language, attention, emotions, and problem solving capabilities. A variety of diseases cause dementia including Alzheimer's disease, stroke, and other neurodegenerative disorders. According to a 2000 report from the World Health Organization (WHO), approximately 6%-10% of the population 65 years and older in North America have dementia, with Alzheimer's disease accounting for two-thirds of those cases.

For their population-based, longitudinal study of aging and dementia, Maria Corrada, Sc.D., and colleagues invited members who were originally part of The Leisure World Cohort Study and 90 years of age or older as of January 1, 2003. As of December 31, 2007 there were 950 participants in The 90+ Study and 539 who had completed a full evaluation that included neurological testing, functional ability assessments and a questionnaire covering demographics, past medical history, and medication use. Evaluations were repeated every 6-12 months with a final dementia questionnaire completed shortly after death.

Analysis was completed on 330 participants who were primarily women (69.7%) between the ages of 90 to 102, and who showed no signs of dementia at baseline. Researchers identified 140 new cases of dementia during follow-up with 60% of those cases attributed to Alzheimer's disease (AD), 22% vascular dementia, 9% mixed AD and vascular dementia and 9% with other or unknown cause.

Dr. Corrada explained, "Our findings show dementia incidence rates almost double every five years in those 90 and older." Researchers found the overall incidence rate based on 770 person-years of follow-up was 18.2% per year. Rates increased with age from 12.7% per year in the 90-94 age group, to 21.2% per year in the 95-99 age group, to 40.7% per year in the 100+ age group. Incidence rates were very similar for men and women. Previous results from The 90+ Study found higher estimates of dementia prevalence in women (45%) compared to men (28%), a result also seen in other similar studies.

Prior reports estimate there were 2 million Americans aged 90 and older in 2007 and the number is expected to reach 8.7 million by 2050, making the oldest-old the fastest growing segment of the U.S. population. "In contrast to other studies, we found that the incidence of dementia increases exponentially with age in both men and women past age 90," said Dr. Corrada. "Given the population projections for this age group along with our findings, dementia in the oldest-old threatens to become an epidemic with enormous public health impact."

*Article: "Dementia Incidence Continues to Increase with Age in the Oldest-Old: The 90+ Study." Maria M. Corrada, Ron Brookmeyer, Annalia Paganini-Hill, Daniel Berlau, Claudia H. Kawas. Annals of Neurology; Published Online: February 23, 2009 (DOI: 10.1002/ana.21915); Print Issue Date: February 2010.*

### **News Release : Optical system promises to revolutionize undersea communications**

In a technological advance that its developers are likening to the cell phone and wireless Internet access, Woods Hole Oceanographic Institution (WHOI) scientists and engineers have devised an undersea optical communications system that - complemented by acoustics - enables a virtual revolution in high-speed undersea data collection and transmission.

Along with the "transfer [of] real-time video from un-tethered [submerged] vehicles" up to support vessels on the surface, "this combination of capabilities will make it possible to operate self-powered ROVs [remotely operate vehicles] from surface vessels without requiring a physical connection to the ROV," says WHOI Senior Engineer Norman E. Farr, who led the research team. This will not only represent a significant technological step forward, but also promises to reduce costs and simplify operations, they say.

Their report will be presented Feb. 23 at the 2010 Ocean Sciences Meeting in Portland Ore.

Compared to communication in the air, communicating underwater is severely limited because water is essentially opaque to electromagnetic radiation except in the visible band. Even then, light penetrates only a few hundred meters in the clearest waters; less in sediment-laden or highly populated waters.

Consequently, acoustic techniques were developed, and are now the predominant mode of underwater communications between ships and smaller, autonomous and robotic vehicles. However, acoustic systems - though capable of long-range communication - transmit data at limited speeds and delayed delivery rates due to the relatively slow speed of sound in water.

Now, Farr and his WHOI team have developed an optical communication system that complements and integrates with existing acoustic systems to enable data rates of up to 10-to-20 megabits per second over a range of 100 meters using relatively low battery power with small, inexpensive transmitters and receivers.

The advance will allow near-instant data transfer and real-time video from un-tethered ROVs and autonomous underwater vehicles (AUVs) outfitted with sensors, cameras and other data-collecting devices to surface ships or laboratories, which would require only a standard UNOLS cable dangling below the surface for the relaying of data.

This would represent a significant advance, Farr says, in undersea investigations of anything from the acidity of water to identifying marine life to observing erupting vents and seafloor slides to measuring numerous ocean properties. In addition, the optical system would enable direct maneuvering of the vehicle by a human.

He likens optical/acoustic system possibilities to the world opened up by “your household wi-fi.”

Co-investigator Maurice Tivey of WHOI adds that “underwater optical communications is akin to the cell phone revolution... wireless communications. The ability to transfer information and data underwater without wires or plugging cables in is a tremendous capability allowing vehicles or ships to communicate with sensors on the seafloor.

“While acoustic communications has been the method of choice in the past it is limited by bandwidth and the bulkiness of transducers,” Tivey says. “Today, sensors sample at higher rates and can store lots of data and so we need to be able to download that data more efficiently. Optical communications allows us to transfer large data sets, like seismic data or tides or hydrothermal vent variations, in a time-efficient manner.”

When the vehicle goes out of optical range, it will still be within acoustic range, the researchers said.

Because it enables communications without the heavy tether-handling equipment required for an ROV, the optical/acoustic system promises to require smaller, less-expensive ships and fewer personnel to perform undersea missions, Farr said.

This July, WHOI plans the first large-scale deployment of the system at the Juan de Fuca Ridge off shore of the Northwestern United States. The WHOI team will employ the human occupied vehicle (HOV) Alvin to deploy the optical system on a sub sea data concentrator to collect and transmit geophysical data from wellheads situated at the undersea ridge. Ultimately, Farr says, the system will “allow us to have vehicles [at specific undersea locations] waiting to respond to an event. It’s a game-changer.”

WHOI scientists collaborating on the research with Farr - who is in the Applied Ocean Physics and Engineering (AOPE) department - and Tivey, chair of the Geology and Geophysics department, are Jonathan Ware, AOPE senior engineer, Clifford Pontbriand, AOPE engineer, and Jim Preisig, AOPE associate scientist. *The work was funded by the National Science Foundation’s Division of Ocean Sciences.*

### **New tool developed to help guide pancreatic cyst treatment**

As a result of improved imaging technology, pancreatic cysts are increasingly diagnosed in asymptomatic individuals who undergo scans for other reasons. And while most of these cysts follow a benign course, a small but significant number are either malignant at the time of diagnosis or have the potential to develop into pancreatic cancer during a patient's lifetime.

The dilemma for both patient and clinician is determining which cysts to leave alone and which to surgically remove. Existing treatment guidelines don't clearly address many treatment options beyond the removal of part of the pancreas - a major undertaking for an asymptomatic lesion.

Now, a UCLA–Veterans Affairs research team has developed an evaluation tool to help guide asymptomatic pancreatic cyst treatment. Published in the February issue of the journal *Gastroenterology*, the tool takes into account overall health, age, cyst size, surgical risk and patients' views about quality of life.

"Surgery may not be the best initial approach for all patients diagnosed with a specific pancreatic cyst. The new tool may help with decision-making and mapping out a treatment plan," said study author Dr. Brennan Spiegel, director of the UCLA–VA Center for Outcomes Research and Education at the David Geffen School of Medicine at UCLA and the VA Greater Los Angeles Healthcare System.

The diagnosis of asymptomatic cysts has increased fivefold over the past decade, due partly to an aging population and to improved diagnostics. Current imaging techniques - including computed tomography (CT), magnetic resonance imaging (MRI) and endoscopic ultrasound, in which a small camera is inserted down the throat and into the stomach and small bowel to image the pancreas - combined with pancreatic cyst fluid analysis, offer an 80 percent accuracy in cyst diagnosis.

"Pancreatic cysts are most often diagnosed in an older population, and although many are benign, these must be carefully tracked, since a small percentage can develop into pancreatic cancer," said study author Dr. James J. Farrell, associate professor of digestive diseases at the Geffen School of Medicine and director of UCLA's Pancreatic Diseases Program.

Using decision-analysis software, the research team evaluated a set of hypothetical patients ranging in age from 65 to 85 with a variety of asymptomatic pancreatic cysts, ranging in size from half a centimeter to greater than 3 cm and located in the head of the pancreas, the most common site for branch duct cysts.

The evaluation tool compared four competing treatment strategies: surgical removal of the cyst, annual non-invasive imaging surveillance with MRI or CT, annual endoscopic ultrasound and no treatment.

While the tool takes into account patient age, health, cyst size and surgical risk, it also considers whether the patient values overall survival, no matter the quality of life, or if he or she prefers balancing quantity and quality of life by pursuing less invasive medical measures, which may lead to shorter survival but a better quality of life.

The researchers found that to maximize overall survival, regardless of the quality of life, surgical removal was the dominant strategy for a cyst greater than 2 cm, despite the patient's age or other health issues - this is smaller than the 3 cm threshold supported by current treatment guidelines for surgical intervention. Surveillance was the dominant strategy for any cyst less than 1 cm, which is similar to current guidelines.

For patients focused on optimizing both quantity and quality of life, either the "do nothing" approach or surveillance strategy appeared optimal for those between the ages of 65 and 75 with cysts less than 3 cm. For patients over age 85, non-invasive surveillance dominated if quality of life was important, most likely because surgical benefits are often outweighed by the poor quality of life experienced post-operatively in this population.

"The evaluation tool offers greater insight into not only key risk factors for deciding pancreatic cyst treatment but also what patients want and value," said study author Dr. Benjamin M. Weinberg, a gastroenterologist in the division of digestive diseases at UCLA's Geffen School of Medicine and the department of gastroenterology at the VA Greater Los Angeles Healthcare System. The researchers noted that data and information on how to use the new evaluation tool are available in the study manuscript, and that the tool is ready for use by clinicians.

Future research aimed at further understanding the disease process, exploring the rate at which benign cysts turn malignant, and delineating the natural history of a malignant cyst that doesn't undergo treatment may also help improve management of pancreatic cysts, the researchers said.

"We are learning more and more about the development and treatment of pancreatic cysts," said study author Dr. James S. Tomlinson, assistant professor of surgical oncology at UCLA's Geffen School of Medicine and the department of surgery at the VA Greater Los Angeles Healthcare System. "The more prognostic tools available to assist both the clinician and the patient in the complex decision-making associated with cystic disease of the pancreas, the more appropriate the management of this disease."

The researchers noted that current management of pancreatic cysts remains uncertain and challenging.

To date, no prospective randomized trials have been carried out for this disease. To optimize individual care, clinicians need evidence-based guidance to help select between competing strategies.

*The study was funded by a Veterans Affairs Health Services Research and Development grant, a Career Development Transition Award grant, the CURE Digestive Diseases Research Center and a National Institutes of Health career development grant.*

## **Water may not run uphill, but it practically flies off new surface**

GAINESVILLE, Fla. - Engineering researchers have crafted a flat surface that refuses to get wet. Water droplets skitter across it like ball bearings tossed on ice. The inspiration? Not wax. Not glass. Not even Teflon.

Instead, University of Florida engineers have achieved what they label in a new paper a "nearly perfect hydrophobic interface" by reproducing, on small bits of flat plastic, the shape and patterns of the minute hairs that grow on the bodies of spiders.

"They have short hairs and longer hairs, and they vary a lot. And that is what we mimic," said Wolfgang Sigmund, a professor of materials science and engineering. A paper about the surface, which works equally well with hot or cold water, appears in this month's edition of the journal *Langmuir*.

Spiders use their water-repelling hairs to stay dry or avoid drowning, with water spiders capturing air bubbles and toting them underwater to breathe. Potential applications for UF's ultra-water-repellent surfaces are many, Sigmund said. When water scampers off the surface, it picks up and carries dirt with it, in effect making the surface self-cleaning. As such, it is ideal for some food packaging, or windows, or solar cells that must stay clean to gather sunlight, he said. Boat designers might coat hulls with it, making boats faster and more efficient.

Sigmund said he began working on the project about five years ago after picking up on the work of a colleague. Sigmund was experimenting with microscopic fibers when he turned to spiders, noted by biologists for at least a century for their water-repelling hairs.

As a scientist and engineer, he said, his natural tendency was to make all his fibers the same size and distance apart. But he learned that spider hairs are both long and short and variously curved and straight,

forming a surface that is anything but uniform. He decided to try to mimic this random, chaotic surface using plastic hairs varying in size but averaging about 600 microns, or millionths of a meter.

The results came as a great surprise.

“Most people that publish in this field always go for these perfect structures, and we are the first to show that the bad ones are the better ones,” Sigmund said. “Of course this is a finding in a lab. This is not something you expect from theory.”

To be sure, water-repelling surfaces or treatments are already common, spanning shoe wax to caulk to car windshield treatments. Scientists have also reproduced other biologically inspired water repelling surfaces, including ones patterned after lotus leaves.

But Sigmund said the UF surface may be the most or among the most water phobic. Close-up photographs of water droplets on dime-sized plastic squares show that the droplets maintain their spherical shape, whether standing still or moving. Droplets bulge down on most other surfaces, dragging a kind of tail as they move. Sigmund said his surface is the first to shuttle droplets with no tail. Also, unlike many water-repelling surfaces, the UF one relies entirely on the microscopic shape and patterns of the material - rather than its composition.

In other words, physics, not chemistry, is what makes it water repellent. Theoretically, that means the technique could transform even the most water-sopping materials – say, sponges – into water-shedding ones. It also means that Sigmund’s surfaces need never slough off dangerous chemicals. Provided the surface material itself is made safe, making it water repellent introduces no new risks. Although he hasn’t published the research yet, Sigmund said a variation of the surface also repels oil, a first for the industry.

Sigmund said making the water or oil-repelling surfaces involves applying a hole-filled membrane to a polymer, heating the two, and then peeling off the membrane. Made gooey by the heat, the polymer comes out of the holes in the desired thin, randomly sized fibers.

While inexpensive, it is hard to produce successful surfaces with great reliability, and different techniques need to be developed to make the surfaces in commercially available quantities and size, Sigmund said. Also, he said, more research is needed to make the surfaces hardy and resistant to damage.

UF patents have already drawn a great deal of industry attention, he said. “We are at the very beginning but there is a lot of interest from industry, because our surface is the first one that relies only on surface features and can repel hot water, cold water, and if we change the chemistry, both oil and water.”

*Doctoral student Shu-Hau Hsu and undergraduate Eli Rubin contributed to the research, funded in part by a scholarship from Ohio-based OMNOVA Solutions Foundation.*

### **Intelligent People Have "Unnatural" Preferences and Values That Are Novel in Human Evolutionary History**

Higher intelligence is associated with liberal political ideology, atheism, and men's (but not women's) preference for sexual exclusivity

More intelligent people are statistically significantly more likely to exhibit social values and religious and political preferences that are novel to the human species in evolutionary history. Specifically, liberalism and atheism, and for men (but not women), preference for sexual exclusivity correlate with higher intelligence, a new study finds.

The study, published in the March 2010 issue of the peer-reviewed scientific journal *Social Psychology Quarterly*, advances a new theory to explain why people form particular preferences and values. The theory suggests that more intelligent people are more likely than less intelligent people to adopt evolutionarily novel preferences and values, but intelligence does not correlate with preferences and values that are old enough to have been shaped by evolution over millions of years.

"Evolutionarily novel" preferences and values are those that humans are not biologically designed to have and our ancestors probably did not possess. In contrast, those that our ancestors had for millions of years are "evolutionarily familiar."

"General intelligence, the ability to think and reason, endowed our ancestors with advantages in solving evolutionarily novel problems for which they did not have innate solutions," says Satoshi Kanazawa, an evolutionary psychologist at the London School of Economics and Political Science. "As a result, more intelligent people are more likely to recognize and understand such novel entities and situations than less intelligent people, and some of these entities and situations are preferences, values, and lifestyles."

An earlier study by Kanazawa found that more intelligent individuals were more nocturnal, waking up and staying up later than less intelligent individuals. Because our ancestors lacked artificial light, they tended to wake up shortly before dawn and go to sleep shortly after dusk. Being nocturnal is evolutionarily novel.

In the current study, Kanazawa argues that humans are evolutionarily designed to be conservative, caring mostly about their family and friends, and being liberal, caring about an indefinite number of genetically



unrelated strangers they never meet or interact with, is evolutionarily novel. So more intelligent children may be more likely to grow up to be liberals.

Data from the National Longitudinal Study of Adolescent Health (Add Health) support Kanazawa's hypothesis. Young adults who subjectively identify themselves as "very liberal" have an average IQ of 106 during adolescence while those who identify themselves as "very conservative" have an average IQ of 95 during adolescence.

Similarly, religion is a byproduct of humans' tendency to perceive agency and intention as causes of events, to see "the hands of God" at work behind otherwise natural phenomena. "Humans are evolutionarily designed to be paranoid, and they believe in God because they are paranoid," says Kanazawa. This innate bias toward paranoia served humans well when self-preservation and protection of their families and clans depended on extreme vigilance to all potential dangers. "So, more intelligent children are more likely to grow up to go against their natural evolutionary tendency to believe in God, and they become atheists."

Young adults who identify themselves as "not at all religious" have an average IQ of 103 during adolescence, while those who identify themselves as "very religious" have an average IQ of 97 during adolescence.

In addition, humans have always been mildly polygynous in evolutionary history. Men in polygynous marriages were not expected to be sexually exclusive to one mate, whereas men in monogamous marriages were. In sharp contrast, whether they are in a monogamous or polygynous marriage, women were always expected to be sexually exclusive to one mate. So being sexually exclusive is evolutionarily novel for men, but not for women. And the theory predicts that more intelligent men are more likely to value sexual exclusivity than less intelligent men, but general intelligence makes no difference for women's value on sexual exclusivity. Kanazawa's analysis of Add Health data supports these sex-specific predictions as well.

One intriguing but theoretically predicted finding of the study is that more intelligent people are no more or no less likely to value such evolutionarily familiar entities as marriage, family, children, and friends.

*The article "Why Liberals and Atheists Are More Intelligent" will be published in the March 2010 issue of Social Psychology Quarterly, a publication of the American Sociological Association. A copy can be obtained by bona fide journalists by emailing a request to pubinfo@asanet.org.*

### **Stroke incidence rising among younger adults, decreasing among elderly**

#### **Study highlights:**

- \* Stroke, often considered a disease of old age, is declining in the elderly and increasing at younger ages.
- \* The percentage of strokes occurring in people under age 45 has grown significantly since the 1990s.

#### **American Stroke Association meeting report:**

SAN ANTONIO - More young people are having strokes while older people are having fewer, according to data from Ohio and Kentucky presented at the American Stroke Association's International Stroke Conference 2010.

The average age of stroke patients in 2005 was nearly three years younger than the average age of stroke patients in 1993-1994 - a significant decrease, researchers said. Moreover, the percentage of people 20 to 45 having a stroke was up to 7.3 percent in 2005 from 4.5 percent in 1993-1994.

"This is scary and very concerning," said Brett M. Kissela, M.D., the study's lead author and Associate Professor, Co-Director of the Neurology Residency Program, and Vice-Chair of Education and Clinical Services at the University of Cincinnati Neuroscience Institute. "What was shocking was the proportion of patients under age 45. The proportion is up, the incidence rate is up."

Stroke has traditionally been considered a disease of old age, so the findings are of great public health significance because of the potential for greater lifetime burden of disability among younger patients.

Kissela said he became interested in studying the issue after observing an increase in young stroke patients admitted to his hospital.

Researchers examined data from the Greater Cincinnati/Northern Kentucky region, which includes about 1.3 million people. But Kissela said the trend noted is likely occurring throughout the United States because the higher prevalence of risk factors such as obesity and diabetes seen in the young here are also seen throughout the country. They recorded the age of people hospitalized for their first-ever stroke from the summer of 1993 to the summer of 1994, then compared it to calendar years 1999 and 2005.

In 1993-94, the average age of first stroke was 71.3 years old. The average age dropped to 70.9 in 1999 and was down to 68.4 by 2005. Researchers also found racial differences in stroke incidence. For blacks, the incidence of strokes among those over age 85 dropped significantly by 2005. For whites, the incidence decreased significantly starting at age 65 by 2005.

In both races, the incidence rates for strokes in 20 to 45 year olds increased, although the increase was only statistically significant among whites, doubling from 12 per 100,000 people to 25 per 100,000.

Kissela said it's hard to know with certainty what is driving this change, but speculated the increased prevalence of diabetes, hypertension and obesity is a major contributor.

"As physicians, we need to look for these potent risk factors even in young people," he said. "Stroke is a life-changing, devastating disease. It can affect young people, and we hope these data will serve as a wake-up call.

"From a public health standpoint, we need to do our best to prevent stroke at any age and monitor for stroke and stroke risk factors in all patients."

*Co-authors are: Kathleen Alwell, R.N.; Jane Khoury, Ph.D.; Charles J. Moomaw, Ph.D.; Daniel Woo, M.D.; Opeolu Adeoye, M.D.; Matthew L. Flaherty, M.D.; Pooja Khatri, M.D.; Simona Ferioli, M.D.; Joseph P. Broderick, M.D.; and Dawn Kleindorfer, M.D. Author disclosures can be found on the abstract.*

### **New clues found linking larger animals to colder climates**

#### **Scientists at UH publish breakthrough research on 163-year-old puzzle**

HOUSTON – Thanks to a pair of University of Houston researchers who found a possible new solution to a 163-year-old puzzle, ecological factors can now be added to physiology to explain why animals grow bigger in the cold.

Their results were published in the February issue of the *American Naturalist*, offering new insight to Bergmann's rule that animals grow larger at high, cold latitudes than their counterparts closer to the equator. While traditional explanations have been based on body temperature being the driving force of this phenomenon, this group of community ecologists hypothesize that better food makes high-latitude animals bigger.

Chuan-Kai Ho, a Ph.D. graduate from UH in ecology and evolution, his adviser and UH professor of biology and biochemistry Steven Pennings, and their collaborator Thomas Carefoot from the University of British Columbia opened up a new line of study into Bergmann's rule. The research program in Pennings' lab over the last decade has offered the most extensive work done on the general problem of latitudinal variation in plant-herbivore interactions. This latest finding from Pennings' groundbreaking research at UH on this subject came from one of Ho's doctoral dissertation chapters.

"Because the *American Naturalist* is one of the top journals in our field, publishing at this level is a mark of great success for a Ph.D. student," Pennings said. "It's also a reflection of the strength of our graduate program in the ecology and evolution division of UH's department of biology and biochemistry."

Ho, now a postdoctoral student at Texas A&M at Galveston's Armitage & Quigg Laboratory, also has another chapter from his UH dissertation on salt marsh food webs published in *Ecology*, another top journal in the field. Pennings received a doctoral dissertation improvement grant for Ho in 2007-2008 from the National Science Foundation that provided funding for Ho to run chemical analyses on leaves from different latitudes to assess their nutritional content.

Studying three different plant-eating species – grasshoppers, planthoppers and sea snails – collected from along the Atlantic coast to Japan, respectively, the researchers fed these herbivores plants from both high and low latitudes and found that they all grew better when fed plants from the higher latitudes. This indicates that Bergmann's rule could reflect that plants from high latitudes provide better food than those from low latitudes. These latest findings, according to Ho, indicate that studies of Bergmann's rule should consider ecological interactions in addition to the more traditional theories of physiology based on responses to temperature.

Over the years, work in Pennings' lab has shown that, although low-latitude plants are less nutritious and better protected by chemical defenses, they experience heavy damage from herbivores, which are more abundant at low latitudes. Future study, Pennings adds, should focus on why there are more herbivores at lower latitudes despite the lower-quality food sources. A likely explanation is that herbivore populations are limited at high latitudes by a short growing season and high death rates during cold winters.

"While the explanations discovered in our current study only apply to herbivores, it may be that carnivores and omnivores also might grow larger as a consequence of eating larger herbivores," Ho said. "Examining such patterns and underlying mechanisms in nature will help us understand what currently is going on and what might happen down the line to our ecosystems."

### **UCLA study finds genetic link between misery and death**

#### **Researchers develop novel strategy to probe 'genetic haystack'**

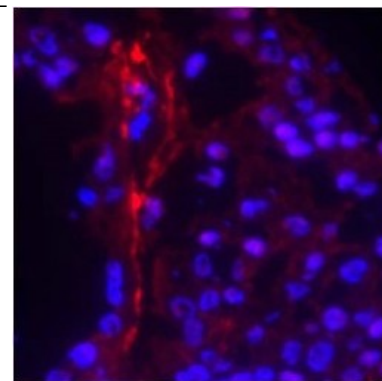
**By Mark Wheeler** February 24, 2010

In ongoing work to identify how genes interact with social environments to impact human health, UCLA researchers have discovered what they describe as a biochemical link between misery and death. In addition, they found a specific genetic variation in some individuals that seems to disconnect that link, rendering them more biologically resilient in the face of adversity.

Perhaps most important to science in the long term, Steven Cole, a member of the UCLA Cousins Center for Psychoneuroimmunology and an associate professor of medicine in the division of hematology-oncology, and his colleagues have developed a unique strategy for finding and confirming gene-environment interactions to more efficiently probe what he calls the "genetic haystack."

The research appears in the current online edition of Proceedings of the National Academy of Sciences.

Using an approach that blends computational, in vivo and epidemiological studies to focus their genetic search, Cole and his colleagues looked at specific groups of proteins known as transcription factors, which regulate gene activity and mediate environmental influences on gene expression by binding to specific DNA sequences. These sequences differ within the population and may affect a gene's sensitivity to environmental activation.



*Nerves (red) and tumor cells (blue) interact to send stress signals to disease sites in the body.*

Specifically, Cole analyzed transcription factor binding sequences in a gene called IL6, a molecule that is known to cause inflammation in the body and that contributes to cardiovascular disease, neurodegeneration and some types of cancer.

"The IL6 gene controls immune responses but can also serve as 'fertilizer' for cardiovascular disease and certain kinds of cancer," said Cole, who is also a member of UCLA's Jonsson Comprehensive Cancer Center and UCLA's Molecular Biology Institute. "Our studies were able to trace a biochemical pathway through which adverse life circumstances - fight-or-flight stress responses - can activate the IL6 gene.

"We also identified the specific genetic sequence in this gene that serves as a target of that signaling pathway, and we discovered that a well-known variation in that sequence can block that path and disconnect IL6 responses from the effects of stress."

To confirm the biochemical link between misery and death, and the genetic variation that breaks it, the researchers turned to epidemiological studies to prove that carriers of that specific genetic variation were less susceptible to death due to inflammation-related mortality causes under adverse social-environmental conditions.

They found that people with the most common type of the IL6 gene showed an increased risk of death for approximately 11 years after they had been exposed to adverse life events that were strong enough to trigger depression. However, people with the rarer variant of the IL6 gene appeared to be immune to those effects and showed no increase in mortality risk in the aftermath of significant life adversity.

This novel method of discovery - using computer modeling and then confirming genetic relationships using test-tube biochemistry, experimental stress studies and human genetic epidemiology - could speed the discovery of such gene and environmental relationships, the researchers say.

"Right now, we have to hunt down genetic influences on health through blind searches of huge databases, and the results from that approach have not yielded as much as expected," Cole said. "This study suggests that we can use computer modeling to discover gene-environment interactions, then confirm them, in order to focus our search more efficiently and hopefully speed the discovery process.

"This opens a new era in which we can begin to understand the influence of adversity on physical health by modeling the basic biology that allows the world outside us to influence the molecular processes going on inside our cells."

*Other authors on the study were Jesusa M. G. Arevalo, Rie Takahashi, Erica K. Sloan and Teresa E. Seeman, of UCLA; Susan K. Lutgendorf, of the University of Iowa; Anil K. Sood, of the University of Texas; and John F. Sheridan, of Ohio State University. Funding was provided by the National Institutes of Health, the UCLA Norman Cousins Center and the James L. Pendleton Charitable Trust. The authors report no conflict of interest.*

### **'Rubbish patch' blights Atlantic**

**By Victoria Gill** Science reporter, BBC News, Portland

Scientists have discovered an area of the North Atlantic Ocean where plastic debris accumulates. The region is said to compare with the well-documented "great Pacific garbage patch".

Kara Lavender Law of the Sea Education Association told the BBC that the issue of plastics had been "largely ignored" in the Atlantic. She announced the findings of a two-decade-long study at the Ocean Sciences Meeting in Portland, Oregon, US.

The work is the conclusion of the longest and most extensive record of plastic marine debris in any ocean basin.

Scientists and students from the SEA collected plastic and marine debris in fine mesh nets that were towed behind a research vessel.

The nets dragged along were half-in and half-out of the water, picking up debris and small marine organisms from the sea surface.

The researchers carried out 6,100 tows in areas of the Caribbean and the North Atlantic - off the coast of the US. More than half of these expeditions revealed floating pieces of plastic on the water surface. These were pieces of low-density plastic that are used to make many consumer products, including plastic bags.

Dr Lavender Law said that the pieces of plastic she and her team picked up in the nets were generally very small - up to 1cm across. "We found a region fairly far north in the Atlantic Ocean where this debris appears to be concentrated and remains over long periods of time," she explained. "More than 80% of the plastic pieces we collected in the tows were found between 22 and 38 degrees north. So we have a latitude for [where this] rubbish seems to accumulate," she said.

The maximum "plastic density" was 200,000 pieces of debris per square kilometre. "That's a maximum that is comparable with the Great Pacific Garbage Patch," said Dr Lavender Law.

But she pointed out that there was not yet a clear estimate of the size of the patches in either the Pacific or the Atlantic. "You can think of it in a similar way [to the Pacific Garbage Patch], but I think the word 'patch' can be misleading. This is widely dispersed and it's small pieces of plastic," she said.

The impacts on the marine environment of the plastics were still unknown, added the researcher.

"But we know that many marine organisms are consuming these plastics and we know this has a bad effect on seabirds in particular," she told BBC News.

Nikolai Maximenko from University of Hawaii, who was not involved in the study, said that it was very important to continue the research to find out the impacts of plastic on the marine ecosystem.

He told BBC News: "We don't know how much is consumed by living organisms; we don't have enough data.

"I think this is a big target for the next decade - a global network to observe plastics in the ocean."

### **Health care volunteers and disasters: First, be prepared**

#### ***Penn physician offers lessons from the medical response following devastating Haiti earthquake***

PHILADELPHIA – A surge in volunteers following a major disaster can overwhelm a response system, and without overall coordination, can actually make a situation worse instead of better. The outpouring of medical volunteers who responded to the devastating earthquake that rocked Haiti in January provides a roadmap for health care providers during future disasters, say the authors of a New England Journal of Medicine "Perspectives" piece that will be published online February 24. Thousands of doctors and nurses stepped up to help following the quake, but many were frustrated by difficulties connecting with a system that could immediately take advantage of their skills in the disaster zone. But lead author Raina Merchant, MD, an emergency physician and Robert Wood Johnson Foundation Clinical Scholar at the University of Pennsylvania School of Medicine, says that volunteers can enhance their effectiveness by preparing for a disaster before it occurs and thinking critically about their ability to respond.

Among Merchant and her colleagues' recommendations for health care workers who wish to volunteer during global disasters:

- \* Seek formal training in disaster medicine to prepare for working with limited resources under hazardous conditions. Short courses are offered by the American Medical Association, the American Red Cross, the Federal Emergency Management Agency and various surgical and trauma medical specialty associations.

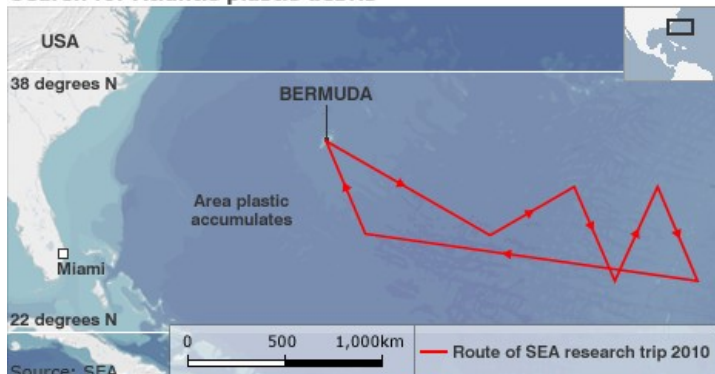
- \* Register with existing volunteer organizations, which often offer specialized training and advance verification of credentials and licensure to speed deployment to needy areas.

- \* Have a clear understanding of what working in the disaster area will require, from working in severe temperatures with poor sanitation and risk of violent crime and exposure to infectious diseases. Underlying medical conditions and the emotional challenges of witnessing extreme pain and suffering of victims are also important considerations.

- \* Seek counsel from travel medicine experts who can provide advice and access to immunizations, prophylactic medications, and education on protection from infections including HIV, tuberculosis, Hepatitis A and mosquito-borne illnesses such as malaria and dengue.

The authors also urge volunteers to consider where in the disaster cycle – early response, when the bulk of volunteers tend to come forward, or recovery and reconstruction – their skills would be most appropriate, and to

Search for Atlantic plastic debris



be mindful of the need to support relief efforts even after the world's attention has turned to other news. "Once immediate needs are addressed, the recovery phase begins, and there is often a prolonged delay before local health care systems can function even minimally," they write. "Health care volunteers are often less numerous during this time although the need for medical assistance remains vast."

*Other authors of the piece include Janet E. Leigh, BDS, DMD, a Robert Wood Johnson Health Policy Fellow, and Nicole Lurie, MD, MSPH, the Assistant Secretary for Preparedness and Response in the Department of Health and Human Services.*

### **Children can have recurrent strokes**

#### ***Study highlights importance of recognizing symptoms quickly***

Children can have strokes, and the strokes can recur, usually within a month, according to pediatric researchers. Unfortunately, the strokes often go unrecognized the first time, and the child does not receive treatment before the recurrence.

Pediatric neurologist Rebecca Ichord, M.D., director of the Pediatric Stroke Program at The Children's Hospital of Philadelphia, reported today on a study of arterial ischemic stroke in children at the International Stroke Conference 2010 in San Antonio, Texas. The conference was sponsored by the American Stroke Association.

An arterial ischemic stroke results from a blockage or constriction in an artery in or leading to the brain.

Ichord and colleagues at Children's Hospital followed 90 children with a median age of about 6 years old, treated for stroke between 2003 and 2009. Twelve patients (13 percent) had a recurrent stroke during the study period, most of them within a month of the first stroke. In six of the 12 children with recurrent strokes, no one diagnosed the initial stroke until a recurrent stroke occurred.

"Strokes don't occur only in the elderly," said Ichord. "They can also affect children as young as infants. Our findings reinforce how important it is to diagnose stroke in children as quickly as possible so that medical caregivers can provide emergency treatment and take measures to prevent recurrence."

Strokes can arise in children as a complication of other illnesses, such as sickle cell disease, which obstructs blood circulation, or from an undetected heart condition. A whiplash injury to a child's neck may damage an artery and leave it vulnerable to a blood clot that causes a stroke. Signs of a stroke are the same as in adults—a sudden loss of neurologic functions such as vision or speech, unsteady gait, or weakness on one side of the face or in limbs. What is different in children, said Ichord, is that symptoms may be subtle, examination is difficult and children are less able to describe their symptoms.

Emergency treatment for a stroke typically involves assuring adequate breathing and circulation, supplying intravenous fluids and improving blood supply to the brain. Medications such as aspirin or blood thinners are given to lower the risk of a recurrent stroke. In the aftermath of a stroke, rehabilitation is critical to promote recovery. "Because a stroke can recur, we need improved awareness of pediatric stroke among primary health care providers, and more research on the best ways to prevent a recurrence after a child suffers a first stroke," added Ichord.

### **Newborns' blood used to build secret DNA database**

**Ewen Callaway**, reporter

Texas health officials secretly transferred hundreds of newborn babies' blood samples to the federal government to build a DNA database, [a newspaper investigation has revealed](#).

According to The Texas Tribune, the Texas Department of State Health Services (DSHS) routinely collected blood samples from newborns to screen for a variety of health conditions, before throwing the samples out.

But beginning in 2002, the DSHS contracted Texas A&M University to store blood samples for potential use in medical research. These accumulated at rate of 800,000 per year. The DSHS did not obtain permission from parents, who sued the DSHS, which settled in November 2009.

Now the Tribune reveals that wasn't the end of the matter. As it turns out, between 2003 and 2007, the DSHS also gave 800 anonymised blood samples to the Armed Forces DNA Identification Laboratory (AFDIL) to help create a national mitochondrial DNA database.

This came to light after repeated open records requests filed by the Tribune turned up documents detailing the mtDNA programme. Apparently, these samples were part of a larger programme to build a national, perhaps international, DNA database that could be used to track down missing persons and solve cold cases.

Jim Harrington, the civil rights attorney who filed [the blood spot lawsuit](#) (pdf) last year on behalf of five Texas parents and who directs the Texas Civil Rights Project, suggests to the Tribune that the DSHS settled with the parents to avoid risking a court case that might have revealed the DNA database. "This explains the mystery of why they gave up so fast," he says.

Email exchanges (pdfs here and here) between state officials and Texas A&M, obtained by the Tribune, point to attempts to conceal efforts to use the DNA for any kind of research. The university had hoped to issue a press release detailing such efforts, but it acceded to the state's request to keep quiet.

Why did the DSHS want to keep it a secret? The Tribune quotes one Texas health official's explanation: *"Genetic privacy is a big ethical issue & even though ... approval is required for use of the spots in most situations and great care is taken to protect the identity of the spots, a press release would most likely only generate negative publicity."*

The fear of a negative reaction is understandable. Concerns over genetic privacy are growing - for example a recent study found that [even anonymous collections of DNA can potentially be traced back to individuals](#). However, the DSHS appears only to have handed over mitochondrial DNA, which is next to impossible to trace to individuals.

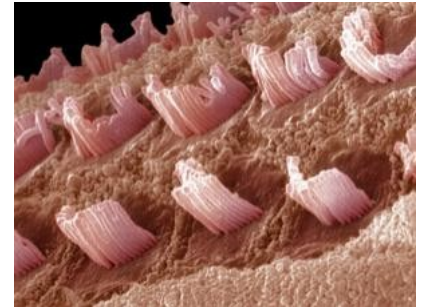
Handling public fears about genetic privacy is certainly tricky, but concealing such an affair is not the answer - and only increases public mistrust.

### **Ten days to save hearing after deafening sound**

DYING ear cells have been revived with a shot of gene therapy.

Ear cells have a hair-like structure that enables them to pick up sound vibrations. They are vital for hearing in mammals but are easily damaged by loud noise, which can lead to deafness.

A gene called Math1 has already been used to generate new hair cells in guinea pigs, from the supporting cells that surround them. Now David He at Creighton University in Omaha, Nebraska, and colleagues have shown that the same gene can repair guinea pigs' existing, damaged hair cells - as long as you get to them in time.



*Race against time to save ear cells (Image: Fred Hossler/Getty)*

He's team exposed guinea pigs to the audio equivalent of 200 rounds of gunfire. After this, the animals couldn't hear anything quieter than a chainsaw. When the researchers injected the animals with a Math1-loaded virus in one ear, hearing recovered almost completely.

The team tested the guinea pigs' hearing by monitoring the electrical activity in their brainstems in response to various noises. Then they viewed the newly grown cells in samples under a microscope. The hair cells also expressed a green protein, showing they had taken up the gene. Although the gene is only temporarily expressed, this is enough to make proteins that repair the cells for life, he says. However, cells could only be saved if they were treated within 10 days of being damaged.

He presented the work at the Association for Research in Otolaryngology meeting in Anaheim, California.

### **Exploiting the body's own ability to fight a heart attack**

Scientists trying to find a way to better help patients protect themselves against harm from a heart attack are taking their cues from cardiac patients.

The work has its roots in a perplexing curiosity that physicians have long observed in their patients: When faced with a heart attack, people who have had a previous one oftentimes fare better than patients who have never had one. Scientists have been working for 25 years to understand one reason why – a process known as ischemic preconditioning, where a temporary restriction of blood flow somehow strengthens cardiac tissues down the road.

In the latest research, published online Feb. 25 in the journal *Circulation Research*, a group led by Paul Brookes, Ph.D., and graduate student Andrew Wojtovich at the University of Rochester Medical Center have developed new methods in the effort to track down one of the key molecular agents involved. That molecule, known as the mitochondrial ATP-sensitive potassium channel, or mKATP, is central to ischemic preconditioning, but it has proven elusive for scientists seeking to isolate and describe it.

The Rochester team has created a new way – faster, less expensive, and easier than current methods – to measure the activity of mKATP. The team has also identified a molecule, known as PIP2, that can restore the channel's activity even once it has stopped working properly. The new work is expected to provide new clues about how the channel, which is thought to be central to our heart health, is regulated in the heart.

The ultimate goal of ischemic preconditioning, of course, is not to condition the heart by purposely causing a lack of blood flow to it. Rather, scientists like Brookes hope to use their knowledge to develop a new medication or treatment to help all patients better resist heart damage should it occur.

"Preconditioning has been shown to be effective in a variety of models in the laboratory, but it hasn't made it to the clinic yet," said Brookes, associate professor of Anesthesiology and of Pharmacology and Physiology. "One would want to design a drug to get the benefit of ischemic preconditioning without actually impeding blood flow in any way."

Physicians like cardiologist Eugene Storzynsky, M.D., Ph.D., see the phenomenon of ischemic preconditioning play out in their patients. He says that it's not uncommon for a middle-aged heart attack patient

who has had symptoms of heart disease to fare much better than a younger person with no history of heart disease who suddenly has a heart attack.

"The person with chronic heart disease who presents with a new heart attack does not appear nearly as disabled as the younger, healthier person with no history of heart disease, even though they present to the hospital with nearly identical blockages in their heart arteries," said Storzynsky, a heart failure expert who was not involved in the study.

"Of course, the ultimate goal for patients is to prevent heart disease wherever possible," added Storzynsky, assistant professor of Medicine in the Cardiology Division. "People need to make sure they eat a balanced, low-fat, reduced-salt diet, exercise regularly, and control their blood pressure – these actions will cut down one's risk for having a heart attack dramatically."

Brookes' team also discovered that mKATP is inhibited by fluoxetine, whose brand name is Prozac. It's the latest in a list of medications that have been shown in the laboratory to impede ischemic preconditioning, Brookes said. Others include painkillers known as cox-2 inhibitors, as well as beta-blockers that are used frequently to treat high blood pressure and heart problems.

Because medications like anti-depressants and beta-blockers are used so widely in patients who have had heart problems, scientists should take a close look at their possible effects on ischemic preconditioning, Brookes said, noting that the drugs have not been linked to any cardiac difficulties in people.

The new findings came about through a collaboration of several research groups at Rochester that allowed the team to address a problem that has dogged scientists for years. Brookes and a few other scientists had worked on mKATP, which shuttles potassium into and out of the mitochondria, for many years, but the laboratory work involved was so finicky that some other teams have not been able to reproduce the results, leading some scientists to question whether the channel truly exists.

Keith Nehrke, Ph.D., assistant professor in the Nephrology Division of the Department of Medicine, proposed a new way to measure the channel's activity. The new method involves measuring the movement of the element thallium into and out of mitochondria, as a surrogate for potassium. The new method is much faster and less expensive and should be much easier to reproduce by other scientists, Brookes said. He and Nehrke recently received funding from the National Institutes of Health to use the new method in the tiny roundworm known as *C. elegans* to identify the mKATP channel.

Then a retreat of the Department of Pharmacology and Physiology, where Wojtovich is a graduate student, connected the group with other researchers who are experts on potassium channels – Daniel A. Gray, M.D., of the Department of Medicine and Coeli Lopes, Ph.D., of the Aab Cardiovascular Research Institute.

*In addition to Brookes, Wojtovich, Nehrke, Gray and Lopes, authors of the paper include former medical resident Marcin K. Karcz, M.D., now with Unity Health System; and technical associate David M. Williams. The work was funded by the National Heart Lung and Blood Institute, the National Institute of General Medical Sciences, and the American Heart Association.*

## **Intracranial stenting, injecting clot-busting drugs directly to brain may be better than other treatments for urgent ischemic strokes**

### **Study highlights:**

\* Placing stents in the brain and injecting clot-busting drugs directly to the brain had better success rates for acute ischemic stroke than other treatments.

\* There was no excess risk of hemorrhage from either of the two treatments.

### ***American Stroke Association meeting report:***

SAN ANTONIO - Techniques that keep brain arteries open (intracranial stenting) or inject clot-busting drugs directly to the brain (intra-arterial tPA) may be more effective than other urgent ischemic stroke treatments, researchers said at the American Stroke Association's International Stroke Conference 2010.

In a study of 1,056 severe stroke patients treated with one or more therapies within eight hours of symptom onset, blood flow was restored in 76 percent of stented patients and 72 percent of those receiving the clot-busting drug tissue plasminogen activator (tPA) directly to the brain (intra-arterial tPA). Overall, blood flow was restored in only 69 percent of patients treated with other drug techniques or interventions.

Ischemic stroke is caused by blockages in a vessel in or leading to the brain.

### ***Researchers studied several treatment techniques:***

- intra-arterial tPA
- intravenous delivery of tPA via the arm
- intracranial stenting
- Merci Retriever™ – a corkscrew-like device that is threaded into the blocked blood vessel to grab and pull out clots
- glycoprotein IIb/IIIa antagonists
- Penumbra™ aspiration catheter – uses suction to remove blood clots
- angioplasty (without stenting)

But only results for intra-arterial tPA and intracranial stenting reached statistical significance.

“Essentially, there is no standard currently as to which interventions are performed for acute stroke in this country,” said Rishi Gupta, M.D., senior author of the study and an assistant professor at Vanderbilt University Medical Center’s Department of Neurology in Nashville, Tenn. “We decided to study treatment at 12 of the busiest stroke centers in the country to determine which of the therapies currently in use may be yielding the best results in terms of opening the blood vessel without creating hemorrhage.”

Researchers said 534 patients received more than one therapy and 75 percent of the time (or in 400 patients), it was successful.

The next phase of the study will examine whether the initial success of these two treatments continues through three months of follow-up, he said.

*The study’s lead author is Esteban Cheng-Ching, M.D., a neurology resident at the Cleveland Clinic Foundation. Other co-authors are Elad I. Levy, M.D.; Osama Zaidat, M.D.; Sabareesh K. Natarajan, M.D., M.S.; Junaid S. Kalia, M.D.; Tudor G. Jovin, M.D.; Albert J. Yoo, M.D.; Raul G. Nogueira, M.D.; Marilyn Rymer, M.D.; Ashis H. Tayal, M.D.; Daniel P. Hsu, M.D.; David S. Liebeskind, M.D.; Alex Abou-Chebl, M.D.; Ashish Nanda, M.D.; Melissa Tian; Qing Hao, M.D., Ph.D.; Thanh N. Nguyen, M.D.; and Michael Chen, M.D. Author disclosures are on the abstract.*

[Click here download audio clips](#) offering perspective on this research from American Stroke Association spokesperson, Mark Alberts, M.D., Professor of Neurology, Northwestern University Feinberg School of Medicine, Director Stroke Program, Northwestern Memorial Hospital, Chicago.

### **MeCP2 goes global -- redefining the function of the Rett syndrome protein**

A paper published online today in *Molecular Cell* proposes that Methyl CpG binding protein 2 (MeCP2) impacts the entire genome in neurons, rather than acting as a regulator of specific genes. Mutations in MeCP2 cause the autism spectrum disorder Rett Syndrome as well as some cases of neuropsychiatric problems including autism, schizophrenia and learning disabilities.

The discovery of MeCP2’s global reach was made in the laboratory of Adrian Bird, Ph.D. of the University of Edinburgh. Bird’s seminal contributions in the Rett Syndrome field include cloning the MeCP2 protein in the early 1990’s and the dramatic reversal of severe symptoms in fully mature mice models of the disease published in *Science* in 2007. He is a Trustee and Scientific Advisor of the Rett Syndrome Research Trust, a nonprofit organization intensively focused on the development of treatments and cures for Rett Syndrome and related MECP2 disorders.

Rett Syndrome strikes little girls almost exclusively, with first symptoms usually appearing before the age of 18 months. These children lose speech, motor control and functional hand use, and many suffer from seizures, orthopedic and severe digestive problems, breathing and other autonomic impairments. Most live into adulthood, and require total, round-the-clock care.

Historically, MeCP2 has been viewed as a classic transcription factor, but Bird’s data establishes MeCP2 as one of the most abundant neuronal nuclear proteins, with levels 100 to 1,000 times higher than typical transcription factors. In fact, there are nearly as many molecules of MeCP2 in the nucleus as there are nucleosomes, the fundamental repeating structural units of chromatin which in turn make up chromosomes. To put this in perspective, there is enough MeCP2 to cover nearly the entire genome.

Peter Skene, a post-doctoral fellow in the Bird lab and first author of the paper confirmed via chromatin immunoprecipitation and high throughput sequencing that this huge abundance of MeCP2 meticulously tracks the DNA methylation pattern of the cell. As a result, Skene observed that most regions of the genome bind to MeCP2, calling into question the previously assigned role of this protein as a target-specific transcription factor. This may explain why few clear gene targets for MeCP2 have been identified in the last decade.

"The brain contains many types of neurons with different functions, but interestingly it appears that the pattern of MeCP2 binding to chromosomes is broadly similar in all of them. This raises the possibility that the neuronal defect brought about by mutations in this gene affect all neurons in a similar way. If there really is a generic defect shared by many neurons, then the causes of Rett Syndrome may be less complicated than we feared. This idea now needs to be tested by further work," said Professor Bird.

In line with its genome-wide distribution, the scientists found that MeCP2 globally impacts the packaging of the DNA in the cell. Histones are proteins which act as spools around which DNA is wound. This winding, or compaction, allows the 1.8 meters of DNA material to fit inside each of our cells. There are two classes of histones – core histones and linker histones. Core histones form the spool around which DNA winds - resembling beads on a string. The linker histones, such as histone H1, seal the DNA onto the spool formed by the core histones. In this way linker histones act as a padlock to hold the DNA in this structure and stop inappropriate access to the DNA outside of genes. In the absence of MeCP2, the amount of linker histone H1 doubles, suggesting an attempt to compensate for the lack of MeCP2.



The Bird lab also found an increase in histone acetylation in MeCP2-deficient neurons, but not in glia. These chemical modifications lead to an unwinding of the chromatin spools and potentially leave the DNA open for inappropriate expression. This suggests that the role of MeCP2 is to globally suppress the genome.

"Consistent with MeCP2 coating the entire genome, we observed global changes in the chromatin composition and activity. In the absence of MeCP2, we discovered an increase in the spurious transcription of the so-called 'junk DNA' which lies between genes. This suggests to us that rather than targeting specific genes, MeCP2 functions on a genome-wide level and may act as the watchdog of the neuronal genome," said Skene.

"RSRT is pursuing two parallel approaches to interventions for Rett Syndrome. One is to find assays for MeCP2 function and then screen for anything that fixes the defect. The other is to understand as much as possible about what MeCP2 does in the brain and then design rational treatments. Understanding that MeCP2 acts in a global manner rather than as a gene-specific regulator gives us a new perspective on the molecular basis of Rett Syndrome that will aid in guiding drug development and other treatment modalities", comments Monica Coenraads, Executive Director of RSRT and parent of a child with the disorder.

*For an in-depth interview with Adrian Bird please visit the RSRT Blog, <http://rettsyndrome.wordpress.com/>*

### **Do men with early prostate cancer commit suicide more frequently?**

The introduction of prostate-specific antigen (PSA) testing as a screening tool for early detection of prostate cancer (PCa) in the beginning of the 1990s drastically increased the detection of PCa. The risk of suicide is increased among cancer patients including men with PCa. To assess the risk of suicide among men diagnosed with PCa subsequent to PSA testing, a nation-wide study was carried out in Sweden. The results are published in the March issue of *European Urology*, the scientific journal of the European Association of Urology (EAU).

Anxiety related to a crisis reaction may develop into a depression, and several studies have shown that there is a high anxiety level among screeners in various screening programs. However, as in most countries, men who underwent PSA testing in Sweden at the time represent an opportunistic screening population and not a true population-based screening program by invitation. Therefore, they may have been more health conscious, less prone to develop depression, and more prepared to accept the potential side effects of curative treatment than the general population.

The number of suicides registered for cases in the Prostate Cancer Base Sweden (a database in which a number of different registers are merged) cohort was compared with the expected number of suicides in an age-matched general male Swedish population. The strengths of this study include the population-based design with inclusion of approximately 98% of all men in Sweden diagnosed with PCa between 1997 and 2006.

There was no evidence for an increased risk of suicide among men diagnosed with early nonpalpable PCa detected by PSA testing. The suicide rate, however, was twice as high among men diagnosed with locally advanced or metastatic disease compared with the general male population. This is important to acknowledge in order to focus on the need to identify signs of depression and optimise treatment among this category of patients.

***Suicide Risk in Men with Prostate-Specific Antigen–Detected Early Prostate Cancer: A Nationwide Population-Based Cohort Study from PCBaSe Sweden***

*Anna Bill-Axelsson, Hans Garmo, Mats Lambe, Ola Bratt, Jan Adolfsson, Ullakarin Nyberg, Gunnar Steineck, Pär Stattin. *European Urology* Volume 57, issue 3, pages 363-550, March 2010*

#### **Doctor and Patient**

### **A Surgeon Learns of the Choking Game**

**By PAULINE W. CHEN, M.D.**

The patient was already on the operating room table when the other transplant surgeons and I arrived to begin the surgery that would remove his liver, kidneys, pancreas, lungs and heart. He was tall, with legs that extended to the very end of the table, a chest barely wider than his 16-year-old hips, and a chin covered with pimples and peach fuzz.

He looked like any one of the boys I knew in high school.



**Image Source/Getty Images**

Those of us in the room that night knew his organs would be perfect - he had been a healthy teenager before death - but the fact that he had not died in a terrible, mutilating automobile or motorcycle crash made us all that much more certain.

The boy had hanged himself and had been discovered early, though not early enough to have survived.

While I had operated on more than a few suicide victims, I had never come across someone so young who had chosen to die in this way. I asked one of the nurses who had spent time with the family about the circumstances of his death. Was he depressed? Had anyone ever suspected? Who found him?

"He was playing the choking game," she said quietly.

I stopped what I was doing and, not believing I had heard correctly, turned to look straight at her.

“You know that game where kids try to get high,” she explained. “They strangle themselves until just before they lose consciousness.” She put her hand on the boy’s arm then continued: “Problem was that this poor kid couldn’t wiggle out of the noose he had made for himself. His parents found him hanging by his belt on his bedroom doorknob.”

The image of that boy and of the dangling homemade noose comes rushing back whenever I meet another victim or read about the grim mortality statistics associated with this so-called game. But one thing has haunted me even more in the years since that night. As a doctor who counts adolescents among her patients, I knew nothing about the choking game before I cared for a child who had died “playing” it.

Until recently, there has been little attention among health care professionals to this particular form of youthful thrill-seeking. What has been known, however, is that children ages 7 to 21 participate in such activities alone or in groups, holding their breath, strangling one another or dangling in a noose in the hopes of attaining a legal high.

Two years ago the Centers for Disease Control and Prevention reported 82 deaths attributable to the choking game and related activities. This year the C.D.C. released the results of the first statewide survey and found that one in three eighth graders in Oregon had heard of the choking game, while more than one in 20 had participated.

The popularity of the choking game may boil down to one fact: adolescents believe it is safe. In one recent study, almost half of the youths surveyed believed there was no risk associated with the game. And unlike other risk-taking behaviors like alcohol or drug abuse where doctors and parents can counsel teenagers on the dangers involved, no one is countering this gross misperception regarding the safety of near strangulation.

Why? Because like me that night in the operating room, many of my colleagues have no clue that such a game even exists.

This month in the journal *Pediatrics*, researchers from the Rainbow Babies and Children’s Hospital in Cleveland reported that almost a third of physicians surveyed were unaware of the choking game. These doctors could not describe any of the 11 warning signs, which include bloodshot eyes and frequent and often severe headaches. And they failed to identify any one of the 10 alternative names for the choking game, startlingly benign monikers like Rush, Space Monkey, Purple Dragon and Funky Chicken.

“Doctors have a unique opportunity to see and prevent this,” said Dr. Nancy E. Bass, an associate professor of pediatrics and neurology at Case Western Reserve University and senior author of the study. “But how are they going to educate parents and patients if they don’t know about it?”

In situations where a patient may be contemplating or already participating in choking activities, frank discussions about the warning signs can be particularly powerful. “The sad thing about these cases,” Dr. Bass observed, “is that every parent says, ‘If we had known what to look for, we probably could have prevented this.’” One set of parents told Dr. Bass that they had noticed knotted scarves and ties and a bowing closet rod in their son’s room weeks before his death.

“They had the telltale signs,” Dr. Bass said, “but they never knew what to look for.”

Nonetheless, broaching the topic can be difficult for both parents and doctors. Some parents worry that talking about such activities will paradoxically encourage adolescents to participate. “But that’s kind of a naïve thought,” Dr. Bass countered. “Children can go to the Internet and YouTube to learn about the choking game.” In another study published last year, for example, Canadian researchers found 65 videos of the choking game from postings to YouTube over an 11-day period. The videos showed various techniques of strangulation and were viewed almost 175,000 times. But, Dr. Bass added, “these videos don’t say that kids can die from doing this.”

Still, few doctors discuss these types of activities with their adolescent patients. Only two doctors in Dr. Bass’s study reported ever having tackled the topic because of a lack of time. “Talking about difficult topics is really hard to do,” Dr. Bass noted, “when you just have 15 minutes to follow up.”

But it is even harder when neither doctor nor patient has any idea of what the activity is or of its lethal consequences.

Based on the results of their study, Dr. Bass and her co-investigators have started programs that educate doctors, particularly those in training, about the warning signs and dangers of strangulation activities. “The choking game may not be as prominent as some of the other topics we cover when we talk with patients,” Dr. Bass said, “but it results in death.”

And, she added, “If we don’t talk to doctors about this issue, they won’t know about the choking game until one of their patients dies.”

## Disease gene blocker sneaks past cell defences

\* 25 February 2010 by Linda Geddes

SNIPPETS of RNA that switch off disease-causing genes can now slip into cells unaided. This could help efforts to use RNA interference (RNAi) to treat diseases such as cancer and diabetes.

For a gene to be expressed as a protein, it must first be copied into messenger RNA (mRNA). RNAi blocks this process by sending in RNA snippets that bind to specific mRNAs.

To do this, the gene-blocking RNA must first get into the cell. A variety of elaborate strategies have been suggested as ways to get it there, such as attaching the blocking RNA to fragments of bacteria or carbon nanotubes.

Now Anastasia Khvorova and colleagues at RXi Pharmaceuticals in Worcester, Massachusetts, have come up with a simpler approach.

RNA molecules cannot easily pass unaided into cells because they are charged or "polar"; this means they dissolve easily in water but not fats. To cross the cell membrane, molecules need to be soluble in both.

### *Crossing the cell membrane*

So Khvorova's team chemically modified RNA molecules to reduce their negative charge, and make them smaller (see diagram). This seemed to do the trick. "These compounds get inside the cell within seconds," says Khvorova, who presented her work at an RNAi Silencing Conference in Keystone, Colorado, last month.

RXi says that in studies of human and animal cells its molecules have been shown to block at least 17 genes, some of which are implicated in disease. It hopes to find many more, but the unusually short strands of RNA it uses may not be able to block the RNA of all genes.

Studies in mice show that the molecules can enter many different cell types, including immune, eye and liver cells, and switch off genes there, RXi says. However, to tackle cancer or inflammatory disease, RXi's RNA would have to be injected into the bloodstream. From there it might find its way not just into cancer cells, for example, but also into healthy cells, and block genes there, warns John Rossi at the City of Hope cancer centre in Duarte, California, who researches an alternative approach to RNAi. Even for diseases where the RNA could be injected directly into target tissue, it might still reach cells other than the intended ones.

Rossi adds, however, that RXi's self-delivering RNA might be useful in cell-culture or animal experiments as a means of rapidly screening RNA sequences to find candidates that could be delivered by other means.

## Emerging tick-borne disease

### *A domestic ecological mystery*

Stories of environmental damage and their consequences always seem to take place far away and in another country, usually a tropical one with lush rainforests and poison dart frogs.

In fact, similar stories starring familiar animals are unfolding all the time in our own backyards - including gripping tales of diseases jumping from animal hosts to people when ecosystems are disrupted.

This time we're not talking hemorrhagic fever and the rainforest. We're talking tick-borne diseases and the Missouri Ozarks. And the crucial environmental disruption is not the construction of roads in the rainforest, it is the explosion of white-tailed deer populations.

An interdisciplinary team at Washington University in St. Louis has been keeping a wary eye on emerging tick-borne diseases in Missouri for the past 20 years. Team members include ecologists Brian F. Allan and Jonathan M. Chase, molecular biologists Robert E. Thach and Lisa S. Goessling, and physician Gregory A. Storch.

The team recently developed a sophisticated DNA assay, described in the March 2010 issue of *Emerging Infectious Diseases*, that allows them to identify which animal hosts are transmitting pathogens to ticks.

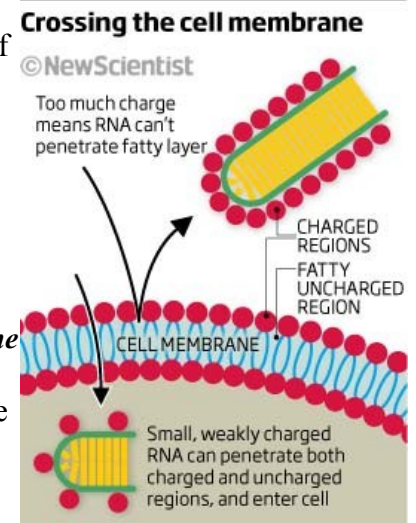
"This new technology is going to be the key to understanding the transmission of diseases from wildlife to humans by ticks," Allan says.

### **Three new tick-borne diseases**

Missouri has three common species of ticks. The black-legged tick (*Ixodes scapularis*) that carries Lyme disease is found here, but is far less common than in other regions of the country.

Missouri also has American dog ticks (*Dermacentor variabilis*), which carry Rocky Mountain Spotted Fever, but again this is a less frequently encountered species.

The most common tick is *Amblyomma americanum*, called the lone star tick because the adult female has a white splotch on her back. It is a woodland species originally found in the southeastern United States whose range now extends northward as far as Maine. Until recently, this tick, which is an aggressive and indiscriminate biter, was considered a nuisance species, not one that played a role in human disease.



Then in 1986 a physician noticed bacterial clusters called morulae in a blood smear from a critically ill man that looked like those formed by bacteria in the genus Ehrlichia (named for the German microbiologist Paul Ehrlich). At the time Ehrlichia were thought to cause disease only in animals.

The bacterium was later identified as a new species, Ehrlichia chaffeensis, and the disease was named human ehrlichiosis. In 1993 E. chaffeensis DNA was found in lone star ticks collected from several states.

Ehrlichiosis typically begins with vague symptoms that mimic those of other bacterial illnesses. In a few patients, however, it progresses rapidly to affect the liver, and may cause death unless treated with antibiotics.

In 1999, a second Ehrlichia species was identified as an agent of human disease. The DNA of the newly identified bacterium was also found in lone star ticks.

Gregory A. Storch, M.D., the Ruth L. Siteman Professor of Pediatrics at the Washington University School of Medicine in St. Louis, led the team that identified the second Ehrlichia species. The discovery was described in the New England Journal of Medicine in 1999.

Blood samples from patients in the St. Louis area who might have a tick-borne disease are still sent to Storch's lab for analysis. But the ehrlichioses weren't the only emerging diseases the tick was carrying. In the 1980s, reports had started to trickle in from Missouri, North Carolina and Maryland of an illness accompanied by a bulls-eye rash. Called STARI, for southern tick-associated rash illness, it resembled Lyme disease but didn't seem to be as severe. The lone star tick was also incriminated in these cases. STARI is thought to be caused by a bacterium named Borrelia lonestari, after its tick vector.

### The question

"The question," says Thach, Ph.D., professor of biology in Arts & Sciences and of biochemistry and molecular biophysics in the School of Medicine, "is where do infectious diseases come from?"

"Most seem to come from nature - they exist in other animals - and then make the leap from animals to people, Thach says." Assuming this model applies to the lone star tick diseases, what is their animal reservoir and why are they jumping?

Lone star ticks need blood meals to power their metamorphoses (they go through three stages: larva, nymph and adult) and egg laying. They sometimes bite coyotes, foxes and other animals, but their favorite hosts are wild turkey and white-tailed deer. Especially white-tailed deer, which seem to be playing a major role in maintaining large lone star tick populations and setting the stage for tick diseases to jump to people.

### Suspicion grows

Fieldwork conducted by Allan, Ph.D., a post-doctoral research fellow at Washington University's Tyson Research Center in the oak-history forests that grace the rolling hills of the Missouri Ozarks, was reinforcing the team's suspicions about deer.

In forests managed by the Missouri Department of Conservation and by the Nature Conservancy, Allan was looking at the effect on tick numbers of management practices such as selective logging and prescribed burns.

Allan's results show that management practices sometimes have counterintuitive effects on tick numbers. For example, he reported in the Journal of Medical Entomology in September 2009 that prescribed burns increase tick numbers and human risk of exposure to lone star tick diseases.

To make sense of this counterintuitive result all you need to do is follow the deer. A prescribed burn leads to a flush of new plant growth. Deer, which are selective browsers, are attracted by the tender greenery. They flood into the burn sites, and drop blood-sated ticks as they browse.

### Getting blood from a tick

Although deer were looking shady, the case against them was still largely circumstantial. Could the scientists get definitive evidence?

Allan found a way. He read about an assay that had been developed in Jeremy Gray's lab at University College Dublin to identify animal reservoirs of Lyme disease. ("There are twice as many cases of Lyme disease in Western Europe as there are in the United States," says Thach, "and there is a lot of Lyme research being done there.") Allan asked Thach whether his lab would be willing to develop a similar assay for the lone star tick diseases. "With my colleague Lisa Goessling," Thach says, "we developed the technique here and used it to analyze the ticks Brian brought in from the woods."

"The technology for identifying mosquito blood meals has existed for some time," Allan says, "because they take many blood meals over a short period of time, so the blood is usually still fresh when you capture them. And they keep coming back for another meal, so it's very easy to capture them."



*A. americanum*, known as the lone star tick because adult females sport a star on their backs, has recently been shown to be the vector for several new diseases. US Centers for Disease Control

It's much harder to get blood from a tick, which usually takes only one blood meal per life stage," Allan continues. "By the time we capture the tick eight months to a year may have elapsed. The tick has had a long time to digest that blood, so there may be only a tiny amount of DNA left - if there's any."

The team does two assays on the tick DNA: one to identify pathogenic bacteria and the other to identify the animal that provided the blood and with it the bacteria.

### **Analyzing DNA in the blood**

The first step in the assay is to pulverize the ticks to release the DNA, which is then amplified using a procedure called the polymerase chain reaction, or PCR. This provides enough DNA for identification.

Following amplification is a step called reverse line blot hybridization. Probes, which are short sequences of DNA unique to a bacterium or to a host animal, are deposited in lines on a membrane. The membrane is then rotated, and the products of the PCR step - tagged with a chemiluminescent (light-generating) dye - are laid down in lines perpendicular to the probe lines.

Wherever two lines cross, DNA from the tick sample mixes with probes for either bacterial or animal DNA. If the two match, the molecules will bond, or hybridize. When the membrane is later washed, tick-sample DNA that has not hybridized washes off. DNA that has hybridized sticks and shows up as a chemiluminescent spot on the membrane. Reading the spots, tells the scientists which bacteria the tick was carrying and which animal provided its last blood meal.

Assay results showed that most of the nymphal lone star ticks infected with *E. chaffeensis* fed upon a white-tailed deer in the larval life stage. "So deer are definitely a primary reservoir for this bacterium," says Thach. "But we also found some kind of squirrel - which we have more recently identified as the common gray squirrel - and what appears to be some kind of rabbit."

In general, the results suggest deer are probably "weakly competent reservoirs" for the tick diseases, meaning that ticks that bit deer stood only a small chance of picking up one of the pathogens. On the other hand, deer have huge "reservoir potential," because there are so many of them.

The bottom line: a sprinkling of deer is ok; crowds of deer are a problem.

### **Too many deer**

Are the bacteria that cause the new tick-borne diseases truly new or have they existed for a long time in wildlife reservoirs like the white-tailed deer without causing human disease?

"We don't know the answer," says Allan, "but my guess is these tick-borne diseases are probably being unleashed by human-mediated environmental change." By human-mediated environmental change he means deer protection, the human behaviors that have led to an explosion in white-tailed deer populations.

"Some state agencies plant food plots for deer, we've created deer forage in the form of crop fields and suburban plantings, and we've taken away almost all of their predators - except cars," Allan says.

To be sure, white-tailed deer were once nearly eliminated from the state. In 1925 there were thought to be only 395, according to the Missouri Department of Conservation. The hunting season was closed that year and again from 1938 through 1944, and deer were re-located to help reestablish them in the state.

In 2009, Lonnie Hanson of the Missouri Department of Conservation estimated the herd at 1.4 million. Nationwide the pattern is similar. Nobody is sure how many deer there are, but estimates range from 8 to 30 million, levels everyone agrees are excessive.

"If you had to point to one factor that led to the emergence of tick-borne diseases in the eastern United States, it would have to be these unnaturally large populations of deer," Allan



*STARI, a disease carried by lone star ticks, resembles Lyme disease in that it is characterized by a bulls-eye rash, but it is caused by a different bacterium and seems to be less virulent.*  
Wunderling/Creative Commons

## **Why symptoms of schizophrenia emerge in young adulthood**

### **Brain differences caused by known schizophrenia gene may explain late development of classic symptoms**

In reports of two new studies, researchers led by Johns Hopkins say they have identified the mechanisms rooted in two anatomical brain abnormalities that may explain the onset of schizophrenia and the reason symptoms don't develop until young adulthood. Both types of anatomical glitches are influenced by a gene known as DISC1, whose mutant form was first identified in a Scottish family with a strong history of schizophrenia and related mental disorders. The findings could lead to new ways to treat, prevent or modify the disorder or its symptoms.

In one of the studies, published in the March issue of Nature Neuroscience, researchers examined DISC1's role in forming connections between nerve cells. Numerous studies have suggested that schizophrenia results from abnormal connectivity. The fact that symptoms typically arise soon after adolescence, a time of massive reorganization of connections between nerve cells, supports this idea.

The scientists began their study by surveying rat nerve cells to see where DISC1 was most active. Unsurprisingly, they found the highest DISC1 activity in connections between nerve cells. To determine what DISC1 was doing in this location, the researchers used a technique called RNA interference to partially shut off DISC1 activity. Consequently, they saw a transient increase and eventual reduction in size and number of dendritic spines, spikes on nerve cells' branch-like extensions that receive input from other nerve cells.

To determine how DISC1 regulates dendritic spine formation, the researchers studied which brain proteins interact with the protein expressed by the DISC1 gene. They identified one, called Kal-7, which earlier studies suggested is critical for proper dendritic spine formation. Further experiments suggested that the DISC1 protein acts as temporary holding place for Kal-7, binding it until it can be released to trigger a molecular cascade that results in dendritic spine formation.

Study leader Akira Sawa, M.D., Ph.D., professor of psychiatry and director of the program in molecular psychiatry at the Johns Hopkins University School of Medicine, says it is becoming clear that having a defective DISC1 gene might lead to an abnormally small number and size of dendritic spines, which could lead nerve cells to maintain weaker connections with unusually low numbers of neighboring neurons. Such abnormal connectivity has long been seen in autopsied brains from schizophrenia patients.

"Connections between neurons are constantly being made and broken throughout life, with a massive amount of broken connections, or 'pruning,' happening in adolescence," Sawa says. "If this pruning doesn't happen correctly, it may be one reason for the pathogenesis of schizophrenia," he adds.

In the second study, published in the Feb. 25 issue of Neuron, Sawa's team generated a new animal model of schizophrenia by temporarily shutting off the DISC1 gene in mice in the prefrontal cortex, a brain area known to differ in schizophrenic people. The new model allowed them to study other roles for DISC1 in the brain.

The researchers created their novel model by, again, using RNA interference. They injected short pieces of the nucleic acid RNA engineered to shut off the DISC1 gene into cavities in the developing brains of mouse fetuses two weeks after conception. Tests showed that these snippets of RNA migrated into cells in the prefrontal cortex, part of the brain located near the forehead. This shutoff was temporary, with the gene's function fully restored within three weeks, or about a couple of weeks after birth. At various times after the gene was reactivated, the scientists examined the animals' brains and behavior, looking for differences from normal mice. Sawa's team found that in the DISC1 shutoff group, nerve cells in the prefrontal cortex that produce dopamine, one of the chemical signals that nerve cells use to communicate, were markedly immature as the animals entered adolescence. Furthermore, the animals showed signs of a deficit of interneurons, nerve cells that connect other neurons in neural pathways. They also found several behavioral differences between these mice compared to normal mice as the animals entered adolescence. For example, those in the shutoff group reacted more strongly to stimulants, displaying more locomotion than normal mice. Interestingly, these effects were somewhat mitigated when the researchers gave the animals clozapine, a drug used to treat schizophrenia.

Taken together, Sawa says, results of both studies suggest that these anatomical differences, which seem to be influenced by the DISC1 gene, cause problems that start before birth but surface only in young adulthood.

"If we can learn more about the cascade of events that lead to these anatomical differences, we may eventually be able to alter the course of schizophrenia. During adolescence, we may be able to intervene to prevent or lessen symptoms," Sawa says.

*Other Johns Hopkins researchers who participated in the Nature Neuroscience study include Akiko Hayashi-Takagi, Manabu Takaki, Saurav Seshadri, Yuichi Makino, Anupama J. Seshadri, Koko Ishizuka, Jay M. Baraban, and Atsushi Kamiya. Other Johns Hopkins researchers who participated in the Neuron study include Minae Niwa, Atsushi Kamiya, Hanna Jaaro-Peled, Saurav Seshadri, Hideki Hiyama, and Beverly Huang.*

## **China, Kenya to search for ancient Chinese wrecks**

### **The Associated Press**

BEIJING - China and Kenya plan to search for ancient Chinese ships wrecked almost 600 years ago off Africa's east coast.

An agreement was signed for a three-year project funded by China's Commerce Ministry to explore waters near the popular tourist towns of Malindi and Lamu, the official Xinhua News Agency reported Friday.

Exploration work will be conducted for up to three months each year, with the first group of Chinese archaeologists due to arrive as early as July, Xinhua said.

The sunken ships are believed to have been part of a massive fleet led by Ming dynasty admiral Zheng He that reached Malindi in 1418. Kenyan lore has long told of shipwrecked Chinese sailors settling in the region and marrying local women.

Between 1405 and 1433, Zheng He - whose name is also spelled Cheng Ho - led armadas with scores of junks and thousands of sailors on voyages to promote trade and recognition of the new dynasty, which had taken power in 1368. Zheng's seven voyages marked a high point in Chinese power. But imperial rulers soon lost interest in the outside world and canceled further exploration more than a half century before Columbus reached the New World.

Zheng's story has been heavily promoted by China's government in recent years as evidence of China's tradition of nonaggression abroad, although historical records show the treasure fleets carried significant firepower and participated in at least three major military actions.

### **Multiple sclerosis, Italian researchers discover a possible onset mechanism for the disease**

A non-pathogenic bacterium is capable to trigger an autoimmune disease similar to the multiple sclerosis in the mouse, the model animal which helps to explain how human diseases work. This is what a group of researchers from the Catholic University of Rome, led by Francesco Ria (Institute of General Pathology) and Giovanni Delogu (Institute of Microbiology), have explained for the first time in a recently published article on the Journal of Immunology.

Multiple sclerosis is a disease due to an inflammatory reaction provoked by the immune system. It causes the disruption of the coating of the nerve fibres in the Central Nervous System.

"We do not know what causes multiple sclerosis", explains Francesco Ria, immunologist of the Catholic University. "We know that there exist a genetic factor and an environmental factor, but we do not yet possess a satisfactory theory which can explain how exactly this environmental factor works".

Currently, there are two competing theories on the field: according to a first hypothesis, a virus hides within the brain and what causes the disease is the immunologic antiviral reaction. On the other hand, the second hypothesis states that a viral or bacterial pathogen similar to specific molecules of the Central Nervous System causes an inflammation which provokes a reaction of the immune system. This reaction ends up destroying the brain cells. The latter is called the autoimmune hypothesis.

This is the hypothesis that the researchers coming from the Institutes of General Pathology, Microbiology and Anatomy of the Catholic University of Rome have been testing with their two-year long work. To demonstrate the viability of this idea, scientists have fooled the mouse immune system, modifying subtly a bacterium of the common family of mycobacteria (the same family to which also the bacterium causing tuberculosis belongs) to make it look like to myelin, the protein coating nerve cells. This modified mycobacterium is completely innocuous. As all external agents, though, it is capable to trigger the reaction of the T-cells of the immune systems. They intervene to destroy it. Since they are innocuous bacteria, although very common in the environment, and since they induce an immune reaction, they are the ideal bacteria scientists can use to study the environmental factor contributing, together with the genetic factor, to cause multiple sclerosis.

"Normally, T-cells cannot penetrate into the Central Nervous System", adds Rea, "because the hematoencephalic barrier prevents them from doing so. But the bacterium modifies the characteristics of the T-cells and allows them to overcome the barrier. In 15 days the bacterium disappears completely from the body".

Yet these T-cells can now enter into the brain. This way, they begin to attack the myelin of the nerve cells, and here is how the immune disease breaks out.

"We basically demonstrate – explains Rea – that in an animal model it is possible to be infected with something not carrying any disease, and later on develop a purely autoimmune disease".

Yet there is another element in this complex research, sponsored by the Italian Association of Multiple Sclerosis (AISM). "Normally – clarifies Rea – to understand which diseases we have encountered, we measure the antibodies produced by that specific pathogen. But there is a whole world of infectious agents which do not induce the production of antibodies, as is the case in our research: mycobacteria and many other bacteria produce a very low and variable number of antibodies. It is thus very hard to establish whether a population has encountered that specific infectious agent. So, we demonstrate that those infectious agents which are more likely to produce an autoimmune reaction are just those which do not induce antibody production".

Obviously, this is only the first step to better understand the way this very complex and devastating disease works. Ria and Delogu are not stopping here: "We want to try to understand the exact characteristics which this infectious agent should have", they explain. "Might it truly be a good experimental model for multiple

sclerosis? If we had prolonged the action of the bacteria, would we have favoured or hampered the development of the disease? And what about the myelin-like bacterium protein: where should it lie? On the surface, or inside? These are all questions – conclude the two researchers – which we will be trying to answer in the next years, in the hope to defeat this terrible illness. We could even imagine to develop a vaccine by which we could prevent the immune response associated to multiple sclerosis".

### **Breast cancer screening: No added value through mammography**

#### ***Results of German national multicenter trial reveal: Current recommendation for surveillance of women at elevated risk of breast cancer need revision***

Do we need a revision of current recommendations for breast cancer screening? According to a recent prospective multicenter cohort study published in the "Journal of Clinical Oncology", this appears advisable at least for young women carrying an increased risk of breast cancer. The results of the EVA trial confirm once more that magnetic resonance imaging (MRI) is substantially more accurate for early diagnosis of breast cancer than digital mammography or breast ultrasound: MRI is three times more sensitive for breast cancer than digital mammography. For the EVA trial, almost 700 women were enrolled. Aim of the trial was to refine existing guidelines for surveillance of women at high and moderately increased risk of breast cancer. Findings suggest that in these women, MRI is essential for early diagnosis – and that a mammogram or an ultrasound examination does not increase the "cancer yield" compared to what is achieved by MRI alone. Researchers conclude that annual MRI is not only necessary, but in fact sufficient for screening young women at elevated risk of breast cancer. In women undergoing screening MRI, mammograms will have no benefit and should be discontinued. Moreover, MRI screening is important not only for women at high risk, but also for those at moderately increased risk. (doi: 10.1200/JCO.2009.23.0839).

Between 2002 and 2007, the EVA trial recruited 687 women who carried a moderately increased risk of breast cancer (lifetime risk of 20% and over). Women underwent 1679 screening rounds consisting of annual MRI, annual digital mammography and half-annual screening ultrasound examinations. During this time span, 27 women received a new diagnosis of invasive cancer or DCIS (Ductal Carcinoma In Situ).

Of all imaging methods under investigation (digital mammography, ultrasound and MRI), MRI offered by far the highest sensitivity: MRI identified 93% of breast cancers. 37% of cancers were picked up by ultrasound. The lowest sensitivity was achieved by digital mammography, which identified only one-third of breast cancers (33%). These results confirm once more that MRI is essential for surveillance not only of women at high risk, but also for women at moderately increased risk of breast cancer. Moreover, the results contradict current guidelines according to which mammography is considered indispensable for breast cancer screening. One aim of the EVA trial was to question this concept and to ask whether it is still appropriate to require that MRI should only be used in addition to mammography. The results speak for themselves: If an MRI is available, then the added value of mammography is literally negligible. Researchers conclude that MRI is necessary as well as sufficient for screening young women at elevated risk of breast cancer. Since mammography appears to be unnecessary in women undergoing MRI, its use is no longer justifiable, and current guidelines should be revised to reflect this.

#### **Current guidelines questionable**

Current guidelines for women at high familial risk of breast cancer recommend annual MRI (with or without ultrasound) and annual MRI starting at age 25-30. "These guidelines were set up based on little or no scientific evidence, and mainly reflect expert opinion", summarizes Prof. Christiane Kuhl, radiologist at the University of Bonn and principal investigator of the EVA trial. "In the light of the results of the EVA trial, such recommendations should be revisited". This seems even more important because digital mammography uses x-rays (ionizing radiation) to detect breast cancer. "The radiation dose associated with regular mammographic screening is clearly acceptable and safe", underscores Kuhl. "However, regular mammographic screening usually starts at age 40-50". The situation is different if systematic annual mammographic screening is started at age 25-30. "Not only because these women will undergo more mammograms and therefore will experience a cumulative lifetime radiation dose that will be substantially higher, but also because the breast tissue of young women is more vulnerable to the mutagenic effects of radiation". This appears to be especially true for BRCA mutation carriers. "Accordingly, we impose more radiation on less radiation-tolerant breast tissue – for a very limited, if any, diagnostic benefit". Therefore, Kuhl advocates a revision of existing guidelines: "It is no longer justifiable to insist on annual mammographic screening women in their thirties if they have access to screening MRI".



## **MRI is a mature technology**

In the past, MRI was used strictly in addition to mammography only. The allegedly high rate of "false positive" diagnoses and the allegedly insufficient sensitivity for DCIS were the main reason to discourage its use as a stand-alone method for breast cancer screening. "In this multicenter trial, with basic quality assurance implemented not only for mammography, but also for MRI, we were able to prove that false positive diagnoses are avoidable if MRI studies are interpreted with adequate radiologist expertise". In the EVA cohort, the Positive Predictive Value achieved with MRI was already even higher than that of mammography or breast ultrasound. "Moreover, we found that MRI offered the highest sensitivity especially for DCIS", adds Dr. Kuhl. "It is simply wrong to state that we need a mammogram to detect intraductal cancer".

## **The most frequent error in medicine**

INDIANAPOLIS – The most frequent error in medicine seems to occur nearly one out of three times a patient is referred to a specialist. A new study found that nearly a third of patients age 65 and older referred to a specialist are not scheduled for appointments and therefore do not receive the treatment their primary care doctor intended.

According to a new study appearing in the February 2010 issue of the *Journal of Evaluation in Clinical Practice*, only 71 percent of patients age 65 or older who are referred to a specialist are actually scheduled to be seen by that physician. Furthermore, only 70 percent of those with an appointment actually went to the specialist's office. Thus, only 50 percent (70 percent of 71 percent) of those referred to a specialist had the opportunity to receive the treatment their primary care doctor intended them to have, according to the findings by researchers from the Regenstrief Institute and the Indiana University School of Medicine.

The Institute of Medicine, in its seminal report "To Err is Human," defines a medical error as a "wrong plan" or a failure of a planned action to be completed.

"Patients fail to complete referrals with specialists for a variety of reasons, including those that the health care system can correct, such as failure of the primary care doctor's office to make the appointment; failure of the specialist's office to receive the request for a consultation—which can be caused by something as simple as a fax machine without paper – or a failure to confirm availability with the patient," said Michael Weiner M.D., M.P.H., first author of the study.

"There will always be reasons – health issues or lack of transportation, for example – why a referred patient cannot make it to the specialist he or she needs, but there are many problems we found to be correctable using health information technology to provide more coordinated and patient-focused care. Using electronic medical records and other health IT to address the malfunction of the referral process, we were able to reduce the 50 percent lack of completion of referrals rate to less than 20 percent, a significant decrease in the medical error rate," said Dr. Weiner.

The JECF study followed 6,785 primary care patients seen at an urban medical institution, all over age 65, with a mean age of 72. Nearly all (91 percent) of the patients were covered by Medicare.

"This is not necessarily the fault of patients or doctors alone, but it may take both working together – along with their health system – to correct this problem. Our study highlights how enormous a problem this is for patients who were not getting the specialized care they needed. Although our findings would likely differ among institutions, unfortunately overall trends are similar in other parts of the country" said Dr. Weiner.

*Dr. Weiner is director of the Regenstrief Institute's Health Services Research Program, director of the Indiana University Center for Health Services and Outcomes Research, and director of the VA Health Services Research and Development Center of Excellence on Implementing Evidence-Based Practice at the Roudebush VA Medical Center.*

*Co-authors of the study are Anthony J. Perkins, M.S., of the Regenstrief Institute and the IU Center for Aging Research, and Christopher M. Callahan, M.D., a Regenstrief Institute investigator and Cornelius and Yvonne Pettinga Professor in Aging Research at the IU School of Medicine. Dr. Callahan is founding director of the IU Center for Aging Research. This study was supported by the National Institute on Aging.*

## **Roman remains are 'elite' African**

***Archaeologists have revealed the remains of what they say was a "high status" woman of African origin who lived in York during Roman times.***

Academics say the discovery goes against the common assumption that all Africans in Roman Britain were low status male slaves.

Remains of the Ivory Bangle Lady, as she has been named, were studied in Reading using forensic techniques. She was first discovered in the Bootham area of York in August 1901. Her remains were in a stone coffin near Sycamore Terrace in the city.

Her grave dates back to the second half of the 4th Century. She was buried with items including jet and elephant ivory bracelets, earrings, beads and a blue glass jug.

She also had a rectangular piece of bone, which is thought to have originally been mounted in a wooden box, which was carved to read, "Hail, sister, may you live in God".

The grave goods and skeletal remains of the Ivory Bangle Lady were studied by the archaeology department of the University of Reading. The university's Dr Hella Eckardt said a study of the skull's size and facial features along with analysis of the chemical signature of the food and drink she had consumed led to their conclusion that she was of high status and of African origin.



*This reconstruction shows how the Ivory Bangle Lady may have looked*

Dr Eckardt said: "Multi-cultural Britain is not just a phenomenon of more modern times.

"Analysis of the 'Ivory Bangle Lady' and others like her, contradicts common popular assumptions about the make up of Roman-British populations as well as the view that African immigrants in Roman Britain were of low status, male and likely to have been slaves."

The Ivory Bangle Lady will feature in an exhibition about the diversity of the population of Roman York at the Yorkshire Museum in August.



*Bracelets of ivory and jet were among the woman's grave goods*