

7000 Years of Iranian History Turned to Bricks

LONDON, (CAIS) -- The 7000-year-old mound of Pardis in the Qarchak region is currently being bulldozed by a factory for brick production.

The mound is located in an area owned by individuals using the earth from the mound for producing bricks in their nearby factory, an informed source who preferred to remain anonymous.

The individual in question had destroyed the site without the fear of prosecution as he must have had the support of the ruling clerics, either by having some family ties or have included them in this lucrative but treacherous act against Iranian heritage.

The upper strata of the ancient site have been devastatingly damaged and ruins of artefacts are visible nearby, said the source, who has recently visited the site located near the city of Varamin in southern Tehran.

Meanwhile, the director of the Archaeology Research Centre of Iran (ARCI) warned cultural officials of the illegal excavations at the site during an interview with the Persian service of CHN published on Wednesday.

The excavations have completely destroyed about 70 percent of the site, said Mohammad-Hassan Fazeli Nashli. However, he refused to give more details about the excavations.

"Despite the unique character of the site and its potential to become a site specific museum, the Tehran Cultural Heritage, Tourism and Handicrafts Department has no plans for the site, which is in danger of destruction," he added.

"Based on the third season of archaeological excavations carried out at Pardis, the site could shed light on the nature and the date of many important developments that occurred in the central Iranian Plateau," explained Fazeli Nashli, who is also the director of the archaeological team currently working at the site.

A joint team of Iranian archaeologists and experts from Kingston University, Durham University, and the University of Leicester in Britain took part in the third season of archaeological excavations in April 2006.

Iron necklaces, bracelets, and some other ornaments were discovered in the graves of the site's cemetery during the excavations.

Discovery of the ruins of a great number of kilns used for pottery making in the region negated the theory that 7000 years ago, pottery was not mass-produced in the central Iranian Plateau.

They also unearthed the remains of a potter's wheel, which had been made of an amalgamation of mud and animals' horns.

2 beta blockers found to also protect heart tissue

DURHAM, N.C. – A newly discovered chemical pathway that helps protect heart tissue can be stimulated by two of 20 common beta-blockers, drugs that are prescribed to millions of patients who have experienced heart failure.

Researchers from Duke University Medical Center tested 20 beta blockers and found that two of them -- alprenolol and carvedilol -- could stimulate a pathway recently found to protect heart tissue.

This finding could guide future drug development and in particular help heart failure patients, says Howard Rockman, M.D., senior author of the study and chief of the Duke Cardiology Division.

"To our surprise, we found that these two beta blockers can actually stimulate the beta receptor to activate a pathway in the cell that promotes cell survival. We have the first evidence that these two drugs have greater potential to repair the heart and to protect it, and possibly even to reverse some heart damage," Dr. Rockman said.

Until now, scientists believed that all beta-blockers worked by binding to and blocking the beta-adrenergic receptor, a molecule on the cell surface that responds to the hormone adrenalin. Blocking the receptor moderates increases in heart rate and heart function that could be damaging to patients whose hearts are already overstressed.

The two beta-blockers identified by the current study also serve to stimulate a different signaling beta-arrestin pathway. Beta arrestin is a protein known as an "off-switch" for beta-adrenergic receptors. These two drugs activated a beta-arrestin pathway that produces beneficial effects in the heart tissue.

"These two drugs were found to stimulate the pathway that produces certain proteins that are protective to the heart," Rockman said.

The new study, published online in Proceedings of the National Academy of Sciences, was funded by that National Institutes of Health.

"Based on these findings, we hope to design drugs that strongly bind in this way and activate this pathway," Rockman said. "We call these drugs biased-ligands or super receptor blockers, because they are designed to block the harmful actions of adrenalin at the beta receptor, but at a molecular level will activate other pathways that protect the cell." Rockman and colleagues discovered the heart-protection factors in a study published last year.

He noted that carvedilol (marketed for many years as Coreg and now as available in generic forms) is known as a very effective beta blocker, but alprenolol has not been fully developed as a beta blocker drug for heart failure patients. Beta blockers now are part of a standard of care for heart failure patients, who have weakened hearts and cannot tolerate much adrenalin, which is released all day long in people as they perform any exertion, even reading an exciting novel. Every year, 400,000 new cases of heart failure are diagnosed and the number is growing as the population ages.

"The next step is to test the drugs in animals to learn which might promote protection and which might cause more negative effects," Rockman said. "Cell studies can be tricky to replicate in organisms and we will have to see what happens, but these cellular results are very exciting and encouraging and could be a boon to heart failure patients."

Other authors on the study include Il-Man Kim, Douglas Tilley, Juhsien Chen, Natasha Salazar, Erin Whalen and Jonathan Violin of the Duke Department of Medicine, in addition to Dr. Rockman, who is a professor of medicine, cell biology and molecular genetics at Duke.

Oceans are 'too noisy' for whales

By Richard Black Environment correspondent, BBC News website

Levels of noise in the world's oceans are causing serious problems for whales, dolphins and other marine mammals, a report warns.

The International Fund for Animal Welfare (Ifaw) says undersea noise blocks animals' communication and disrupts feeding.

Naval sonar has been implicated in the mass deaths of some cetaceans. In some regions, the level of ocean noise is doubling each decade, and Ifaw says protective measures are failing.

"Humanity is literally drowning out marine mammals," said Robbie Marsland, UK director of Ifaw.

"While nobody knows the precise consequences for specific animals, unless the international community takes preventive measures we are likely to discover only too late the terrible damage we're causing."

In its global assessment of cetacean species, released last month, the International Union for the Conservation of Nature (IUCN) concluded that ocean noise posed a significant threat.



Noise from oil exploration is implicated in the plight of gray whales near Sakhalin

Across the spectrum

Whales and dolphins use sound in ways that are clearly important to their survival, though not completely understood. Baleen whales, such as blue and humpback whales, produce low frequency calls that can travel thousands of kilometres through water. Dolphins and toothed whales generate higher frequency clicks used to locate prey.

Noise generated by ships' engines and propellers, and by seismic airguns used in oil and gas exploration, produce a range of frequencies that can interfere with both these groups of species, Ifaw concludes.

Its report - Ocean Noise: Turn it down - cites research showing that the effective range of blue whales' calls is only about one-tenth of what it was before the era of engine-driven commercial shipping. It also notes that high-energy military sonar systems have driven the mass strandings and deaths of beaked whales.

The sonar is thought to disrupt the animals' diving behaviour so much that they suffer a condition rather like "the bends" which human divers can contract if they surface too quickly.

Pressure from conservation groups has led to restrictions on the use of sonar by the US Navy.

In some places, companies involved in oil and gas exploration limit their use of seismic airguns.

But Ifaw argues these restrictions are not enough. The use of high-energy sonar and seismic airguns should be completely prohibited in sensitive areas, it says. National legislation, such as the UK's Marine Bill, should comprehensively restrict the exposure of cetaceans to noise.

The UK branch of the Whale and Dolphin Conservation Society (WDCS) has sounded alarm bells recently over oil and gas exploration in the Moray Firth, home to a small population of bottlenose dolphins.

The Ifaw report is not the first to raise the threat posed by ocean noise, and it will not be the last.

The problem is that most of the activities causing the problem - commercial shipping, mineral extraction - are part and parcel of the modern, interconnected economy.

A further obstacle to legislation is that much of the noise is generated on the high seas, which are largely unregulated.

Study reveals how viruses collectively decide the fate of a bacterial cell

A new study suggests that bacteria-infecting viruses – called phages – can make collective decisions about whether to kill host cells immediately after infection or enter a latent state to remain within the host cell.

The research, published in the September 15 issue of the *Biophysical Journal*, shows that when multiple viruses infect a cell, this increases the number of viral genomes and therefore the overall level of viral gene expression. Changes in viral gene expression can have a dramatic nonlinear effect on gene networks that control whether viruses burst out of the host cell or enter a latent state.

"What has confounded the virology community for quite some time is the observation that the cell fate of a bacteria infected by a single virus can be dramatically different than that infected by two viruses," said Joshua Weitz, an assistant professor in the School of Biology at the Georgia Institute of Technology. "Our study suggests that viruses can collectively decide whether or not to kill a host, and that individual viruses 'talk' to each other as a result of interactions between viral genomes and viral proteins they direct the infected host to produce."

To study viral infections, Weitz teamed with postdoctoral fellow Yuriy Mileyko, graduate student Richard Joh and Eberhard Voit, who is a professor in the Wallace H. Coulter Department of Biomedical Engineering, the David D. Flanagan Chair Georgia Research Alliance Eminent Scholar in Biological Systems and director of the new Integrative BioSystems Institute at Georgia Tech.

Nearly all previous theoretical studies have claimed that switching between "lysis" and "latency" pathways depends on some change in environmental conditions or random chance. However, this new study suggests that the response to co-infection can be an evolvable feature of viral life history.

For this study, the researchers analyzed the decision circuit that determines whether a virus initially chooses the pathway that kills the host cell – called the lytic pathway – or the pathway where it remains dormant inside the host cell – called the lysogenic pathway.

When the lytic pathway is selected, the virus utilizes bacterial resources to replicate and then destroys the host cell, releasing new viruses that can infect other cells. In contrast, in the lysogenic pathway, the viral genome inserts itself into the bacterial genome and replicates along with it, while repressing viral genes that lead to lysis. The virus remains dormant until host conditions change, which can result in a switch to the lytic pathway.

The decision of the genetic circuit that controls whether a virus initially chooses lysis or lysogeny is not random. Instead, cell fate is controlled by the number of infecting viruses in a coordinated fashion, according to the new study, which was funded by the Defense Advanced Research Projects Agency, the National Science Foundation and the Burroughs Wellcome Fund.

"In the case of perhaps the most extensively studied bacteriophage, lambda phage, experimental evidence indicates that a single infecting phage leads to host cell death and viral release, whereas if two or more phages infect a host the outcome is typically latency," explained Weitz, who is a core member of the new Integrative BioSystems Institute at Georgia Tech. "We wanted to know why two viruses would behave differently than a single virus, given that the infecting viruses possess the same genetic decision circuit."

To find out, the researchers modeled the complex gene regulatory dynamics of the lysis-lysogeny switch for lambda phage. They tracked the dynamics of three key genes – *cro*, *cI* and *cII* – and their protein production. The decision circuit involved both negative and positive feedback loops, which responded differently to changes in the total number of viral genomes inside a cell. The positive feedback loop was linked to the lysogenic pathway and the negative feedback loop was linked to the lytic pathway.

With a single virus, *cro* dominated and the lytic pathway prevailed. If the number of co-infecting viruses exceeded a certain threshold, the positive feedback loop associated with *cI* dominated, turning the switch to the lysogenic pathway. The differences in bacterial cell fate were stark and hinged upon whether or not one or two viruses were inside a given cell.

The researchers found that the *cII* gene acted as the gate for the system. Increasing the number of viruses drove the dynamic level of *cII* proteins past a critical point facilitating production of *cI* proteins leading to the lysogenic pathway.

"The decision circuit is a race between two pathways and in the case of a single virus, the outcome is biased toward lysis," explained Weitz. "In our model, when multiple viruses infect a given cell, the overall production of regulatory proteins increases. This transient increase is reinforced by a positive feedback loop in the latency pathway, permitting even higher production of lysogenic proteins, and ultimately the latent outcome."

The central idea in the model proposed by Weitz and collaborators is that increases in the overall amount of viral proteins produced from multiple viral genomes can have a dramatic effect on the nonlinear gene networks that control cell fate.

"Many questions still remain, including to what extent subsequent viruses can change the outcome of previously infected, but not yet committed, viruses, and to what extent microenvironments inside the host impact cell fate," added Weitz. "Nonetheless, this study proposes a mechanistic explanation to a long-standing paradox by showing that when multiple viruses infect a host cell, those viruses can make a collective decision rather than behaving as they would individually."

Cold and Lonely: Does Social Exclusion Literally Feel Cold?

When we hear somebody described as "frosty" or "cold", we automatically picture a person who is unfriendly and antisocial. There are numerous examples in our daily language of metaphors which make a connection between cold temperatures and emotions such as loneliness, despair and sadness. We are taught at a young age that metaphors are meant to be descriptive and are not supposed to be taken literally. However, recent studies suggest that these metaphors are more than just fancy literary devices and that there is a psychological basis for linking cold with feelings of social isolation.

Psychologists Chen-Bo Zhong and Geoffrey Leonardelli from the University of Toronto's Rotman School of Management wanted to test the idea that social isolation might generate a physical feeling of coldness. They divided a group of volunteers into two groups. One group recalled a personal experience in which they had been socially excluded--rejection from a club, for example. This was meant to tap into their feelings of isolation and loneliness. The other group recalled an experience in which they had been accepted into a group.

Then, the researchers had all the volunteers estimate the temperature in the room, on the pretense that the building's maintenance staff wanted that information. The estimates ranged widely, from about 54 degrees F to a whopping 104 degrees F. Here's the interesting part: Those who were told to think about a socially isolating experience gave lower estimates of the temperature. In other words, the recalled memories of being ostracized actually made people experience the ambient temperature as colder.

"We found that the experience of social exclusion literally feels cold," Zhong said. "This may be why people use temperature-related metaphors to describe social inclusion and exclusion."

In another experiment, instead of relying on volunteers' memories, the researchers triggered feelings of exclusion by having the volunteers play a computer-simulated ball tossing game. The game was designed so that some of the volunteers had the ball tossed to them many times, but others were left out.

Afterwards, all the volunteers rated the desirability of certain foods and beverages: hot coffee, crackers, an ice-cold Coke, an apple, and hot soup. The findings were striking. As reported in the September issue of *Psychological Science*, a journal of the Association for Psychological Science, the "unpopular" volunteers who had been ostracized during the computer game were much more likely than the others to want either hot soup or hot coffee. Their preference for warm food and drinks presumably resulted from physically feeling cold as a result of being excluded.

"It's striking that people preferred hot coffee and soup more when socially excluded," Leonardelli said. "Our research suggests that warm chicken soup may be a literal coping mechanism for social isolation."

These results open up new opportunities in exploring the interaction between environment and psychology, such as the study of mood disorders (e.g., Seasonal Affective Disorder). Research on Seasonal Affective Disorder has focused on the idea that lack of sunlight during winter results in feelings of depression in normally healthy people. The current study indicates that the cold temperatures may also contribute to feelings of sadness and isolation felt during the winter months. In addition, this study suggests that raising the thermostat a bit might be an easy method of promoting group interaction and cooperation in social settings.

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Responsive local governments most attractive to young adults

Young adults staying in or coming to Pennsylvania are attracted to regions that have more units of government and they are not deterred by the large number of local governments in the state, according to a new study.

"Voters like to be close to their local government officials and give input directly to them," says study co-author Stephen Goetz, professor of agricultural and regional economics and director of the Northeast Regional Center for Rural Development at Penn State.

"Employers choose communities with local governments that supply an educated workforce, transportation infrastructure, police and fire protection, and other goods and services that allow firms to maximize their profits. Families follow the employers there and seek places with desired government services such as roads, libraries, parks and schools," he adds.

A team of researchers used a new economic measure of state and county government fragmentation to test if fragmentation drove away young residents from the state.

Georg Grassmueck, assistant professor of Business, Lycoming College; Goetz; and Martin Shields, associate professor of economics, Colorado State University, published their findings in the paper, "Youth Out-Migration from Pennsylvania: The Roles of Government Fragmentation vs. the Beaten Path Effect," in a recent issue of the Journal of Regional Analysis and Policy.

Pennsylvania has 2,567 municipalities including nine classes of counties, four classes of cities and two classes of townships. Boroughs are not classified. Generally, each class of municipality operates under its own code of laws, which determines its structure and powers.

The researchers studied the movement of young adults between Pennsylvania counties between 1995 and 2000 and considered a variety of factors such as housing prices, employment and unemployment figures, school student and teacher numbers, and a list of social gathering places. A primary component of the model is the use of government expenditure data to measure fragmentation, as opposed to the old formula using the number of government units per capita.

Governments with greater expenditures are likely to have more population and economic as well as political power affecting economic growth, according to the study.

Young adults who move are relocating to counties with a relatively higher percentage of young adults and with services needed by that age group. The model also shows that a destination county with higher employment growth relative to a person's original county attracted the young adults.

"These results suggest that young adults find the availability of employment opportunities a more important economic indicator in the moving decision than the level of earnings, which were not important statistically," the researchers said.

Also, entertainment venues seem to play an important role in attracting young adults, but not necessarily artistic venues such as museums and galleries. Health-related facilities also appeared as a key factor in the study, perhaps confirming a trend toward healthier living.

"Our findings contradict a 2003 Brookings Institution study that attributed the state's brain drain of young adults to a large number of small and inefficient local governments in Pennsylvania that was hindering economic development," say the authors.

The study suggests the opposite -- that destination counties with greater fragmentation in local governments attracted even more young adults while those counties with consolidated governments attracted fewer individuals.

"The study serves as a starting point in future discussions on governmental organizational form and economic growth," says Goetz. "Amenities, natural and artificial, matter in the moving decision but any public policy seeking to increase amenities is costly and may be difficult to accomplish.

"Local governments in Pennsylvania need to focus on providing and producing the best and most responsive public goods and services possible to attract and retain households, especially those headed by relatively young adults," he adds.

Avoid coupon redeemers: Their stigma is contagious (unless they're attractive)

Less than 2 percent of Americans use coupons, likely because of fear of being viewed as cheap or poor. A new study in the Journal of Consumer Research demonstrates that not only do coupon users face stigmatization; people who stand near them do too.

Authors Jennifer J. Argo (University of Alberta) and Kelley J. Main (University of Manitoba) studied a phenomenon called "stigma-by-association," which has already been documented in regard to physical disabilities and alcoholism. In a series of studies, the authors found that coupon stigma is real and it transfers to people who are in close proximity to coupon users.

"One implication that arises from society's fascination with wealth and status is that when consumers engage in behaviors that differ from this view they risk being sanctioned," the authors explain. "Using a retail context, we conducted four experiments to demonstrate that the presence of one consumer redeeming a coupon results in a second non-coupon redeeming shopper being stigmatized-by-association (i.e., perceived as cheap)."

The researchers interviewed shoppers who observed people using various kinds of coupons. They tested participants' impressions of the coupon shoppers and people standing near them. They found that people had negative ideas about the people using coupons, especially low-value coupons. This stigma was more likely to be transferred if the shoppers knew each other well, stood in the same line, or were of similar (average) attractiveness.

In addition, the authors discovered two ways to avoid catching the coupon stigma: standing in a different checkout lane or being highly attractive. In fact, being highly attractive also protected coupon redeemers from being stigmatized.

"Thus, in a naturally occurring environment, where our interest in coupon redemption is not salient, consumers appear to infer that one shopper in the retail environment is cheap based on the behavior of another," the study concludes.

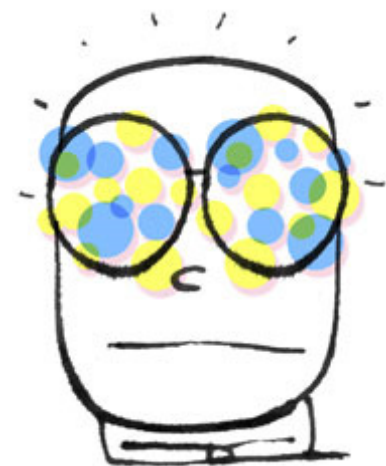
Jennifer J. Argo and Kelley J. Main. "Stigma-by-Association in Coupon Redemption: Looking Cheap Because of Others" *Journal of Consumer Research*: December 2008.

Basics

Gut Instinct's Surprising Role in Math

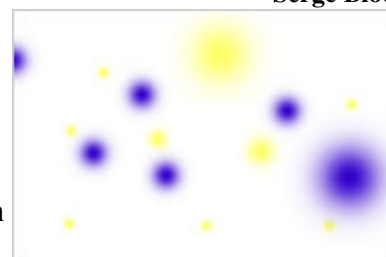
By NATALIE ANGIER

You are shopping in a busy supermarket and you're ready to pay up and go home. You perform a quick visual sweep of the checkout options and immediately start ramming your cart through traffic toward an appealingly unpeopled line halfway across the store. As you wait in line and start reading nutrition labels, you can't help but calculate that the 529 calories contained in a single slice of your Key lime cheesecake amounts to one-fourth of your recommended daily caloric allowance and will take you 90 minutes on the elliptical to burn off and you'd better just stick the thing behind this stack of Soap Opera Digests and hope a clerk finds it before it melts.



One shopping spree, two distinct number systems in play. Whenever we choose a shorter grocery line over a longer one, or a bustling restaurant over an unpopular one, we rally our approximate number system, an ancient and intuitive sense that we are born with and that we share with many other animals. Rats, pigeons, monkeys, babies -- all can tell more from fewer, abundant from stingy. An approximate number sense is essential to brute survival: how else can a bird find the best patch of berries, or two baboons know better than to pick a fight with a gang of six?

Serge Bloch



Interactive Feature

When it comes to genuine computation, however, to seeing a self-important number like 529 and panicking when you divide it into 2,200, or realizing that, hey, it's the square of 23! well, that calls for a very different number system, one that is specific, symbolic and highly abstract. By all evidence, scientists say, the capacity to do mathematics, to manipulate representations of numbers and explore the quantitative texture of our world is a uniquely human and very recent skill. People have been at it only for the last few millennia, it's not universal to all cultures, and it takes years of education to master. Math-making seems the opposite of automatic, which is why scientists long thought it had nothing to do with our ancient, pre-verbal size-em-up ways.

Yet a host of new studies suggests that the two number systems, the bestial and celestial, may be profoundly related, an insight with potentially broad implications for math education.

One research team has found that how readily people rally their approximate number sense is linked over time to success in even the most advanced and abstruse mathematics courses. Other scientists have shown that preschool children are remarkably good at approximating the impact of adding to or subtracting from large groups of items but are poor at translating the approximate into the specific. Taken together, the new research suggests that math teachers might do well to emphasize the power of the ballpark figure, to focus less on arithmetic precision and more on general reckoning.

"When mathematicians and physicists are left alone in a room, one of the games they'll play is called a Fermi problem, in which they try to figure out the approximate answer to an arbitrary problem," said Rebecca Saxe, a cognitive neuroscientist at the Massachusetts Institute of Technology who is married to a physicist. "They'll ask, how many piano tuners are there in Chicago, or what contribution to the ocean's temperature do fish make, and they'll try to come up with a plausible answer."

"What this suggests to me," she added, "is that the people whom we think of as being the most involved in the symbolic part of math intuitively know that they have to practice those other, nonsymbolic, approximating skills."

This month in the journal *Nature*, Justin Halberda and Lisa Feigenson of Johns Hopkins University and Michele Mazzocco of the Kennedy Krieger Institute in Baltimore described their study of 64 14-year-olds who were tested at length on the discriminating power of their approximate number sense. The teenagers sat at a computer as a series of slides with varying numbers of yellow and blue dots flashed on a screen for 200

milliseconds each -- barely as long as an eye blink. After each slide, the students pressed a button indicating whether they thought there had been more yellow dots or blue. (Take a version of the test.)

Given the antiquity and ubiquity of the nonverbal number sense, the researchers were impressed by how widely it varied in acuity. There were kids with fine powers of discrimination, able to distinguish ratios on the order of 9 blue dots for every 10 yellows, Dr. Feigenson said. "Others performed at a level comparable to a 9-month-old," barely able to tell if five yellows outgunned three blues. Comparing the acuity scores with other test results that Dr. Mazocco had collected from the students over the past 10 years, the researchers found a robust correlation between dot-spotting prowess at age 14 and strong performance on a raft of standardized math tests from kindergarten onward. "We can't draw causal arrows one way or another," Dr. Feigenson said, "but your evolutionarily endowed sense of approximation is related to how good you are at formal math."

The researchers caution that they have no idea yet how the two number systems interact. Brain imaging studies have traced the approximate number sense to a specific neural structure called the intraparietal sulcus, which also helps assess features like an object's magnitude and distance. Symbolic math, by contrast, operates along a more widely distributed circuitry, activating many of the prefrontal regions of the brain that we associate with being human. Somewhere, local and global must be hooked up to a party line.

Other open questions include how malleable our inborn number sense may be, whether it can be improved with training, and whether those improvements would pay off in a greater appetite and aptitude for math. If children start training with the flashing dot game at age 4, will they be supernumerate by middle school?

Dr. Halberda, who happens to be Dr. Feigenson's spouse, relishes the work's philosophical implications. "What's interesting and surprising in our results is that the same system we spend years trying to acquire in school, and that we use to send a man to the moon, and that has inspired the likes of Plato, Einstein and Stephen Hawking, has something in common with what a rat is doing when it's out hunting for food," he said. "I find that deeply moving."

Behind every great leap of our computational mind lies the pitter-patter of rats' feet, the little squeak of rodent kind.

Immigrant Sun: Our star could be far from where it started in Milky Way

A long-standing scientific belief holds that stars tend to hang out in the same general part of a galaxy where they originally formed. Some astrophysicists have recently questioned whether that is true, and now new simulations show that, at least in galaxies similar to our own Milky Way, stars such as the sun can migrate great distances.

What's more, if our sun has moved far from where it was formed more than 4 billion years ago, that could change the entire notion that there are parts of galaxies -- so-called habitable zones -- that are more conducive to supporting life than other areas are.

"Our view of the extent of the habitable zone is based in part on the idea that certain chemical elements necessary for life are available in some parts of a galaxy's disk but not others," said Rok Roškar, a doctoral student in astronomy at the University of Washington.

This image is from a computer simulation showing the development and evolution of the disk of a galaxy such as the Milky Way.

"If stars migrate, then that zone can't be a stationary place." If the idea of habitable zone doesn't hold up, it would change scientists' understanding of just where, and how, life could evolve in a galaxy, he said.

Roškar is lead author of a paper describing the findings from the simulations, published in the Sept. 10 edition of the *Astrophysical Journal Letters*. Co-authors are Thomas R. Quinn of the UW, Victor Debattista at the University of Central Lancashire in England, and Gregory Stinson and James Wadsley of McMaster University in Canada. The work was funded in part by the National Science Foundation.

Using more than 100,000 hours of computer time on a UW computer cluster and a supercomputer at the University of Texas, the scientists ran simulations of the formation and evolution of a galaxy disk from material that had swirled together 4 billion years after the big bang. (See a simulation video at http://www.astro.washington.edu/roskar/astronomy/12M_hr_rerun_angle.mpg.)

The simulations begin with conditions about 9 billion years ago, after material for the disk of our galaxy had largely come together but the actual disk formation had not yet started. The scientists set basic parameters to mimic the development of the Milky Way to that point, but then let the simulated galaxy evolve on its own.

If a star, during its orbit around the center of the galaxy, is intercepted by a spiral arm of the galaxy, scientists previously assumed the star's orbit would become more erratic in the same way that a car's wheel might become wobbly after it hits a pothole.



However, in the new simulations the orbits of some stars might get larger or smaller but still remain very circular after hitting the massive spiral wave. Our sun has a nearly circular orbit, so the findings mean that when it formed 4.59 billion years ago (about 50 million years before the Earth), it could have been either nearer to or farther from the center of the galaxy, rather than halfway toward the outer edge where it is now.

Migrating stars also help explain a long-standing problem in the chemical mix of stars in the neighborhood of our solar system, which has long been known to be more mixed and diluted than would be expected if stars spent their entire lives where they were born. By bringing in stars from very different starting locations, the sun's neighborhood has become a more diverse and interesting place, the researcher said.

Such stellar migration appears to depend on the galaxy having spiral arms that twist their way through the galaxy, as are present in the Milky Way, Roškar said.

"Our simulated galaxy is very idealized in the formation of the disk, but we believe it is indicative of the formation of a Milky Way-type of galaxy," he said. "In a way, studying the Milky Way is the hardest thing to do because we're inside it and we can't see it all. We can't say for sure that the sun had this type of migration."

However, there is recent observational evidence that such migration might be occurring in other galaxies as well, he said.

Roškar noted that the researchers are not the first to suggest that stars might be able to migrate great distances across galaxies, but they are the first to demonstrate the effects of such migrations in a simulation of a growing galactic disk.

The findings are based on a few runs of the simulations, but it is expected additional runs using the same parameters and physical properties would produce largely the same results.

"When you swirl cream into a cup of coffee, it will rarely look exactly the same twice, but the general process, and the resulting taste, is always the same," said Wadsley, the team member from McMaster University.

The scientists plan to run a range of simulations with varying physical properties to generate different kinds of galactic disks, and then determine whether stars show similar ability to migrate large distances within different types of disk galaxies. *For more information, contact Roškar at (206) 369-5722 or roskar@astro.washington.edu.*

Herpes drug inhibits HIV in patients infected with both viruses

High rates of co-infection may turn the drug acyclovir into potent new anti-HIV weapon

Researchers at the U.S. National Institutes of Health (NIH), McGill University and other institutions have discovered how a simple antiviral drug developed decades ago suppresses HIV in patients who are also infected with herpes. Their study was published in the Sept. 11 issue of the journal *Cell Host and Microbe*.

An NIH research team led by Dr. Leonid Margolis made the initial discovery, while Dr. Matthias Gotte, Associate Professor in Biochemical Virology at McGill's Department of Microbiology and Immunology, along with colleagues at Emory University, helped explain the precise molecular mechanisms.

According to Dr. Gotte, HIV/herpes co-infection rates are very high and carry significant health burdens for those patients who are already coping with HIV.

"In co-infected individuals, HIV disease progression is enhanced by the presence of herpes," he explained. "Why this is the case is not clear, but there's a lot of evidence for it. Moreover, if you're infected with HIV and herpes, it makes it easier for you to transmit HIV to other people. And if you're infected with herpes alone, it makes it easier for you to acquire HIV."

Though it was long-believed that acyclovir was an ineffective drug against HIV, it was often prescribed to co-infected patients in the hope of indirectly treating HIV by reducing the herpes load. Surprisingly, the NIH team discovered that in the presence of herpes virus HHV-6, acyclovir actually attacks HIV directly and is able to suppress its reproduction.

Acyclovir is a "prodrug," which is converted into its active form only after it is administered to a patient. The research team demonstrated that the herpes virus contains an enzyme not present in HIV and it is this enzyme that converts acyclovir into a compound capable of attacking in HIV. Acyclovir by itself is simply inactive against HIV and therefore the drug can only work in people infected with both viruses.

The researchers are hopeful this discovery may open a new front in the war on HIV, particularly in parts of the developing world where rates of co-infection are extremely high.

"No anti-retroviral kills HIV completely," Dr. Gotte said. "We need to administer at least three drugs to hold it in check. This potentially gives us another weapon in the armory, and it's cheap and accessible, which matters a lot in the developing world."

Did evolution come before life?

* 08:00 15 September 2008

* **Bob Holmes**

A rudimentary form of natural selection likely existed in the primordial soup even before life arose on Earth. If so, the complex "ecosystem" of prebiotic molecules may have made the eventual arrival of life much more probable. Most experts presume that life arose from complex molecules such as nucleic acids and proteins, which were assembled from a mix of simpler units strung together with chemical bonds.

To examine how this might occur, Martin Nowak and Hisashi Ohtsuki, mathematical biologists at Harvard University, used simple equations to model the growth of such chains of building-blocks.

The model shows that because longer chains require more assembly reactions, they should be much less common than short chains. And if some assembly reactions run faster than others, then chains built from these fast-assembling sequences of building blocks grow to be most abundant.



Threshold of life

This bare-bones equivalent of natural selection makes the prebiotic soup an interesting place, they say.

"It generates a rich evolutionary dynamic – or what I would want to call a 'prevolutionary' dynamic – where you have diversity, you have information, you have complicated chemistry," says Nowak.

Such a system, full of novel, interacting molecules, would be the ideal milieu to generate a molecule with attributes that would favour the assembly of copies of itself. Nowak's prebiotic selection could then act to refine this ability by ensuring that better replicators become more common.

At some point, Nowak's model predicts, the best replicator may get fast and accurate enough to dominate the population, sucking up all the resources and driving all the other prebiotic sequences extinct. This is the threshold of life. "Ultimately, life destroys pre-life," says Nowak. "It eats away the scaffold that has built it."

'Murky area'

In showing that selection actually precedes the origin of life, and helps to shape it, Nowak helps bridge the gap between nonliving and living systems. In a sense, he says, the prebiotic soup is constantly testing possible replicators, making it much more probable that one might eventually reach the threshold of life.

Nowak's model helps clarify a murky area of research on prebiotic mixtures, but it offers little direct guidance to experimentalists, says Irene Chen, an origin-of-life researcher also at Harvard.

"The tricky part is figuring out exactly what the relevant chemicals to use are," she says. "Martin's model is basically agnostic about that question."

Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0806714105)

Is re-emerging superbug the next MRSA?

Loyola physicians warn little-known bacteria *Clostridium difficile* next emerging disease threat, killing 1,000s in the United States

MAYWOOD, Ill. – Dr. Ed Corboy had no idea what was afflicting his 80-year-old mother, Joan Corboy.

All he knew for certain was that since being treated for what was a routine diarrheal infection, she seemed to be wasting away and none of her doctors or other health specialists could explain why.

"She lost almost 55 pounds between July Fourth and Christmas in 2006," said Corboy, a resident of Wilmette. "She was so sick, so weak and despite the best care of her doctors, she was getting weaker. It was clear she was in big trouble."

Afraid that his mother was running out of time, Corboy called the Centers for Disease Control in Atlanta for advice. Dr. Clifford McDonald told him the infection his mother probably had was of the NAP1 type of the bacteria *Clostridium difficile*, a virulent strain of a common intestinal bacteria currently plaguing hospitals that now rivals the superbug Methicillin-resistant staphylococcus aureus (MRSA) as one of the top emerging disease threats to humans.

"Disease caused by *Clostridium difficile* can range from nuisance diarrhea to life-threatening colitis that could lead to the surgical removal of the colon, and even death," said Dr. Stuart Johnson, associate professor of medicine, division of infectious diseases, Loyola University Chicago Stritch School of Medicine. "It's a very hardy strain and it seems to persist."

C-diff, as it is better known, is a bacterium that was discovered in 1978 to be the cause of antibiotic-associated diarrhea and colitis, said Johnson, one of the world's top C-diff researchers and physicians, and who successfully treated Joan Corboy's infection. Although C-diff sickens about 500,000 Americans a year and has reached epidemic proportions in 38 states including Illinois, most people have not yet heard of it.

"I don't think that people appreciate the urgency and severity of this disease," said Dr. Dale Gerding, professor of medicine, division of infectious diseases, Stritch School of Medicine, and associate chief of staff for Research, Hines VA Hospital. "In the past, it was thought to be a nuisance illness. Now it is a fatal illness and a lot of physicians have not figured that out as yet."

Hospitals in Quebec have been particularly hard hit by C-diff. In the 12 hospitals affected, about 2,000 deaths were directly attributable to the antibiotic resistant strain between the 2003 and 2004. In the United Kingdom, deaths from C-diff leaped by 28% in 2007 to more than 8,000, according to the nation's Department of Health.

"What was surprising was not just the rates, but the number of severe cases," said Johnson, who helped treat Joan Corboy's illness.

Similar to MRSA, C-diff is an infection that is mainly acquired in a hospital or nursing home, although like MRSA there is some evidence that a community-acquired strain may be developing, according to the CDC.

"When a patient is in the hospital getting antibiotics for some type of infection, one of the potential complications is that the normal bacterium that lives in the colon is disturbed with that antibiotic. That makes you susceptible to an infection with *Clostridium difficile*," Johnson said. "The great majority of cases occur in people who have recently used antibiotics."

When C-diff is not actively dividing, it forms very tough spores that can exist on surfaces for months and years, making it very difficult to kill, Johnson said. "Antibiotics are very effective against the growing form of the bacteria but it doesn't do anything to the spores," Johnson said. "If there are spores they can sit around like stealth bombs. Once the antibiotic is gone, these spores can germinate again and spread their toxins."

Since its discovery, C-diff has grown increasingly resistant to antibiotics, according to Johnson and Gerding, who has been studying the bacteria since 1980. Though it is appearing more often in younger people, those 65 years and older face a greater risk of developing infection from C-diff and has more severe outcomes and higher death rates. Relapse is common with about 25 percent of patient experiencing a second bout of disease within two months after their first. Patients who have had two or more episodes of disease have a 30 percent to 65 percent risk of another bout.

Symptoms of C-diff include profuse diarrhea and abdominal pain and distention of the abdomen. An infection is also frequently accompanied by fever, nausea and dehydration. In some rare cases blood may be present in the stool. The infection is spread by spores that contaminate the hospital environment and hands of healthcare workers who can transmit the spores to patients. The resistance of the spores to hospital cleaning agents and to alcohol hand disinfectants makes it extremely difficult to eradicate.

Common bronchodilator linked to increased deaths

CHICAGO --- A common bronchodilator drug which has been used for more than a decade by patients with chronic obstructive pulmonary disease (COPD) has been linked to a one-third higher risk of cardiovascular-related deaths. The drug, ipratropium, is sold under the brand names Atrovent and Combivent, the latter a combination product that contains ipratropium.

A new study from Northwestern University's Feinberg School of Medicine found that veterans with recently diagnosed COPD using ipratropium were 34 percent more likely to die of a heart attack or of arrhythmia than COPD patients using only albuterol (another bronchodilator) or patients not using any treatment.

The study is published in the Sept. 15 issue of the *Annals of Internal Medicine*.

"This medication may be having some systemic cardiovascular effect that is increasing the risk of death in COPD patients," said Todd Lee, lead author and research assistant professor in the Institute for HealthCare Studies at the Feinberg School.

COPD is an umbrella term for respiratory diseases that include chronic bronchitis and emphysema. The primary cause is smoking. An estimated 12 million people in the U.S. have COPD. The disease is the fourth leading cause of death in the U.S. and is expected to grow to the third leading cause by 2020 due largely to an aging population with a higher historical rate of smoking.

Todd noted his study is observational and indicates the need for researchers to take a closer look at this medication, which has been considered safe for many years. The study looked at the cause of death of 145,000 veterans with newly diagnosed COPD from 1999 to 2003.

"The safety of drugs for COPD patients has flown under the radar," Lee said. "We decided to look into the safety of respiratory medications for COPD patients because of some concerns that had been raised in asthma drugs. We were curious as to whether there were safety problems with these medications in patients with COPD."

Todd said patients and providers should be aware of the potential risk. "When they make treatment decisions they need to weigh these potential risks against other medications that are available for COPD," he noted.

Astronomers image planet around Sun-like star

* 21:47 15 September 2008

* NewScientist.com news service

* **Rachel Courtland**

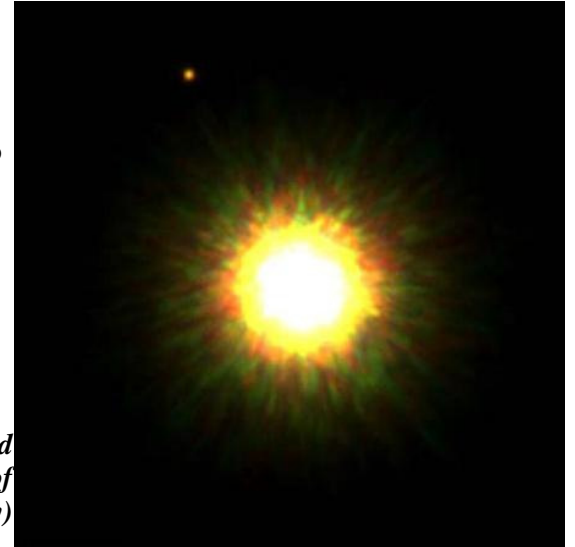
Astronomers have snapped what may turn out to be the first picture of a planet orbiting a star similar to the Sun. If confirmed, it could challenge estimates of how far away planets can form from their host stars.

The planet weighs 8 times as much as Jupiter and appears close to a young star that weighs slightly less than the Sun. Both objects are roughly 500 light years away from Earth.

More than 300 extrasolar planets have been found orbiting distant stars. Most have been discovered by looking for stellar wobbles that suggest gravitational tugs by a close-in companion.

But taking a snapshot of these planets has proved difficult because they tend to be close to their stars, and the stars far outshine them.

This near-infrared image shows the star IRSX J160929.1-210524, and what appears to be a planetary companion, weighing 8 times the mass of Jupiter (upper left) (Image: Gemini Observatory)



To search for planets farther out, Ray Jayawardhana of the University of Toronto and colleagues decided to look at young stars. That's because gas giant planets like Jupiter retain the heat from their formation – and are therefore brighter – in their youth than they are later in life.

In a survey of more than 85 stars using the Gemini North telescope in Hawaii, the team found one potential planet that is 8 times as massive, 10 times as hot and roughly 30,000 times as bright as Jupiter near a star called IRSX J160929.1-210524. The star is 85% as massive as the Sun but less than 0.1% its age, at an estimated 5 million years old.

The planet appears to orbit the star at a distance of 330 astronomical units (1 AU is the distance from the Earth to the Sun). By comparison, Neptune, the most distant planet in our solar system, orbits the Sun at roughly 30 AU.

That distance is so large that it contradicts models of planetary formation, which suggest that planets coalesce from a disc of gas and dust left over from the Sun's birth. Such discs are thought to contain too little material at such distances to form planets.

Many paths to planethood?

Instead, the planet may have formed closer to its host star, then migrated outwards due to collisions in the disc. Alternatively, it may have formed like a stellar companion to its host star, collapsing from its own collection of gas and dust.

"It's significant that nature may have more than one way of making planetary companions for stars like the Sun," Jayawardhana told New Scientist.

The new find is not the first planet-like object to have been spotted orbiting a Sun-like star. A similar object was reported in 2005, orbiting the star GQ Lupi.

But it is not clear whether GQ Lupi's companion is a planet or a brown dwarf, a "failed" star that – unlike real stars – cannot sustain nuclear fusion in its core.

Objects between 13 and 75 Jupiter masses are often considered to be brown dwarfs. The body orbiting GQ Lupi is now estimated to be between 4 and 35 Jupiter masses, says Ralph Neuhauser of the Astrophysical Institute and University Observatory in Jena, Germany.

In sync

The mass of the new object seems to place it in the planet category, but it still might be a brown dwarf, says Adam Burrows of Princeton University. He models the evolution of brown dwarfs and giant planets and was not associated with the study.

Some planets may actually be more massive than the 13-Jupiter-mass threshold of a brown dwarf, he says, because the manner in which the objects form is important.

"Right now they're just at the cutting edge discovering things," Burrows told New Scientist. But follow-up observations of the object's spectrum could help determine whether its composition matches that of a brown dwarf or a planet.

The team is also not yet sure whether the planet is gravitationally bound to the star. Over the next few years, they will watch the system to see whether the star and its companion move across the sky together against background stars.

But it may take decades to trace part of the planet's path around the star, which takes an estimated 6000 years to complete.

Move over mean girls -- boys can be socially aggressive, too

Society holds that when it comes to aggression, boys hit and punch, while girls spread rumors, gossip, and intentionally exclude others, a type of aggression that's called indirect, relational, or social. Now a new analysis of almost 150 studies of aggression in children and adolescents has found that while it's true that boys are more likely to engage in physical aggression, girls and boys alike take part in social aggression.

"These conclusions challenge the popular misconception that indirect aggression is a female form of aggression," according to Noel A. Card, assistant professor of family studies and human development at the University of Arizona and the study's lead author.

The analysis of 148 studies, which comprised almost 74,000 children and adolescents and were carried out largely in schools, looked at both direct aggression, which is usually defined as physical, and indirect aggression, which includes covert behavior designed to damage another individual's social standing in his or her peer group. Conducted by Card and researchers at the University of North Carolina at Chapel Hill and the University of Kansas, the analysis appears in the September/October 2008 issue of the journal *Child Development*.

The researchers suggest that the myth that girls are more likely to be indirectly or socially aggressive than boys has persisted among teachers, parents, and even other researchers because of social expectations that develop early in life and recent movies and books that portray girls as mean and socially aggressive toward one another.

Based on the analysis, the researchers suggest that children who carry out one form of aggression may be inclined to carry out the other form; this is seen more in boys than in girls. They also found ties between both forms of aggression and adjustment problems. Specifically, direct aggression is related to problems like delinquency and ADHD-type symptoms, poor relationships with peers, and low prosocial behavior such as helping and sharing. In contrast, indirect aggression is related to problems like depression and low self-esteem, as well as higher prosocial behavior--perhaps because a child must use prosocial skills to encourage peers to exclude or gossip about others.

The study was funded, in part, by the National Institute of Health.

Summarized from Child Development, Vol. 79, Issue 5, Direct and Indirect Aggression during Childhood and Adolescence: A Meta-Analytic Review of Gender Differences, Intercorrelations, and Relations to Maladjustment by Card, NA (University of Arizona), Stucky, BD (University of North Carolina at Chapel Hill), Sawalani, GM, and Little, TD (University of Kansas). Copyright 2008 The Society for Research in Child Development, Inc. All rights reserved.

Higher urinary levels of commonly used chemical, BPA, linked with cardiovascular disease, diabetes

Higher levels of urinary Bisphenol A (BPA), a chemical compound commonly used in plastic packaging for food and beverages, is associated with cardiovascular disease, type 2 diabetes and liver-enzyme abnormalities, according to a study in the September 17 issue of *JAMA*. This study is being released early to coincide with a Food and Drug Administration (FDA) hearing on BPA.

BPA is one of the world's highest production-volume chemicals, with more than two million metric tons produced worldwide in 2003 and annual increase in demand of 6 percent to 10 percent annually, according to background information in the article. It is used in plastics in many consumer products. "Widespread and continuous exposure to BPA, primarily through food but also through drinking water, dental sealants, dermal exposure, and inhalation of household dusts, is evident from the presence of detectable levels of BPA in more than 90 percent of the U.S. population," the authors write. Evidence of adverse effects in animals has created concern over low-level chronic exposures in humans, but there is little data of sufficient statistical power to detect low-dose effects. This is the first study of associations with BPA levels in a large population, and it explores "normal" levels of BPA exposure.

David Melzer, M.B., Ph.D., of Peninsula Medical School, Exeter, U.K., and colleagues examined associations between urinary BPA concentrations and the health status of adults, using data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004. The survey included 1,455 adults, age 18 through 74 years, with measured urinary BPA concentrations.

The researchers found that average BPA concentrations, adjusted for age and sex, appeared higher in those who reported diagnoses of cardiovascular diseases and diabetes. A 1-Standard Deviation (SD) increase in BPA

concentration was associated with a 39 percent increased odds of cardiovascular disease (angina, coronary heart disease, or heart attack combined) and diabetes.

When dividing BPA concentrations into quartiles, participants in the highest BPA concentration quartile had nearly three times the odds of cardiovascular disease compared with those in the lowest quartile. Similarly, those in the highest BPA concentration quartile had 2.4 times the odds of diabetes compared with those in the lowest quartile.

In addition, higher BPA concentrations were associated with clinically abnormal concentrations for three liver enzymes. No associations with other diagnoses were observed.

"Using data representative of the adult U.S. population, we found that higher urinary concentrations of BPA were associated with an increased prevalence of cardiovascular disease, diabetes, and liver-enzyme abnormalities. These findings add to the evidence suggesting adverse effects of low-dose BPA in animals. Independent replication and follow-up studies are needed to confirm these findings and to provide evidence on whether the associations are causal," the authors conclude. "Given the substantial negative effects on adult health that may be associated with increased BPA concentrations and also given the potential for reducing human exposure, our findings deserve scientific follow-up."

(JAMA. 2008;300[11]:1303-1310. Available pre-embargo to the media at www.jamamedia.org)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Bisphenol A and Risk of Metabolic Disorders

In accompanying editorial, Frederick S. vom Saal, Ph.D., of the University of Missouri, Columbia, and John Peterson Myers, Ph.D., of Environmental Health Sciences, Charlottesville, Va., comment on the findings regarding BPA.

"Since worldwide BPA production has now reached approximately 7 billion pounds per year, eliminating direct exposures from its use in food and beverage containers will prove far easier than finding solutions for the massive worldwide contamination by this chemical due its to disposal in landfills and the dumping into aquatic ecosystems of myriad other products containing BPA, which Canada has already declared to be a major environmental contaminant."

"The good news is that government action to reduce exposures may offer an effective intervention for improving health and reducing the burden of some of the most consequential human health problems. Thus, even while awaiting confirmation of the findings of Lang et al, decreasing exposure to BPA and developing alternatives to its use are the logical next steps to minimize risk to public health."

(JAMA. 2008;300[11]:1353-1355. Available pre-embargo to the media at www.jamamedia.org)

Editor's Note: Please see the article for additional information, including financial disclosures, funding and support, etc.

Sole use of impaired limb improves recovery in spinal cord injury

Animal study shows physical therapy works by increasing growth of nerve fibers and formation of brain cell connections

A new study finds that following minor spinal cord injury, rats that had to use impaired limbs showed full recovery due to increased growth of healthy nerve fibers and the formation of new nerve cell connections. Published in the September 17 issue of The Journal of Neuroscience, these findings help explain how physical therapy advances recovery, and support the use of rehabilitation therapies that specifically target impaired limbs in people with brain and spinal cord injuries.

"After brain and spinal cord injuries, exercise-based physical therapy is the primary rehabilitative strategy in use today," said Stephen Strittmatter, MD, PhD, at Yale University School of Medicine, an expert unaffiliated with the study. "These therapies are so beneficial to patients, but the anatomical and molecular bases of improvement have not been clear," Strittmatter said.

The researchers, led by Irin Maier and senior researcher Martin Schwab, PhD at the University of Zurich and the Swiss Federal Institute of Technology, tested rats with minor surgical injuries to the spinal cord that impaired the use of one forelimb. Slings were placed on the rats that restricted the use of either the injured or uninjured limb. After three weeks, researchers removed the slings and tested the rats on an elevated horizontal ladder.

Rats that relied on their impaired limb because use of their unimpaired limb was restricted showed complete functional recovery: they negotiated the ladder as well as rats that had not been injured. In contrast, rats that had not worn slings and those that wore slings restricting the use of the injured limb performed poorly, showing difficulty grasping and negotiating the horizontal rungs of the ladder.

In all of the rats, healthy nerve fibers, or axons, grew into injured regions of the spinal cord. However, rats that relied on their injured limb showed the most extensive nerve growth. "The study shows that when the axons that remain after a spinal cord injury are more active -- because the animal is forced to use them -- they grow more. This seems to help the animal recover more control of their movements," said John Martin, PhD, at Columbia University, an expert unaffiliated with the study.

These nerve fibers formed more connections, or synapses, in rats relying on their injured limb compared with those relying on their uninjured limb. This finding suggests that forced limb use encourages healthy nerve cells to form new synapses with cells affected by spinal cord injury, perhaps rerouting and rewiring damaged spinal cord circuits that are important for movement.

Using gene chip technology, the researchers found that forced limb use turned on or turned off genes known to be involved in nerve fiber growth and synapse formation in the spinal cord. Knowing which genes are involved in recovery from spinal cord injury may help researchers develop new drug treatments.

"This study shows that a behavioral approach is remarkably effective in promoting both axon growth and recovery after injury," said Martin. "We know that physical therapy is effective after brain and spinal injuries. But these new results suggest that a more aggressive therapy, in which the unimpaired limb is prevented from use and the impaired limb is forced to be used, might lead to new neural connections," he said.

The research was supported by the Swiss National Science Foundation and the Christopher and Dana Reeve Foundation.

Really?

The Claim: Changes in Weather Can Spur Heart Attacks

By ANAHAD O'CONNOR

THE FACTS It sounds counterintuitive, but a link between the onset of cold weather and heart attacks has been hypothesized for some time, with an array of possible culprits:

inflammation from common colds, the stress and indulgence of the holiday season, and higher blood pressure from narrowed blood vessels. Only in recent years have epidemiological studies looked for a connection, and most have found one.

In 2004, for example, a group of British scientists used data from the World Health Organization to look at changes in weather and heart attack rates in women over 50 in 17 countries on four continents. Their study found that a temperature drop of 9 degrees Fahrenheit was associated, in general, with a 7 percent increase in hospital admissions for stroke and a 12 percent rise in admissions for heart attack.

Another study, in France, looked at 700 admissions over two years. It found that in people with hypertension, the risk of suffering a heart attack doubled when the temperature fell below 25. Most studies have had similar findings. But one, by Canadian scientists, that looked at heart attack rates and Chinook winds in Calgary -- which can cause temperatures to swing wildly -- found no relationship.

THE BOTTOM LINE Mixed, but most studies suggest that heart attacks rise when the temperature falls.

Nerves Tangle, and Back Pain Becomes a Toothache

By KATE MURPHY

When people have a heart attack, a classic symptom is shooting pain down the left arm. That symptom, it turns out, has something in common with a far more benign kind of pain: the headache one can get from eating ice cream too fast.

Both are examples of what doctors call referred pain, or pain in an area of the body other than where it originates. Such sensory red herrings include a toothache resulting from a strained upper back, foot soreness caused by a tumor in the uterus, and hip discomfort when the problem is really arthritis in the knee.

Referred pain can make diagnoses difficult and can lead to off-target or wholly unnecessary cortisone injections, tooth extractions and operations. Now, in trying to discover the patterns and causes of the phenomenon, researchers say they are gaining a greater understanding of how the nervous system works and how its signals can go awry.

"The body can really fool you in terms of determining pathology," said Karen J. Berkley, a professor of neuroscience at Florida State University. Her research has focused on referred pain caused by endometriosis -- pain that can be felt as far away as the jaw.

One possible explanation has to do with the way the body's nerve fibers converge on and send signals up the spinal column. Each nerve input carries an astonishing amount of information about the body.



Lief Parsons



Richard Mia

“What we think happens is that the information sometimes loses its specificity as it makes its way up the spinal column to the brain,” Dr. Berkley said. In the constant dynamic of excitation and inhibition that occurs during the transport of innumerable nerve impulses, she went on, “we can’t always discern where a sensory message is coming from.”

Usually the mixed signals come from nerves that overlap as they enter the spinal column -- from the heart and left arm, for example, or from the gallbladder and right shoulder. This so-called adjacency of neural inputs probably explains why some people report a sensation in their thighs when they need to have a bowel movement or feel a tingling in their toes during an orgasm.



Measuring Referred Pain

Moreover, when the stimulus emanates from internal organs, the sensation is often perceived as coming from the chest, arms, legs, hands or feet. “The brain is more used to feeling something out there than in the viscera,” explained Gerald F. Gebhart, director of the Center for Pain Research at the University of Pittsburgh.

In a study published last year, researchers at Aalborg University in Denmark applied irritating substances like capsaicin (the stuff that makes chili peppers hot) to subjects’ small and large intestines. They found increased blood flow and elevated temperatures in referred-pain sites in the trunk and extremities. (The study appeared in *The European Journal of Pain*.)

Pain can also be referred to areas that do not have overlapping nerves. This most often occurs after an injury, according to Dr. Jon Levine, a neuroscientist at the University of California, San Francisco. This, he said, might be because of “pain memory,” which makes the brain more likely to “experience a new sensation as coming from where you were hurt before.”

Several studies using functional magnetic resonance imaging have supported this hypothesis. Areas of the brain corresponding to once injured body parts often lit up when another part was poked or prodded.

Widespread and persistent inflammation in response to a current or past injury may cause what doctors call peripheral sensitization, or excitation of nerves elsewhere in the body. These somatic nerves are on high alert and ready to fire pain signals at the least provocation. Dr. Emeran A. Mayer, a gastroenterologist at the University of California, Los Angeles, who studies referred pain from the gut, said, “The more pain a person has experienced or is experiencing, the more likely we are to see atypical sites of referral.”

Referred pain is also thought to emanate from trigger points -- taut nodules that develop within muscle -- which were first described in the 1960s by Dr. Janet G. Travell, who treated President John F. Kennedy’s back pain. The matrix of trigger points and their predictable pain-referral patterns has “a remarkable correspondence with acupuncture meridians in Chinese medicine,” said Dr. Jay P. Shah, a physiatrist in the rehabilitation medicine department at the National Institutes of Health.

Patients report that their referred pain is precipitated or worsened when the corresponding trigger point is pressed, and alleviated through massage or acupuncture at the trigger point. Though some doctors are skeptical about the trigger point hypothesis, Dr. Shah published a study last year in *The Archives of Physical Medicine and Rehabilitation* indicating that inflammatory chemicals exist at both the trigger points and the locations of referred pain.

Researchers say the varied explanations for referred pain may not be contradictory, but rather an indication that several mechanisms are at work. Dr. Lars Arendt-Nielsen, head of research at the Center for Sensory Motor Interaction at Aalborg, said the growing body of evidence supporting each notion “has changed the way we treat pain to a multifaceted approach.”

Treatments might incorporate not just painkillers but drugs that calm the central nervous system, like anti-epileptics and serotonin reuptake inhibitors.

Acupuncture and trigger-point therapy have also gained acceptance, along with psychological approaches that encourage patients to focus on where the pain is actually coming from rather than where it hurts. Research conducted in 2003 at the University of Bath in England and published in the British journal *Rheumatology* revealed that patients’ referred pain diminished or disappeared if they saw where the pressure was actually being applied.

“Patients and doctors alike,” said Dr. Berkley, of Florida State, “need to remind themselves that where pain is felt may not be where the problem lies.”

Q & A

The Nicotine Blast **By C. CLAIBORNE RAY**

Q. How does nicotine, without tobacco, affect the body?

A. “The effects include the release of epinephrine, which is like adrenaline, and activates the sympathetic nervous system, the so-called flight-or-fight system,” said Dr. Robert Millman, an addiction expert at New York-Presbyterian Hospital/Weill Cornell Medical Center. “It raises the heart rate, increases blood pressure, increases cardiac output and constricts blood vessels. All those things lead to long-term hypertension and heart diseases like congestive heart failure and arrhythmias.”

“The dangers of nicotine may not relate so much to cancer of the lung,” which is tied to tars and other cigarette residues, explained Dr. Millman, the Saul P. Steinberg Distinguished Professor of Psychiatry and Public Health, “but it does relate to heart attacks and cardiovascular accidents, or strokes.”



Victoria Roberts

It is hard to separate the highly addictive drug nicotine from the very efficient delivery system embodied in the cigarette.

“Rapidly acting drugs are generally more addictive than those that act more slowly,” Dr. Millman said. “The effects are felt almost instantaneously and wear off quickly, powerfully reinforcing the tendency to want to do it again and again and again.”

A tolerance also develops, so that more and more of the drug is needed to get the same effect, he said, and then there is the withdrawal syndrome, which with nicotine is associated with psychological problems like depression. The good news is that nicotine delivery by gum, nasal spray or patch is slower than cigarette smoking, so that the nicotine is much less dangerous.

The fastest flights in nature: High-speed spore discharge mechanisms among fungi

Microscopic coprophilous or dung-loving fungi help make our planet habitable by degrading the billions of tons of feces produced by herbivores. But the fungi have a problem: survival depends upon the consumption of their spores by herbivores and few animals will graze on grass next to their own dung. Evolution has overcome this obstacle by producing an array of mechanisms of spore discharge whose elegance transforms a cow pie into a circus of microscopic catapults, trampolines, and squirt guns.

A new paper from Nik Money's lab at Miami University in Oxford, Ohio, in collaboration with Diana Davis and Mark Fischer at the College of Mount St. Joseph in Cincinnati, is published in the open-access journal PLoS ONE and solves the operation of squirt guns that fire spores over distances of more than 2 meters.

The researchers used high speed cameras running at up to 250,000 frames per second to capture these blisteringly fast movements. Spores are launched at maximum speeds of 25 meters per second—impressive for a microscopic cell—corresponding to accelerations of 180,000 g. In terms of acceleration, these are the fastest flights in nature.

The paper is significant for a number of reasons. This is the first study utilizing ultra-high-speed video cameras to capture the events of spore discharge in ascomycete and zygomycete fungi. Previous investigators relied upon models to predict ballistic parameters and produced erroneous estimates of velocities and accelerations. These estimates were then used to suggest that pressures within the spore guns were very high. Fungal cells generate pressure by osmosis and, in the PLoS ONE study, the authors used a combination of spectroscopic methods to identify the chemical compounds responsible for driving water influx into the guns.

These experiments showed that the discharge mechanisms in fungi are powered by the same levels of pressure that are characteristic of the cells that make up the feeding colonies of fungi. Therefore, the long flights enjoyed by spores result not from unusually high pressure, but from the way in which explosive pressure loss is linked to the propulsion of the spores. There appear to be some similarities between the escape of the spores and the expulsion of ink droplets through nozzles on inkjet printers.

Another important aspect of the new work is the way that it has allowed the researchers to test different models for the effect of viscous drag on microscopic particles and identify limitations in previous approaches to modeling. This information is very important for future biophysical studies on spore and pollen movement, which have implications for the fields of plant disease control, terrestrial ecology, indoor air quality, atmospheric sciences, veterinary medicine, and biomimetics.

Finally, the paper was co-authored by 6 undergraduate students, and 3 graduate students who worked for hundreds of hours to obtain the video footage. Some of the videos are so beautiful that student Hayley Kilroy (one of the authors) has set them to music and plans to post them on YouTube.

The authors' research on spore discharge in fungi is currently funded by NSF and NIH. Citation: Yafetto L, Carroll L, Cui Y, Davis DJ, Fischer MWF, et al. (2008) The Fastest Flights in Nature: High-Speed Spore Discharge Mechanisms among Fungi. PLoS ONE 3(9): e3237. doi:10.1371/journal.pone.0003237 <http://dx.plos.org/10.1371/journal.pone.0003237>

Face blindness research shows emotions are key in the study of face recognition

Recognizing the faces of family and friends is usually an effortless process. However, a minority of people have difficulties identifying the person they are meeting or remembering people they have met before. These problems can be quite dramatic, to the point where those affected fail to recognize the face of their spouse or child or even their own face. New research on face blindness demonstrates the importance of using naturalistic emotional faces and bodies for a better understanding of developmental face disorders.

The study, which is published in the open-access journal PLoS ONE this week, by researchers in the Netherlands and at Massachusetts General Hospital, led by Beatrice de Gelder, shows that the presence of emotional information in the face increases neural activity in the area of the brain associated with face recognition (the fusiform face area, or FFA), a finding that could be used to design novel assessment and training programs. The study also provides evidence that body and face sensitive processes are less categorically segregated in people with face blindness and points to a possible cause of face blindness in cortical specialisation.

Recent research has shown that as much as 2% of the population suffers from face recognition difficulties. On analogy with developmental dyslexia, these cases are commonly referred to as developmental prosopagnosia, referring to the possible origin of the adult face recognition deficit in anomalous development of the full face recognition skills.

Faces provide many different types of information, such as gender, age, emotion, familiarity and attractiveness and these details can be called upon and used in different ways in daily life (sometimes the context only requires rapid detection that a face is present, other times, full recognition of all facial attributes, including name retrieval, is required). The contextual requirements and the task settings are thus very important for evaluating face recognition problems and for understanding its neuro-functional basis and possible deficits.

Using functional magnetic resonance imaging, de Gelder and colleagues compared the ability to process faces in a group of individuals reporting life-long problems in recognizing people and with particular difficulties when meeting familiar people unexpectedly--developmental prosopagnosics--with a control group matched for age, sex and education level.

The researchers sought to investigate how the neural underpinnings of face and body processing in prosopagnosia are influenced by emotional information in the face and the body and ran a series of tests on the participants, assessing abilities such as object and face recognition and perception, face matching and face memory.

De Gelder and colleagues found that compared to the control group, the developmental prosopagnosia group displayed a similar activation level in FFA for the emotional faces, but a lower activation in this area for neutral faces; these findings are consistent with the view that there is a higher threshold for the recognition of neutral faces in prosopagnosics. This relative difficulty with neutral faces is based on the idea that faces are more difficult stimuli than many of the other categories with which they are routinely compared.

The scientists explain that emotional stimuli trigger a higher level of arousal and emotion in a face constitutes an additional feature that carries important communicative information, making it more salient. Consistent with this, they observed a higher activity level of activity in the amygdala (the region of the brain associated with emotional reactions) for emotional faces compared to neutral ones.

Since face processing is likely to involve a variety of hierarchical and parallel processes, impairments in different processes will result in different types of behavioral and neuro-anatomical correlates. The results of this study demonstrate the importance of emotional information in face processing and the researchers urge future imaging studies to take into account the modulatory effect of emotion, in order to further untangle the complex nature of developmental prosopagnosia.

Citation: Van den Stock J, van de Riet WAC, Righart R, de Gelder B (2008) Neural Correlates of Perceiving Emotional Faces and Bodies in Developmental Prosopagnosia: An Event-Related fMRI-Study. PLoS ONE 3(9): e3195.

doi:10.1371/journal.pone.0003195 <http://dx.plos.org/10.1371/journal.pone.0003195>

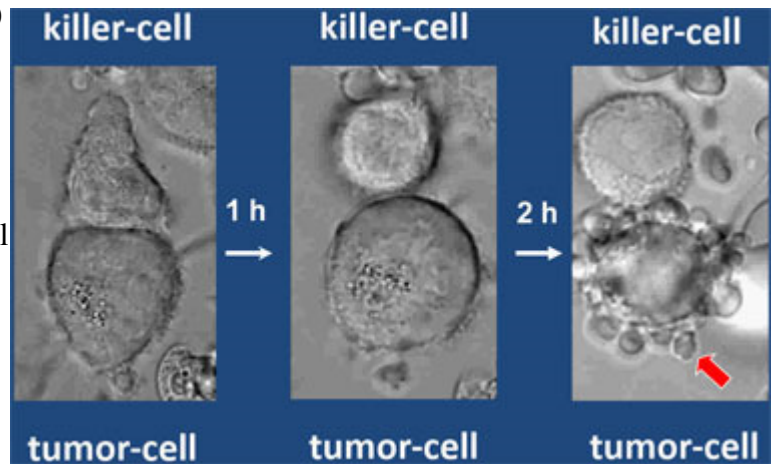
Pores open the door to death

Scientists settle the question as to how our immune defences enter and attack its own cells when they fall prey to viruses and tumour cells

Our body is almost constantly being threatened by pathogens and cancerous cells that appear out of the blue. But the body puts up a fight: specialized cells in the immune system smuggle small molecules (granzymes) into cancer cells and those body cells that have fallen prey to viruses. The molecules then trigger off the diseased cells' built-in suicide program. There are two possible ways in which the granzymes gain entry into the cells under attack. Despite more than twenty years of research, however, it remained unclear as to which of these pathways is used to smuggle the lethal amount of granzymes into a cell. Scientists at the Max Planck Institute

of Neurobiology have now shown that minute pores on the cell surface open the door to the granzymes for a short period of time. These results provide new prospects for improved methods of treatment of chronic virus infections and cancer. (PNAS, 2. September 2008)

During our day-to-day life, we are rarely aware of the battles taking place in our own bodies. The body is almost always in a state of war against countless pathogens. And so, with every litre of blood that is pumped through our bodies, up to five billion white blood cells are sent out on patrol. Some of these cells react to pathogens by producing antibodies specially designed to attack precisely those pathogens that have been discovered. At the same time, they develop memory cells which recognize these pathogens immediately, should they attack anew.



Granzymes going about their deadly work. A killer cell makes contact with a tumour cell (left) and detaches itself after one hour. After a further two hours, blisters appear (right, red arrow) on the surface of the cell that had been attacked. The tumour cells shrinks, dies and disintegrates. Image: Max Planck Institute of Neurobiology / Jenne

In addition to these tacticians, a second group of white blood cells takes up arms against the enemy without further hesitation. The group consists of T-cells and killer cells that specialize in singling out body cells that have already been infected by viruses and tumor cells - swift action is therefore essential. However, these attackers also require tactics: in order to destroy a target cell, the attackers need to smuggle their weapons, known as granzymes, into the afflicted cell. Once inside, the granzymes can carry out their deadly work by manipulating the diseased cell in such a way that it activates its suicide program. But how do the granzymes gain entry into the cell to begin with?

This is a question that scientists have been discussing for over twenty years. Granzymes were believed to gain entry into a cell either via pores or by membrane transport. T-cells and killer cells release a molecule called perforin which creates small holes in the cell membrane. Perforin might thus provide the granzymes with the openings they require. However, granzymes also bind to the surface of the attacked cells and are then internalized by membrane inversions and formation of small vesicles. Since the membrane pores created by perforin holes are fairly small and are quickly closed again by the besieged cell, most scientists favoured the latter theory that the granzymes' main mode of entry into a cell was membrane transport.

To determine what path the lethal dose of granzymes takes to enter a cell is no trivial matter. Such knowledge could be used to develop new therapeutic methods in the fight against viruses and cancer. Some twenty years on, scientists at the Max Planck Institute of Neurobiology now appear to have solved this question. Contrary to the generally accepted view, the membrane holes now seem to be the main point of entry for granzymes. The scientists proved this with artificially manipulated granzymes which no longer bound to membranes and which therefore could not enter the cell via membrane transport. "Interestingly enough, despite this restriction, the attacker cells were observed to be no less effective" declares Dieter Jenne. "We were also able to show that the pores are large enough to allow enough granzymes into the cell before the holes are resealed."

"The exciting thing about these results is not only that we have finally managed to answer a long-standing question", Florian Kurschus explains, "but that our granzyme variations, together with the knowledge that the membrane holes are the most important means of entry into the cell, can lead to improved therapeutic methods in the fight against viruses and cancer." High doses of artificially added granzymes can also damage healthy cells by entering them via membrane transport. The new granzyme variants do not accumulate in healthy cells, however, since they can only avail themselves of the pathway opened by T-cells or killer cells using perforin. In an infected cell that has been recognized by a T-cell or killer cell as an enemy, this door will be opened -wide enough for granzymes to enter and perform their deadly task.

Original work:

Florian Kurschus, Edward Fellows, Elisabeth Stegmann, Dieter Jenne

Granzyme B delivery via perforin is restricted by size, but not by heparan sulfate-dependent endocytosis
PNAS, September 2, 2008 (doi:10.1073/pnas.0801724105)

Why some primates, but not humans, can live with immunodeficiency viruses and not progress to AIDS

Key differences in immune system signaling and the production of specific immune regulatory molecules may explain why some primates are able to live with an immunodeficiency virus infection without progressing to AIDS-like illness, unlike other primate species, including rhesus macaques and humans, that succumb to disease.

Following the identification of HIV (Human Immunodeficiency Virus) as the cause of AIDS 25 years ago, an extensive search was undertaken to identify the source of the virus. These studies led to the discovery that chimpanzees and sooty mangabeys are infected in the wild with simian immunodeficiency viruses (SIV), whose transmission to humans and macaques leads to AIDS.

Surprisingly, the natural hosts for the AIDS viruses, such as the mangabeys and numerous other African primate species who have been found to harbor SIVs in the wild, remain healthy despite infection. Understanding how the natural hosts evolved to resist the development of immunodeficiency disease has long represented a key unsolved mystery in our understanding of AIDS. Furthermore, definition of the mechanisms by which they resist disease could help explain the mechanisms underlying AIDS progression in humans.

A team of scientists from Yerkes National Primate Research Center and the Emory Vaccine Center has discovered that the immune systems of sooty mangabeys are activated to a significantly lower extent during SIV infection than are the immune systems of rhesus macaques, and that this difference may explain why SIV and HIV infection leads to AIDS in some primate species but not others.

"During both HIV infection in humans and SIV infection in macaques, the host immune system becomes highly activated, experiences increased destruction and decreased production of key immune effector cells and progressively fails as a result. In contrast, natural hosts for SIV infection, like sooty mangabeys, do not exhibit aberrant immune activation and do not develop AIDS despite high levels of ongoing SIV replication. Our studies sought to understand the basis for the very different responses to AIDS virus infections in different species," says Mark Feinberg, MD, PhD, the paper's senior author. Feinberg is a former investigator at the Emory Vaccine Center and the Yerkes Research Center and a professor of medicine at the Emory University School of Medicine. He currently serves as vice president of medical affairs and policy for vaccines and infectious diseases at Merck & Co., Inc.

The reasons are found in significant differences in immune signaling in a specific type of dendritic cells in AIDS-susceptible or resistant host species. Dendritic cells are part of the immune system that play a key role in alerting the body to the presence of invading viruses or bacteria, and in initiating immune responses that enable clearance of these infections. They detect the invaders using molecules called Toll-like receptors.

Feinberg's team found that in sooty mangabeys, dendritic cells produce much less interferon alpha--an alarm signal to the rest of the immune system--in response to SIV. As a result, the dendritic cells are not activated during the initial or chronic stages of SIV infection, and mangabeys fail to mount a significant immune response to the virus. In contrast to mangabeys, dendritic cells from humans and macaques that are susceptible to developing AIDS are readily activated by HIV and SIV.

The difference in whether or not dendritic cells become activated upon AIDS virus exposure in specific primate hosts appears to result from species-specific differences in patterns of Toll-like-receptor signaling. Because host immune responses are unable to clear AIDS virus infections, ongoing virus replication leads to unrelenting activation of the immune system in humans and macaques.

Unfortunately, rather than promoting clearance of the infection, chronic dendritic cell stimulation may result in chronic immune activation and significant unintended damage to the immune system in AIDS-susceptible species. Such chronic immune activation is now recognized to be a major driving force for the development of AIDS.

The observation that mangabey dendritic cells are less susceptible to activation by SIV may explain why mangabeys do not exhibit abnormal immune activation and do not develop AIDS. Thus, in mangabeys, the generation of a less vigorous immune response to SIV may represent an effective evolutionary response to a virus that is so resistant to clearance by antiviral immune responses.

The authors suggest new treatment strategies that would steer the immune system away from over-activation, thereby protecting against the unintended damage caused by host immune responses. Such treatment approaches that focus on the host response to the AIDS virus may provide a valuable means of complementing the use of antiretroviral drugs that focus directly on inhibition of virus replication.

Understanding the particular details of Toll-like receptor signaling pathways in the mangabeys may help guide the development of specific therapeutic approaches that could beneficially limit chronic immune activation in HIV-infected humans.

"Better understanding of the biological basis by which sooty mangabeys and the numerous primate species that represent natural hosts for AIDS virus infections have evolved to resist disease promises to teach us a great deal about the emergence of the AIDS pandemic, and about the mechanisms underlying AIDS progression in humans. In addition, such insights will hopefully help inform new approaches to treat HIV infection most effectively." Feinberg says.

"Also, better understanding how natural hosts for SIV remain healthy may provide clues as to the future evolutionary trajectory of human populations in response to the profound selective pressures now being felt in regions of the world where the tragic consequences of HIV infection are most severe."

First authors of the paper are Judith N. Mandl from the Graduate Program in Population Biology, Ecology and Evolution at Emory University and Ashley P. Barry who formerly was with the Emory Vaccine Center and Yerkes National Primate Research Center.

The research was funded by the National Institutes of Health, and included support provided to the Yerkes National Primate Research Center and the Emory Center for AIDS Research.

Reference: Nature Medicine advance online publication: Divergent TLR7 and TLR9 signaling and type I interferon production distinguish pathogenic and nonpathogenic AIDS virus infections.

Inflammatory response to infection and injury may worsen dementia

Inflammation in the brain resulting from infection or injury may accelerate the progress of dementia, research funded by the Wellcome Trust suggests. The findings, published this week in the journal *Biological Psychiatry*, may have implications for the treatment and care of those living with dementia.

Systemic inflammation – inflammation in the body as a whole – is already known to have direct effects on brain function. Episodes of delirium, in which elderly and demented patients become extremely disoriented and confused, are frequently caused by infections, injury or surgery in these patients. For example, urinary tract infections, which are typically bacterial, appear to be particularly potent inducers of psychiatric symptoms.

Until now, there had been little research into the impact of systemic inflammation on the progress of dementia and neurodegenerative diseases. However, with over 700,000 people currently living in the UK with dementia – a figure set to rise with our ageing population – scientists are keen to understand more about the mechanisms behind such diseases.

Now, in a study to mimic the effect of bacterial infection in people with dementia, Dr Colm Cunningham and colleagues at Trinity College Dublin, in collaboration with Professor Hugh Perry at the University of Southampton have shown that the inflammatory response to infection in mice with prior neurodegenerative disease leads to exaggerated symptoms of the infection, causes changes in memory and learning and leads to accelerated progression of dementia.

"Our study clearly shows the damaging effect of systemic infection or inflammation in animal models of dementia," says Dr Cunningham, a Wellcome Trust Research Career Development Fellow.

In previous studies, Dr Cunningham and colleagues showed that infection-induced inflammation can exacerbate nerve cell damage in animal models of dementia. Now, the team has shown that just one episode of systemic inflammation could be sufficient to trigger a more rapid decline in neurological function.

"Doctors and carers need to pay increased attention to protect people with dementia from potential causes of systemic inflammation," says Dr Cunningham. "These include preventing infection, protecting them against falls and carefully weighing up the risk-benefit ratio of non-essential surgery."

Dr Cunningham believes the research may provide clues for helping slow down the progression of neurodegenerative diseases in humans. Although long-term use of non-steroidal anti-inflammatory drugs to treat conditions such as rheumatoid arthritis offers modest protection against the development of Alzheimer's disease, actually treating Alzheimer's patients with these drugs has not had a significant impact on disease progression.

The researchers found that systemic inflammation leads to the production of a protein known as IL-1 β by microglia, the brain's resident immune cells, in the hippocampus region of the brain. This region is involved in memory and learning. The protein is known to exacerbate nerve cell damage in stroke. Inflammatory mediators such as IL-1 β are routinely produced in the blood in response to inflammatory stimuli and prior studies by colleagues in Southampton have shown a correlation between elevated blood IL-1 β levels, recent infection and subsequent cognitive decline.

"The recognition that relatively banal systemic inflammatory events can interact with and exacerbate neurodegenerative processes in the brain opens up potential avenues of treatment for patients with dementia," he says.

Rebecca Wood, Chief Executive of the Alzheimer's Research Trust, commented: "This is really interesting research leading to a significant step forward in our understanding of dementia. Inflammation has been implicated in dementia for some time, which is why falls are of such concern, but this also shows that the

dementia is increased by another common problem of ageing - urinary tract and other infections. It also demonstrates how important it is to lower our dementia risk through maintaining good overall health.

"In the UK, 25 million of us know a close friend or family member with dementia, but research into the condition is severely underfunded. We need far more research like this if we are to reduce dementia's impact on our society."

Cutting calories could limit muscle wasting in later years

GAINESVILLE, Fla. --Chemical concoctions can smooth over wrinkles and hide those pesky grays, but what about the signs of aging that aren't so easy to fix, such as losing muscle mass? Cutting calories early could help, say University of Florida researchers who studied the phenomenon in rats.

A restricted-calorie diet, when started in early adulthood, seems to stymie a mitochondrial mishap that may contribute to muscle loss in aging adults, the researchers reported recently in the journal PLoS One.

In rats, the scientists found pockets of excess iron in muscle cell mitochondria, the tiny power plants found in every cell. The excess iron affects the chemistry inside the mitochondria, sparking the formation of harmful free radicals that can lead a mitochondrion straight to the emergency exit, said Christiaan Leeuwenburgh, Ph.D., a UF professor of aging in the UF College of Medicine and the Institute on Aging. Leeuwenburgh was the senior author of the study and of a related report published online this month in *Aging Cell* that details the damage done by excess iron in mitochondria.

"We become less efficient at an old age and we need to understand why this is," Leeuwenburgh said. "One thing, maybe, is the accumulation of redox-active metals in cells. If the mitochondria become unhappy or are ready to kick the bucket, they have proteins in the inner and outer membranes that they can open up and commit suicide. They're tricky beasts."

The suicidal mitochondria can damage the rest of the muscle cell, leading to cell death and perhaps to muscle wasting, a big problem for adults as they reach their mid-70s, Leeuwenburgh added.

"Muscle is critical for your overall well-being," Leeuwenburgh said. "As you walk, muscle functions partly as a pump to keep your blood going. Muscle is an incredible source of reserves."

The researchers found increasing amounts of iron in the muscle cells of aging rats fed a typical unrestricted diet. The older the rats got, the more iron accumulated in the mitochondria and the more damage was done to its RNA and DNA. Rats of the same ages that were kept on a calorie-restricted diet -- about 60 percent of the food typically ingested -- seemed to maintain more normal iron levels in mitochondria, the researchers reported.

"The novel thing here is that iron is accumulating in places it does not normally accumulate," said Mitch Knutson, Ph.D., a UF assistant professor of food science and human nutrition and a study co-author. "Such iron accumulation in muscle was quite unexpected. This may be of concern because more people are genetically predisposed to developing iron overload than we originally thought."

The problem occurs when metals such as iron accumulate in the mitochondria and react with oxygen. Iron can change the chemical structure of oxygen, triggering its metamorphosis into a free radical, an unstable atom that can upset the delicate balance inside the mitochondria. The result? Leeuwenburgh describes it sort of like internal rust.

"Not all free radicals are harmful," Leeuwenburgh said. "To just use antioxidants to neutralize all free radicals is a huge misconception because some radicals are helpful. You just need to try and target very specific free radicals that form in specific parts of the body."

Researchers don't know exactly what causes iron to accumulate in mitochondria in aging animals, but a breakdown in how iron is transported through cells could be one reason why, Leeuwenburgh said. Understanding how caloric restriction limits the problem in rats could help researchers better understand how to combat it, he added.

Russell T. Hepple, Ph.D., an associate professor of kinesiology and medicine at the University of Calgary in Canada, said the findings are another step forward in linking iron to muscle cell death, but there are more questions researchers must answer.

"They've shown that apoptosis (cell death) goes up in aging muscle but where does that happen?" Hepple asked. "There are more than muscle cells in muscle. (For example) in older adults there are inflammatory cells."

Can nutrients improve behaviour?

By Fergus Walsh Medical correspondent, BBC News

Inside Polmont Young Offenders' Institute One thousand young offenders from three prisons in England and Scotland are being recruited for a major trial to see if nutritional supplements can improve behaviour.

The study is being organised by neuroscientist Professor John Stein, of the University of Oxford, whose brother is the chef Rick Stein.

I met them and some of the volunteers at Polmont Young Offenders Institute near Falkirk.

Rick Stein has prepared food for the Queen, presidents and prime ministers. But his guests at Polmont were young offenders. Most were serving long sentences for crimes of violence. None of them had ever tasted marinated raw fish before.

The restaurateur, author and TV chef is not part of the trial getting underway in three prisons.

Instead, he was there to give some celebrity support to his brother John, a neuroscientist at Oxford.

Fish oils

Professor Stein believes that food supplements - Omega 3 fish oils in particular - can improve reduce the anti-social behaviour of prisoners.

Rick Stein takes a less scientific approach, and is simply passionate about fish and its health benefits.

He said: "I really believe that fish is good for the brain - what our grandmothers taught us turned out to be true.

"In layman's terms, as I see it, fish oil lubricates the brain and makes it far faster.

"We are what we eat. If you have a balanced diet you will be healthier and that must include fish."

Rick Stein is not re-modelling the prison menu at Polmont.

Raw fish was not on the menu for most of the inmates that day - for them black pudding was the popular choice. Healthy options are already available - but few chose them.

Daily capsules

Instead, prisoners on the trial will take four capsules a day with their main meal. Half the volunteers will get the micro-nutrients and half placebo or dummy capsules. The researchers will compare the disciplinary record of the two groups over four months. A smaller, pilot study at Aylesbury Young Offenders Institute in 2002 showed that inmates receiving the supplements committed a third fewer offences.

Professor Stein believes the trial, which will report in two years, will prove a success. He believes a lot of young offenders commit crime because they fail to pick up social signals.

"My theory is that micro-nutrients - in particular the fatty acids found in Omega 3 fish oils - improve the function of nerve cells in the brain which deal with visual, social signals. "When you don't have them it means you can react badly in an impulsive or aggressive manner. "In short, fish oils are needed to make the brain work properly."

Serious science

Although the study had a celebrity launch, there is serious science behind it. It is funded by a £1.4m grant from the Wellcome Trust, the UK's biggest independent funder of medical research.

Dr Mark Walport, Wellcome Trust director, said: "If this study shows that nutritional supplementation affects behaviour, it could have profound significance for nutrition guidelines not only within the criminal justice system, but in the wider community, in schools, for example.

"We are all used to nutritional guidelines for our physical health, but this study could lead to revisions taking into account our mental health, as well."

Crows make monkeys out of chimps in mental test

* 00:01 17 September 2008

* NewScientist.com news service

* **Emma Young**

Crows seem to be able to use causal reasoning to solve a problem, a feat previously undocumented in any other non-human animal, including chimps.

Alex Taylor at the University of Auckland, New Zealand, and his team presented six New Caledonian crows with a series of "trap-tube" tests.

A choice morsel of food was placed in a horizontal Perspex tube, which also featured two round holes in the underside, with Perspex traps below.

For most of the tests, one of the holes was sealed, so the food could be dragged across it with a stick and out of the tube to be eaten. The other hole was left open, trapping the food if the crows moved it the wrong way.



A New Caledonian crow, Corvus moneduloides (Image: Pawel Ryszawa/Wikimedia Commons)

Three of the crows solved the task consistently, even after the team modified the appearance of the equipment. This suggested that these crows weren't using arbitrary features – such as the colour of the rim of a hole – to guide their behaviour. Instead they seemed to understand that if they dragged food across a hole, they would lose it.

Not-so great apes

To investigate further, the team presented the crows with a wooden table, divided into two compartments. A treat was at the end of each compartment, but in one, it was positioned behind a rectangular trap hole. To get the snack, the crow had to consistently choose to retrieve food from the compartment without the hole.

A recent study of great apes found they could not transfer success at the trap-tube to success at the trap-table. The three crows could, however.

"They seem to have some kind of concept of a hole that isn't tied to purely visual features, and they can use this concept to figure out the novel problem," Taylor says. "This is the most conclusive evidence to date for causal reasoning in an animal."

Three of the crows did fail at both tasks, however. The team plans further work to investigate why.
Journal reference: Proceedings of the Royal Society B (DOI: 10.1098/rspb.2008.1107)

Mother's flu shot protects newborns

Newborns can be protected from seasonal flu when their mothers are vaccinated during pregnancy, according to a study led by researchers at the Johns Hopkins Bloomberg School of Public Health. The researchers observed a 63 percent reduction in proven influenza illness among infants born to vaccinated mothers while the number of serious respiratory illnesses to both mothers and infants dropped by 36 percent. The study is the first to demonstrate that the inactivated influenza vaccine provides protection to both mother and newborn. The findings were presented during the National Vaccine Advisory Committee meeting in Washington, D.C. on September 17 and will be published in the October 9 issue of the *New England Journal of Medicine*.

The inactivated influenza vaccine (the flu shot) is not licensed for infants younger than six months. The alternative nasal flu vaccine is not available for children under age 2. The flu shot has been recommended for pregnant women in the U.S. since 1997, although approximately 15 percent of pregnant women are vaccinated each year.

"Even though there is no flu vaccine for these children, our study shows that a newborn's risk of infection can be greatly reduced by vaccinating mom during pregnancy. It's a two for one benefit," said Mark Steinhoff, MD, the study's senior author and professor in the Bloomberg School's Department of International Health. "Infants under six months have the highest rates of hospitalization from influenza among children in the U.S. These admission rates are higher than those for the elderly and other high-risk adult groups."

The study was conducted in Bangladesh in collaboration with researchers from the International Centre for Diarrheal Disease Research (ICDDR,B). Researchers observed 340 mothers and their infants as part of the larger Mother's Gift vaccine evaluation study. The mothers were randomly selected to receive either flu vaccine or pneumococcal vaccine.

"Pregnant woman should be encouraged to be vaccinated for the flu to protect their infants and themselves," said Steinhoff.

Additional authors of the study include K. Zaman, S.E. Arifeen, M. Rahman, R. Raqui, N. Shahid and R.F. Breiman from the International Centre for Diarrheal Disease Research in Bangladesh. E. Wilson is with the Bloomberg School of Public Health and S. B. Omer is with Emory University.

The research was supported by the Bill & Melinda Gates Foundation, United States Agency for International Development (USAID), the NPVO Research Fund, Wyeth Pharmaceuticals Inc., the Thrasher Research Fund, Aventis Pasteur, ICDDR,B and the Johns Hopkins Bloomberg School of Public Health.

Top-Selling Prescription Drug Mismarketed to Women

Ithaca, N.Y. – Lipitor has been the top-selling drug in the world and has accounted for over \$12 billion in annual sales. It has been prescribed to both men and women to lower cholesterol and reduce the risk of heart attack and stroke in patients with common risk factors for heart disease. However, a new study appearing in the *Journal of Empirical Legal Studies* was unable to find high quality clinical evidence documenting reduced heart attack risk for women in a primary prevention context. Furthermore, advertising omits label information relevant to women.

Theodore Eisenberg of Cornell Law School and Martin T. Wells of Cornell University assembled studies for a meta analysis of drugs' effects on cardiovascular risk, taking into account all relevant studies reporting risks for both men and women.

Not one of the studies that included women with a mixture of risk factors for heart attacks provided statistically significant support for prescribing Lipitor or other statins to protect against cardiovascular problems. Pfizer's claims of clinical proof that Lipitor reduces risk of heart attack in patients with multiple risk factors for heart disease does not appear to be scientifically supported for large segments of the female population.

In addition, Lipitor's advertising repeatedly fails to report that clinical trials were statistically significant for men but not for women. Unqualified advertising claims of protection against heart attacks may therefore be misleading. Pfizer's advertising also does not disclose critical portions of the Lipitor FDA-approved label, which acknowledges the absence of evidence with respect to women.

"Our findings indicate that each year, reasonably healthy women spend billions of dollars on drugs in the hope of preventing heart attacks but that scientific evidence supporting their hope does not exist," the authors conclude.

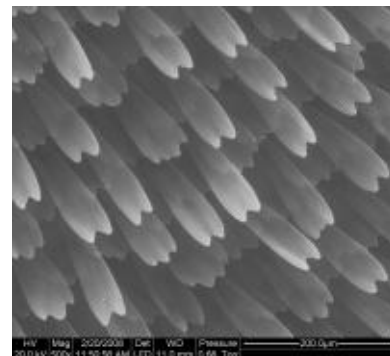
This study is published in the September 2008 issue of the Journal of Empirical Legal Studies. Media wishing to receive a PDF of this article may contact journalnews@bos.blackwellpublishing.net.

[To view the abstract for this article, please click here.](#)

Coating copies microscopic biological surfaces

Someday, your car might have the metallic finish of some insects or the deep black of a butterfly's wing, and the reflectors might be patterned on the nanostructure of a fly's eyes, according to Penn State researchers who have developed a method to rapidly and inexpensively copy biological surface structures.

"Only a small fraction of mutations in evolutionary processes are successful," says Akhlesh Lakhtakia, the Charles Godfrey Binder (Endowed) Professor of Engineering Science and Mechanics. "But, evolution has gone on for at least a billion years. A huge range of biological surface architectures have been created and are available."



Enlarged view of surface of butterfly wings after application of coating using CEFR.

Lakhtakia and his colleagues, Carlo G. Pantano, distinguished professor of materials science and engineering, and director of Penn State's Materials Research Institute, and Raúl J. Martín-Palma, visiting professor, Penn State, and professor department of applied physics, Universidad Autónoma de Madrid, used the conformal evaporated film by rotation (CEFR) technique, to produce coatings that capture the micro and nano structure of biological surfaces in a thin coating of glass. The results appear in recent issues of Applied Physics Letters and Nanotechnology.

In the CEFR technique, the researchers thermally evaporate the material that forms the coating in a vacuum chamber. The object receiving the coating is fixed to a holder and rotated about once every two seconds. The researchers have coated butterfly wings and a fly, creating replicas of these templates with identical surface characteristics. The researchers are using chalcogenide glasses composed of varying combinations of germanium, antimony and selenium.

"With the right temperature, which is room temperature, and the right pressure and rotation speed, the coating process takes about 10 minutes and deposits a 500- nanometer layer," says Lakhtakia.

Some biostructures, such as moth's eyes, which are duplicated to produce moth's-eye lenses, can be mechanically created by engineers, but it is painstaking and expensive work. These lenses, that capture nearly all available light, have applications in optoelectronic and photovoltaic applications. Other biostructures do not lend themselves to synthetic reproduction.



The magnified head of a fly coated with chalcogenic glass.

"In that case, perhaps we need to replicate the actual structure," says Lakhtakia. "One insect has an iridescent shell that does not change colors as many shiny ones do. No one has made this type of material artificially because we do not know the mechanism by which it retains its color, but making a template from the actual insect would replicate the fine structure of the surface."

Many things in the natural world are colored not by pigment, but by surface structure. The way light interacts with the surface creates the color, rather than any tint or chemical. Reproducing the surface reproduces the color. Surface properties include not just visible light characteristics, but also infra red, thermal, stickiness and other characteristics.

Martín-Palma, Pantano and Lakhtakia's work creates either a replica template or a mold depending on what they coat. The replica of a template can be used to create a mold in a harder, less damageable material to make many copies. Molds can be combined and multiplied to create the desired surfaces.

The researchers initially looked at surfaces with optical properties because they are easy to see and identify. The structural black of some butterflies invites investigation of thermal properties as well. Creating surfaces

that have micro or nanoscale patterns on solar cells, heat exchangers, reflectors and lenses can produce devices that work more efficiently.

"The whole world of biomimetics and bioinspiration is just beginning to emerge," says Martín-Palma. "Butterfly wings come in a large variety of surface structures. Eventually we may be able to take these biological structures and modify them to create other properties that do not already exist on biological surfaces."

While the researchers are still experimenting with butterfly wings, they would like to use CEFR on lotus leaves because they are super hydrophobic. Surfaces that repel water could be very useful. They also plan to look at other plant materials as potential surfaces for solar cells. Lakhtakia and Martín-Palma are organizing a small conference next year on biomimetics and bioinspiration.

Pantano suggested the use of chalcogenide glass for its infrared properties, but the researchers have also tried other glasses and materials like polymers to reproduce other surfaces and their properties.

This work was supported by the Ministerio de Educacion y Ciencia (Spain) and the Penn State National Science Foundation National Nanotechnology Infrastructure Network. The researchers have filed a provisional patent application on this work.

UNC scientists turn human skin cells into insulin-producing cells

CHAPEL HILL – Researchers at the University of North Carolina at Chapel Hill School of Medicine have transformed cells from human skin into cells that produce insulin, the hormone used to treat diabetes.

The breakthrough may one day lead to new treatments or even a cure for the millions of people affected by the disease, researchers say.

The approach involves reprogramming skin cells into pluripotent stem cells, or cells that can give rise to any other fetal or adult cell type, and then inducing them to differentiate, or transform, into cells that perform a particular function – in this case, secreting insulin.

Several recent studies have shown that cells can be returned to pluripotent state using "defined factors" (specific proteins that control which genes are active in a cell), a technique pioneered by Dr. Shinya Yamanaka, a professor at Kyoto University in Japan.

However, the UNC study is the first to demonstrate that cells reprogrammed in this way can be coaxed to differentiate into insulin-secreting cells. Results of the study are published online in the *Journal of Biological Chemistry*.

"Not only have we shown that we can reprogram skin cells, but we have also demonstrated that these reprogrammed cells can be differentiated into insulin-producing cells which hold great therapeutic potential for diabetes," said study lead author Yi Zhang, Ph.D., Howard Hughes Medical Institute investigator, professor of biochemistry and biophysics at UNC and member of the Lineberger Comprehensive Cancer Center.

"Of course, there are many years of additional studies that are required first, but this study provides hope for a cure for all patients with diabetes," said John Buse, MD, Ph.D., president of the American Diabetes Association and professor and chief of the endocrinology division in the UNC School of Medicine's department of medicine.

About 24 million Americans suffer from diabetes, a disease that occurs when the body is unable to produce or use insulin properly. Virtually all patients with type I diabetes, the more severe of the two types, must rely on daily injections of insulin to maintain their blood sugar levels.

Recent research exploring a possible long-term treatment – the transplantation of insulin-producing beta cells into patients – has yielded promising results. But this approach faces its own challenges, given the extreme shortage of matched organ donors and the need to suppress patients' immune systems.

The work by Zhang and other researchers could potentially address those problems, since insulin-producing cells could be made from diabetic patients' own reprogrammed cells.

Zhang is collaborating with Buse to obtain skin samples from diabetes patients. He said he hoped his current experiments will take this approach one step closer to a new treatment or even a cure for diabetes.

The research was funded by the Howard Hughes Medical Institute and the National Institutes of Health. Study co-authors include postdoctoral fellows Keisuke Tateishi, M.D.; Jin He, Ph.D.; Olena Taranova, Ph.D.; Ana C. D'Alessio, Ph.D.; and graduate student Gaoyang Liang, all from the UNC School of Medicine's department of biochemistry and biophysics. Note: Zhang can be reached at yi_zhang@med.unc.edu.

PHOTO IN THE NEWS: DNA-Based Neanderthal Face Unveiled

David Braun

Meet Wilma--named for the redheaded Flintstones character--the first model of a Neanderthal based in part on ancient DNA evidence.

Artists and scientists created Wilma (shown in a photo released yesterday) using analysis of DNA from 43,000-year-old bones that had been cannibalized. Announced in October 2007, the findings had suggested that at least some Neanderthals would have had red hair, pale skin, and possibly freckles.

Created for an October 2008 National Geographic magazine article, Wilma has a skeleton made from replicas of pelvis and skull bones from Neanderthal females. Copies of male Neanderthal bones--resized to female dimensions--filled in the gaps. (The National Geographic Society owns both National Geographic News and National Geographic magazine.)

"For the first time, anthropologists can go beyond fossils and peer into the actual genes of an extinct species of human," said National Geographic's senior science editor, Jamie Shreeve, who oversaw the project.



Reconstruction by Kennis & Kennis, photograph by Joe McNally/NGS

"We saw an opportunity to literally embody this new science in a full-size Neanderthal female, reconstructed using the latest information from genetics, fossil evidence, and archaeology."

For more on Neanderthals, watch Neanderthal Code, airing Sunday, September 21, on the National Geographic Channel.

Observatory

Permafrost May Not Thaw Even During Global Warming

By HENRY FOUNTAIN

One of the potential consequences of a warmer world, according to scientists who study such things, is the deep thawing of the permafrost. Thawing could release huge quantities of carbon into the atmosphere, as vegetation, bones and other organic material, long locked up in the deep freezer that is the permafrost, decompose.

But a study published in Science suggests that the impact of warming on the permafrost may not be as bad as forecast. The evidence comes in the form of a wedge of ancient ice found at an old mining site in the Yukon in Canada.

Ice wedges form in permafrost when the ground cracks because of cold, and spring meltwater seeps in and freezes. Over hundreds of years, the wedge builds up, like an in-ground icicle.

Duane G. Froese of the University of Alberta, the lead author of the study, said ice wedges could provide clues to the long-term stability of the permafrost. The problem is figuring out how old they are.

In this case, the top of the wedge was a couple of yards deep in the permafrost, and the researchers found volcanic ash on its top surface. By dating the ash (which presumably came from eruptions in what is now southeastern Alaska), Dr. Froese and his colleagues were able to say how long the ice has been there: about 740,000 years. Because the ash had to have been deposited after the wedge formed, that's "very clear proof," Dr. Froese said, that the ice is at least that old.

That means the ice survived through several warming periods, including the last major one, 120,000 years ago. "The general view is that everything would have melted out back then," Dr. Froese said. The new finding suggests that wasn't the case, and that models of future melting need to be rethought.

"But I don't want people to think we don't have to worry about global climate change," Dr. Froese said. The top couple of yards of permafrost are still likely to melt as temperatures warm, and there's plenty of carbon stored in them. "But the deeper part of the permafrost is probably relatively stable," he said.

Hormone discovery points to benefits of 'home grown' fat

A hormone found at higher levels when the body produces its own "home grown" fat comes with considerable metabolic benefits, according to a report in the September 19th issue of the journal Cell, a Cell Press publication. The newly discovered signaling molecule is the first example of a lipid-based hormone--most are made up of proteins--although the researchers said they expect it will not be the last.

The findings in mice raise the paradoxical notion that treatments designed to boost the body's fat production might actually be one solution to the growing epidemic of obesity and related metabolic diseases. Likewise, diets supplemented with the fat hormone, a fatty acid known as palmitoleate, might also come with long-term benefits. The results also reveal that, as with most things, when it comes to fat it's not fair to generalize.

"Most people think that fat is bad and the more you have the worse it is," said Gökhan Hotamisligil of Harvard School of Public Health. "To a certain extent that may be true, but it's far too simplistic. Rather than being one chemical entity, fats are actually a huge soup of things with hundreds of molecules and many

different structures. In the blood, high fatty acids and triglycerides are often considered bad and low levels good, but it's not quite that way. It depends what constitutes this soup rather than how much you have."

Hotamisligil, along with study first author Haiming Cao and their colleagues, made their discovery while studying mice that lack two specific fatty acid binding proteins (the lipid chaperones aP2 and mal1) only in their fat tissue. Those proteins bind lipids and control the fat composition of cells. Earlier studies showed that mice lacking one of those proteins become more sensitive to insulin. In addition, mice lacking both become resistant to virtually all aspects of metabolic syndrome, a cluster of obesity-associated ailments that includes diabetes, fatty liver disease, and atherosclerosis.

To further explore the animals' apparently "excellent health," the researchers measured their plasma lipid levels initially expecting to find lower than normal values. But, in fact, they found the mice to have higher circulating fatty acid levels.

"Despite those higher fatty acid levels, the animals are spectacularly healthy seemingly no matter what—even on a high fat diet," Hotamisligil said. Careful analysis of the lipids in those animals showed that their fat displayed a profile normally found in lean, insulin-sensitive mice despite consuming a high-fat diet.

Those results together with earlier studies also suggested that the changes in fat cells were having effects elsewhere in the body, specifically in the muscle and liver. They suspected it to be a protein-based hormone released by the fat, but nothing turned up.

Ultimately, they landed on the relevant actor: the fatty acid palmitoleate. They found that the normally rare fatty acid is the third most abundant free fatty acid in mice lacking those fatty acid binding proteins. In the fat tissue of normal mice, total palmitoleate concentrations drop nearly 50 percent upon exposure to a high fat diet. The mutant animals on the other hand experienced only a 10 percent decline in the fatty acid under the same conditions, evidence to explain their resistance to poor eating habits.

The fat hormone strongly stimulates insulin's effects on muscle and suppresses fat accumulation in the liver, they report. "This lipid is almost as good as insulin at pushing sugar out of the blood and it prevents fat in the liver," Hotamisligil said. "Delivering fat protects against fat, at least in the liver."

That emergence of palmitoleate in the blood is tied to changes in the activity of fat cells that occur when they convert glucose into fatty acids (a process known as de novo lipogenesis) rather than getting it from dietary sources.

"If what we postulate is correct, tricking the body to produce fat may actually be an excellent strategy for metabolic health," Hotamisligil said. Indeed, he added, there is evidence that people who are obese produce less of their own fat.

Of course, all of this assumes that the findings in mice will be applicable to humans. Hotamisligil said that it should be relatively easy to begin testing that idea by measuring palmitoleate levels in healthy people compared to those with various metabolic diseases. Further study by his group will seek to unravel exactly how palmitoleate exerts its influence. They will also delve further into hints from the current study that the fat hormone might also have anti-inflammatory properties.

The researchers include Haiming Cao, Harvard School of Public Health, Boston, MA; Kristin Gerhold, Harvard School of Public Health, Boston, MA; Jared R. Mayers, Harvard School of Public Health, Boston, MA; Michelle M. Wiest, Lipomics Technologies, West Sacramento, CA; Steven M. Watkins, Lipomics Technologies, West Sacramento, CA; and Gokhan S. Hotamisligil, Harvard School of Public Health, Boston, MA.

In pain? Take one masterpiece, three times a day

THE power of art to heal emotional wounds is well known, but could contemplating a beautiful painting have the same effect on physical pain?

To investigate, Marina de Tommaso and a team from the University of Bari in Italy asked 12 men and women to pick the 20 paintings they considered most ugly and most beautiful from a selection of 300 works by artists such as da Vinci and Botticelli.

They were then asked to contemplate either the beautiful paintings, or the ugly painting, or a blank panel while the team zapped a short laser pulse at their hand, creating a pricking sensation.

The subjects rated the pain as being a third less intense while they were viewing the beautiful paintings, compared with contemplating the ugly paintings or the blank panel. Electrodes measuring the brain's electrical activity suggested a reduced response to the pain when the subject looked at beautiful paintings (Consciousness and Cognition, DOI: 10.1016/j.concog.2008.07.002).

While distractions are known to reduce pain in hospital patients, de Tommaso says this is the first result to show that beauty plays a part. "Hospitals have been designed to be functional, but we think that their aesthetic aspects should be taken into account too," she says.

When healing turns to scarring: Research reveals why it happens and how to stop it

For the first time, research from The University of Western Ontario has revealed the mechanisms involved in the origin of scarring or fibrotic diseases, as well as a way to control it. The study, led by Andrew Leask of the CIHR Group in Skeletal Development and Remodeling, is published in the Journal of Clinical Investigation.

"People are generally unaware of how prevalent scarring diseases are, and the impact they have on our health," says Leask, a professor in the Department of Physiology and Pharmacology at Western's Schulich School of Medicine & Dentistry. "Cardiovascular and other diseases including diabetes, cancer, and pulmonary fibrosis all involve scarring, which affects the organs' ability to function. Another example is scleroderma, a progressive scarring disease affecting 300,000 people in the United States and 40,000 Canadians. It's estimated about 40% of all deaths and health care costs in North America are related to scarring or fibrosis."

During tissue repair, specialized cells called myofibroblasts migrate to the wound where they generate the adhesive and tensile forces required for wound closure. Normally, these myofibroblasts then disappear from the wound. But if they persist and continue to make connective tissue, it can become too thick, preventing the organ from functioning properly. So for instance, in the case of diabetes, this scarring could cause the kidney to shut down, requiring dialysis or a transplant.

The research team which included investigators from Mount Sinai Hospital in Toronto and University College London in England, identified that a particular protein called glycogen synthase kinase 3 normally acts as a brake to terminate repair. If this protein is impaired, scarring results after wounding. Investigators also found elevated levels of a protein called endothelin-1. Next, they used a drug, already on the market, which blocks endothelin-1 and found it prevented scarring but did not affect wound closure in mice. While the use of the drug for this purpose would still have to be tested in humans, Leask believes this therapy could stop fibrosis from occurring without affecting normal tissue repair.

The research was supported by the Canadian Foundation for Innovation, CIHR, the Arthritis Research Campaign, the Reynaud's and Scleroderma Foundation, and the Scleroderma Society.

Political attitudes are predicted by physiological traits

Is America's red-blue divide based on voters' physiology?

HOUSTON -- (Sept. 16, 2008) -- Is America's red-blue divide based on voters' physiology? A new paper in the journal Science, titled "Political Attitudes Are Predicted by Physiological Traits," explores the link.

Rice University's John Alford, associate professor of political science, co-authored the paper in the Sept. 19 issue of Science.

Alford and his colleagues studied a group of 46 adult participants with strong political beliefs. Those individuals with "measurably lower physical sensitivities to sudden noises and threatening visual images were more likely to support foreign aid, liberal immigration policies, pacifism and gun control, whereas individuals displaying measurably higher physiological reactions to those same stimuli were more likely to favor defense spending, capital punishment, patriotism and the Iraq War," the authors wrote.

Participants were chosen randomly over the phone in Lincoln, Neb. Those expressing strong political views -- regardless of their content -- were asked to fill out a questionnaire on their political beliefs, personality traits and demographic characteristics.

In a later session, they were attached to physiological measuring equipment and shown three threatening images (a very large spider on the face of a frightened person, a dazed individual with a bloody face and an open wound with maggots in it) interspersed among a sequence of 33 images. Similarly, participants also viewed three nonthreatening images (a bunny, a bowl of fruit and a happy child) placed within a series of other images. A second test used auditory stimuli to measure involuntary responses to a startling noise.

The researchers noted a correlation between those who reacted strongly to the stimuli and those who expressed support for "socially protective policies," which tend to be held by people "particularly concerned with protecting the interests of the participants' group, defined as the United States in mid-2007, from threats." These positions include support for military spending, warrantless searches, the death penalty, the Patriot Act, obedience, patriotism, the Iraq War, school prayer and Biblical truth, and opposition to pacifism, immigration, gun control, foreign aid, compromise, premarital sex, gay marriage, abortion rights and pornography.

The paper concluded, "Political attitudes vary with physiological traits linked to divergent manners of experiencing and processing environmental threats." This may help to explain "both the lack of malleability in the beliefs of individuals with strong political convictions and the associated ubiquity of political conflict," the authors said.

Alford's co-authors were Douglas R. Oxley, Kevin B. Smith, Jennifer L. Miller, John R. Hibbing and Mario Scalora, of the University of Nebraska; Matthew V. Hibbing, of the University of Illinois, Urbana-Champaign; and Peter K. Hatemi, of the Virginia Institute for Psychiatric and Behavioral Genetics.

We are facing a global pandemic of antibiotic resistance, warn experts

Analysis: Antibiotic resistance BMJ Online First

Vital components of modern medicine such as major surgery, organ transplantation, and cancer chemotherapy will be threatened if antibiotic resistance is not tackled urgently, warn experts on bmj.com today.

A concerted global response is needed to address rising rates of bacterial resistance caused by the use and abuse of antibiotics or "we will return to the pre-antibiotic era", write Professor Otto Cars and colleagues in an editorial.

All antibiotic use "uses up" some of the effectiveness of that antibiotic, diminishing the ability to use it in the future, write the authors, and antibiotics can no longer be considered as a renewable source.

They point out that existing antibiotics are losing their effect at an alarming pace, while the development of new antibiotics is declining. More than a dozen new classes of antibiotics were developed between 1930 and 1970, but only two new classes have been developed since then.

According to the European Centre for Disease Prevention and Control, the most important disease threat in Europe is from micro-organisms that have become resistant to antibiotics. As far back as 2000, the World Health Organisation was calling for a massive effort to address the problem of antimicrobial resistance to prevent the "health catastrophe of tomorrow".

So why has so little been done to address the problem of resistance, ask the authors?

Antibiotics are over prescribed, still illegally sold over the counter in some EU countries, and self medication with leftover medicines is commonplace.

There are alarming reports about serious consequences of antibiotic resistance from all around the world. However, there is still a dearth of data on the magnitude and burden of antibiotic resistance, or its economic impact on individuals, health care, and society. This, they suggest, may explain why there has been little response to this public health threat from politicians, public health workers, and consumers.

In addition, there are significant scientific challenges but few incentives to developing new antibiotics, state the authors.

The authors believe that priority must be given to the most urgently needed antibiotics and incentives given for developing antibacterials with new mechanisms of action. In addition, "the use of new antibiotics must be safeguarded by regulations and practices that ensure rational use, to avoid repeating the mistakes we have made by overusing the old ones", they say.

They point out that reducing consumer demand could be the strongest force to driving change—individuals must be educated to understand that their choice to use an antibiotic will affect the possibility of effectively treating bacterial infections in other people.

But, they claim, the ultimate responsibility for coordination and resources rests with national governments, WHO and other international stakeholders.

Not only is there an urgent need for up-to-date information on the level of antibiotic resistance, but also for evidence of effective interventions for the prevention and control of antibiotic resistance at national and local levels, while more focus is needed on infectious diseases, they conclude.

Plants in Forest Emit Aspirin Chemical to Deal with Stress; Discovery May Help Agriculture

BOULDER—Plants in a forest respond to stress by producing significant amounts of a chemical form of aspirin, scientists have discovered. The finding, by scientists at the National Center for Atmospheric Research (NCAR), opens up new avenues of research into the behavior of plants and their impacts on air quality, and it also has the potential to give farmers an early warning signal about crops that are failing.

"Unlike humans, who are advised to take aspirin as a fever suppressant, plants have the ability to produce their own mix of aspirin-like chemicals, triggering the formation of proteins that boost their biochemical defenses and reduce injury," says NCAR scientist Thomas Karl, who led the study. "Our measurements show that significant amounts of the chemical can be detected in the atmosphere as plants respond to drought, unseasonable temperatures, or other stresses."

For years, scientists have known that plants in a laboratory may produce methyl salicylate, which is a chemical form of acetylsalicylic acid, or aspirin. But researchers had never before detected methyl salicylate in an ecosystem or verified that plants emit the chemical in significant quantities into the atmosphere.

The team of scientists reported its findings last week in *Biogeosciences*. The research was funded by the National Science Foundation, NCAR's sponsor.

An unexpected finding

Researchers had not previously thought to look for methyl salicylate in a forest, and the NCAR team found the chemical by accident. They set up specialized instruments last year in a walnut grove near Davis, California,

to monitor plant emissions of certain volatile organic compounds (VOCs). These hydrocarbon compounds are important because they can combine with industrial emissions to affect pollution, and they can also influence local climate.

When the NCAR scientists reviewed their measurements, they found to their surprise that the emissions of VOCs included methyl salicylate. The levels of methyl salicylate emissions increased dramatically when the plants, which were already stressed by a local drought, experienced unseasonably cool nighttime temperatures followed by large daytime temperature increases. Instruments mounted on towers about 100 feet above the ground measured up to 0.025 milligrams of methyl salicylate rising from each square foot of forest per hour.

Karl and his colleagues speculate that the methyl salicylate has two functions. One of these is to stimulate plants to begin a process known as systemic acquired resistance, which is analogous to an immune response in an animal. This helps a plant to both resist and recover from disease.

The methyl salicylate also may be a mechanism whereby a stressed plant communicates to neighboring plants, warning them of the threat. Researchers in laboratories have demonstrated that a plant may build up its defenses if it is linked in some way to another plant that is emitting the chemical. Now that the NCAR team has demonstrated that methyl salicylate can build up in the atmosphere above a stressed forest, scientists are speculating that plants may use the chemical to activate an ecosystem-wide immune response.

"These findings show tangible proof that plant-to-plant communication occurs on the ecosystem level," says NCAR scientist Alex Guenther, a co-author of the study. "It appears that plants have the ability to communicate through the atmosphere."

Implications for farmers

The discovery raises the possibility that farmers, forest managers, and others may eventually be able to start monitoring plants for early signs of a disease, an insect infestation, or other types of stress. At present, they often do not know if an ecosystem is unhealthy until there are visible indicators, such as dead leaves.

"A chemical signal is a very sensitive way to detect plant stress, and it can be an order of magnitude more effective than using visual inspections," Karl says. "If you have a sensitive warning signal that you can measure in the air, you can take action much sooner, such as applying pesticides. The earlier you detect that something's going on, the more you can benefit in terms of using fewer pesticides and managing crops better."

The discovery also can help scientists resolve a central mystery about VOCs. For years, atmospheric chemists have speculated that there are more VOCs in the atmosphere than they have been able to find. Now it appears that some fraction of the missing VOCs may be methyl salicylate and other plant hormones. This finding can help scientists better track the impact of VOCs on the behavior of clouds and the development of ground-level ozone, an important pollutant.

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About the article

Title: "Chemical sensing of plant stress at the ecosystem scale"

Authors: T. Karl, A. Guenther, A. Turnipseed, E.G. Patton, K. Jardine

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'Buckyballs' have high potential to accumulate in living tissue

WEST LAFAYETTE, Ind. - Research at Purdue University suggests synthetic carbon molecules called fullerenes, or buckyballs, have a high potential of being accumulated in animal tissue, but the molecules also appear to break down in sunlight, perhaps reducing their possible environmental dangers.

Buckyballs may see widespread use in future products and applications, from drug-delivery vehicles for cancer therapy to ultrahard coatings and military armor, chemical sensors and hydrogen-storage technologies for batteries and automotive fuel cells.

"Because of the numerous potential applications, it is important to learn how buckyballs react in the environment and what their possible environmental impacts might be," said Chad Jafvert, a professor of civil engineering at Purdue.

The researchers mixed buckyballs in a solution of water and a chemical called octanol, which has properties similar to fatty tissues in animals. Jafvert and doctoral student Pradnya Kulkarni were the first to document how readily buckyballs might be "partitioned," or distributed into water, soil and fatty tissues in wildlife such as fish.

Findings indicated buckyballs have a greater chance of partitioning into fatty tissues than the banned pesticide DDT. However, while DDT is toxic to wildlife, buckyballs currently have no documented toxic effects, Jafvert said.

"This work points out the need for a better understanding of where the materials go in the environment," he said. "Our results show they are going to be taken up by fish and other organisms, possibly to toxic levels. This, however, indicates only the potential of buckyballs to bioaccumulate. They could break down in the environment or in an organism once taken up."

Researchers do not yet know whether buckyballs will break down in the environment or will be metabolized by animals, which would reduce the risk of accumulating in fatty tissues.

"For example, we don't bioaccumulate sugars because we process sugars, but we do bioaccumulate other compounds that we don't metabolize," Jafvert said. "If we have the ability to metabolize buckyballs, we won't bioaccumulate them."

Findings were detailed in a research paper that appeared in August in the journal *Environmental Science and Technology*. The paper was written by Jafvert and Kulkarni.

The researchers determined the "octanol-water partition coefficient," which enables them to show how readily buckyballs would be partitioned.

"The bottom line is, if buckyballs partition favorably from water to octanol, they are also likely to partition favorably from water to fatty tissues," Jafvert said.

The researchers also are investigating whether sunlight breaks down buckyballs and other structures called carbon nanotubes, which also could have widespread industrial applications.

"We need to learn how reactive these materials are in the environment," Jafvert said. "Do they break down? What kinds of products do they form? We have learned so far that buckyballs absorb light, and they do photoreact. That's potentially a good thing because it means it won't hang around for a long period of time, reducing the exposure concentration, which would then reduce any potential toxicity that it may or may not have."

Named after architect R. Buckminster Fuller, who designed the geodesic dome, buckminsterfullerenes, or buckyballs, are soccer-ball-shaped molecules containing 60 carbon atoms. A buckyball has a width of about 1 nanometer, or one-billionth of a meter, which is roughly 10 atoms wide.

The researchers determined precisely how soluble the buckyballs are in water and confirmed that the molecules form clusters, which complicates efforts to understand how they might be dispersed by water in the environment.

"Typically, buckyballs are not found in water because their solubility is so low, but the same could be said of DDT," Jafvert said. "DDT is found in sediment, so you would assume buckyballs would also end up in sediments. That means there is also a chance that marine organisms, like worms that are eating sediment, are going to be potentially accumulating buckyballs unless they break down in the environment."

The research is affiliated with the Center for the Environment and the Birck Nanotechnology Center at Purdue's Discovery Park and is funded by the Environmental Protection Agency and the National Science Foundation through the NSF's Nanoscale Interdisciplinary Research Team, or NIRT. The work is part of a larger NIRT project at Purdue involving researchers in agronomy, civil engineering, agricultural and biological engineering, mechanical engineering, food science, and earth and atmospheric sciences.

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Note to Journalists: An electronic copy of the research paper is available from Emil Venere, (765) 494-4709, venere@purdue.edu

ABSTRACT

Buckminsterfullerene's (C60) Octanol-Water Partition Coefficient (Kow) and Aqueous Solubility

Chad T. Jafvert and Pradnya P. Kulkarni Purdue University, School of Civil Engineering

To assess the risk and fate of fullerene C60 in the environment, its water solubility and partition coefficients in various systems are useful. In this study, the log Kow of C60 was measured to be 6.67, and the toluene-water partition coefficient was measured at log Ktw) 8.44. From these values and the respective solubilities of C60 in water-saturated octanol and water-saturated toluene, C60's aqueous solubility was calculated at 7.96ng/L(1.11°—10-11M) for the organic solvent-saturated aqueous phase. Additionally, the solubility of C60 was measured in mixtures of ethanol-water and tetrahydrofuran-water and modeled with Wohl's equation to confirm the accuracy of the calculated solubility value. Results of a generator column experiment strongly support the hypothesis that clusters form at aqueous concentrations below or near this calculated solubility. The Kow value is compared to those of other hydrophobic organic compounds, and bioconcentration factors for C60 were estimated on the basis of Kow.

UCLA study of satellite imagery casts doubt on surge's success in Baghdad

By tracking the amount of light emitted by Baghdad neighborhoods at night, a team of UCLA geographers has uncovered fresh evidence that last year's U.S. troop surge in Iraq may not have been as effective at improving security as some U.S. officials have maintained.

Night light in neighborhoods populated primarily by embattled Sunni residents declined dramatically just before the February 2007 surge and never returned, suggesting that ethnic cleansing by rival Shiites may have been largely responsible for the decrease in violence for which the U.S. military has claimed credit, the team reports in a new study based on publicly available satellite imagery.

"Essentially, our interpretation is that violence has declined in Baghdad because of intercommunal violence that reached a climax as the surge was beginning," said lead author John Agnew, a UCLA professor of geography and authority on ethnic conflict. "By the launch of the surge, many of the targets of conflict had either been killed or fled the country, and they turned off the lights when they left."

The team reports its findings in the October issue of *Environment and Planning A*, a leading peer-reviewed academic journal that specializes in urban and environmental planning issues.

The night-light signature in four other large Iraqi cities — Kirkuk, Mosul, Tikrit and Karbala — held steady or increased between the spring of 2006 and the winter of 2007, the UCLA team found. None of these cities were targets of the surge.

Baghdad's decreases were centered in the southwestern Sunni strongholds of East and West Rashid, where the light signature dropped 57 percent and 80 percent, respectively, during the same period.

By contrast, the night-light signature in the notoriously impoverished, Shiite-dominated Sadr City remained constant, as it did in the American-dominated Green Zone. Light actually increased in Shiite-dominated New Baghdad, the researchers found.

Until just before the surge, the night-light signature of Baghdad had been steadily increasing overall, they report in "Baghdad Nights: Evaluating the U.S. Military 'Surge' Using Night Light Signatures."

"If the surge had truly 'worked,' we would expect to see a steady increase in night-light output over time, as electrical infrastructure continued to be repaired and restored, with little discrimination across neighborhoods," said co-author Thomas Gillespie, an associate professor of geography at UCLA. "Instead, we found that the night-light signature diminished in only in certain neighborhoods, and the pattern appears to be associated with ethno-sectarian violence and neighborhood ethnic cleansing."

The effectiveness of the February 2007 deployment of 30,000 additional U.S. troops has been a subject of debate. In a report to Congress in September of that year, Gen. David Petraeus claimed "the military objectives of the surge are, in large measure, being met." However, a report the same month by an independent military commission headed by retired U.S. Gen. James Jones attributed the decrease in violence to areas being overrun by either Shiites or Sunnis. The issue now figures in the U.S. presidential race, with Republican presidential candidate John McCain defending the surge and Democratic hopeful Barack Obama having been critical of it.

Reasoning that an increase in power usage would represent an objective measure of stability in the city, Agnew and Gillespie led a team of UCLA undergraduate and graduate students in political science and geography that pored over publicly available night imagery captured by a weather satellite flown by the U.S. Air Force for the Department of Defense.

Orbiting 516 miles above the Earth, Satellite F16 of the Defense Meteorological Satellite Program, Operational Linescan System (DMSP/OLS) contains infrared sensors that calculate, among other things, the amount of light given off in 1.75-square-mile areas. Using geo-referenced coordinates, the team overlaid the infrared reading on a preexisting satellite map of daytime Iraq created by NASA's Landsat mapping program. The researchers then looked at the sectarian makeup in the 10 security districts for which the DMSP satellite took readings on four exceptionally clear nights between March 20, 2006, when the surge had not yet begun, and Dec. 16, 2007, when the surge had ended.

Lights dimmed in those neighborhoods that Gen. Jones pointed to as having experienced ethno-sectarian violence and neighborhood ethnic cleansing in his "Report of the Independent Commission on the Security Forces of Iraq."

"The surge really seems to have been a case of closing the stable door after the horse has bolted," Agnew said.

Long-term obstacles to meeting Baghdad's power needs may have contributed to the decrease in night lights in the city's southwestern parts, the researchers acknowledge. But Baghdad's shaky power supply does not fully account for the effect, they contend, citing independent research showing that decaying and poorly maintained power plants and infrastructure were meeting less than 10 hours of Baghdad's power needs prior to the fall of Saddam Hussein.

"This was the part of the city that had the best sources of connection and the most affluent population, so they could actually generate power themselves, and they were in the habit of doing so well before the U.S. invasion," said Agnew, the president of the American Association of Geographers, the field's leading professional organization. "But we saw no evidence of a widespread continuation of this practice."

In addition to casting doubt on the efficacy of the surge in general, the study calls into question the success of a specific strategy of the surge, namely separating neighborhoods of rival sectarian groups by erecting concrete blast walls between them. The differences in light signatures had already started to appear by the time American troops began erecting the walls under Gen. Petraeus's direction, the researchers found.

"The U.S. military was sealing off neighborhoods that were no longer really active ribbons of violence, largely because the Shiites were victorious in killing large numbers of Sunnis or driving them out of the city all together," Agnew said. "The large portion of the refugees from Iraq who went during this period to Jordan and Syria are from these neighborhoods."

Previous research has used satellite imagery of night-light saturation to measure changes in the distribution of populations in a given area, but the UCLA project is believed to be the first to study population losses and migration due to sectarian violence. The outgrowth of an undergraduate course in the use of remote sensing technologies in the environment, the UCLA project was inspired by a desire to bring empirical evidence to a long-running debate.

"We had no axe to grind," said Agnew. "We were very open. If we had found that the situation was different, we would've reported it. Our main goal was to bring fairly objective and unobtrusive measures to a particularly contentious issue." *The study will be available Sept. 19 at www.envplan.com/abstract.cgi?id=a41200.*

How to prevent liver damage induced by anti-tuberculosis treatment?

About one third of the world's population has latent tuberculosis and roughly 9 million cases of active tuberculosis emerge annually resulting in 2-3million deaths. Most new cases occur in the most populated nations like India and China. Combination chemotherapy containing Isoniazid (INH), Rifampicin (RMP), Pyrazinamide (PZA) with or without ethambutol for initial 2 months followed by a continuation phase of 4-6 months of Isoniazid and Rifampicin is the preferred regimen for successful treatment and for preventing acquired resistance. Drug induced hepatotoxicity is a potentially serious adverse effect of antituberculosis (ATT) regimen. A higher risk of hepatotoxicity has been reported in Indian patients (up to 11.5%) than in their western counterpart (up to 4.3%). The only measure available for managing hepatotoxicity is stopping the offending agents, once there is an evidence of liver damage and reintroducing the same after normalization of liver enzymes. Preventive therapy of contacts causes severe hepatotoxicity more often than curative treatment of clinical tuberculosis. Search for non-toxic and highly effective new compounds for treating tuberculosis or an effective vaccine conferring sustained protective immunity have yet not seen the face of success.

A research article to be published on August 14, 2008 in the World Journal of Gastroenterology addresses this question. The research team led by Dr. Meghna Adhvaryu of Bapalal Vaidya Botanical research center, Department of Biosciences, Veer Narmad South Gujarat University Surat, India in joint effort with Dr. Bhasker Vakharia running a charitable mobile clinic in tribal belt of district Surat, conducted a clinical trial of two Ayurvedic herbs in a modified form used as an adjuvant to conventional ATT to evaluate their ability to prevent hepatotoxicity.

The pathogenesis of hepatotoxicity is not entirely clear but INH and RMP induced damage may involve oxidative stress, lipid peroxidation, choline deficiency leading to lowering of phospholipids protein synthesis with alteration in cell wall configuration, reduced glutathione level and activation of CYP2E1. It is well known that some non toxic herbs are having opposite activities in the form of membrane stabilizing, anti-oxidative and CYP2E1 inhibitory effects. A review of available literature suggests that reduction in lipid peroxide content in tissue and increase in superoxide dismutase, catalase, glutathione, glutathione-s-transferase and glutathione peroxidase activities should help to maintain liver cell integrity and control the increase in level of liver enzymes.

Initially four potential candidate herbs were tested in a guinea pig model of ATT induced hepato-toxicity and marked hepato-protective ability was demonstrated. The research article was published on 21st June 2007 in the World Journal of Gastroenterology. Two herbs viz. Curcuma longa and Tinospora cordifolia were selected for further study due to their higher efficacy, very safe toxicological profile and synergistic action when used in combination.

The results of clinical trial proved the safety and efficacy of the formulation as an adjuvant to conventional ATT in preventing liver damage beyond doubt by limiting the incidence of hepatotoxicity (mild) to 0.06% as against 14% due to conventional treatment alone in the control group. Malnourished, HIV positive, Hepatitis B/C virus carrier. Sick trait positive, relapse cases, cases with extensive or miliary disease, COPD, asthma, Diabetes mellitus, hypertension... all were recruited in both the group, which may account for the higher incidence of hepatotoxicity in control group but at the same time the similar patients in trial group not only escaped liver damage but showed a higher cure rate and better resolution of lesions. This result encourages for

further research and trials with immunocompromised, multidrug resistant and non-responding patients and also latent TB cases who are subjected to a potentially serious risk by preventive treatment.

Looking at the scenario as described earlier, the results of this trial carries utmost significance and applicability at mass level tuberculosis control programs and might help curb the resurgence of TB in developed countries after advent of HIV and AIDS.

Reference: Adhvaryu MR, Reddy MN, Vakharia BC. Prevention of hepatotoxicity due to anti tuberculosis treatment: A novel integrative approach. World J Gastroenterol 2008; 14(30): 4753-4762 <http://www.wjgnet.com/1007-9327/14/4753.asp>

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Research pushes back crop development 10,000 years

Until recently researchers believed the story of the origin of agriculture was one of a relatively sudden appearance of plant cultivation in the Near East around 10,000 years ago spreading quickly into Europe and dovetailing conveniently with ideas about how quickly language and population genes spread from the Near East to Europe. Initially, genetics appeared to support this idea but now cracks are beginning to appear in the evidence underpinning that model.

Now a team led by Dr Robin Allaby from the University of Warwick have developed a new mathematical model that shows how plant agriculture actually began much earlier than first thought, well before the Younger Dryas (the last "big freeze" with glacial conditions in the higher latitudes of the Northern Hemisphere). It also shows that useful gene types could have actually taken thousands of years to become stable.

Up till now researchers believed in a rapid establishment of efficient agriculture which came about as artificial selection was easily able to dominate natural plant selection, and, crucially, as a consequence they thought most crops came from a single location and single domestication event.

However recent archaeological evidence has already begun to undermine this model pushing back the date of the first appearance of plant agriculture. The best example of this being the archaeological site Ohalo II in Syria where more than 90,000 plant fragments from 23,000 years ago show that wild cereals were being gathered over 10,000 years earlier than previously thought, and before the last glacial maximum (18,000-15,000 years ago).

The field of Archaeobotany is also producing further evidence to undermine the quick development model. The tough rachis mutant is caused by a single recessive allele (one gene on a pair or group of genes), and this mutant is easily identifiable in the archaeological specimens as a jagged scar on the chaff of the plant noting an abscission (shedding of a body part) as opposed to the smooth abscission scar associated with the wild type brittle rachis.

Simply counting the proportion of chaff types in a sample gives a direct measure of frequency of the two different gene types in this plant. That study has shown that the tough rachis mutant appeared some 9,250 years ago and had not reached fixation over 3,000 years later even after the spread of agriculture into Europe was well underway. Studies like these have shown that the rise of the domestication syndrome was a slow process and that plant traits appeared in slow sequence, not together over a short period of time.

Genome wide surveys of crops such as einkorn and barley that in the past that have suggested a single origin from a narrow geographical range, supporting the rapid establishment view, have long been in conflict with other gene studies. The most notable conflict is in the case of barley for which there is a large body of evidence that suggests more than one common ancestor was used in its development.

These challenges to the fast model of agricultural development need a new model to explain how and why the development was so slow and demonstrate why artificial selection of just one plant type does not have the expected quick result. This computer model has now been provided by Dr Robin Allaby and his team at the University of Warwick, the Institute of Archaeology, University College London, and Manchester Interdisciplinary Biocentre has outlined the new mathematical model in a paper published in Proceedings of the National Academy of Sciences USA 2008 and in a summary article in the Biologist (2008 55:94-99).

Their paper entitled The genetic expectations of a protracted model for the origins of domesticated crops used computer simulations that showed that over time a cultivated population will become monophyletic (settle into one stable species) at a rate proportional to its population size as compared various gene variations in the wild populations. They found this rate of change matched closely the 3000 years it took the tough rachis mutant to become established.

Ironically, this process is actually accelerated if there is more than one wild source population (in other words if attempts at domestication happen more than once) because any resulting hybrid between those

domesticated populations then has a heightened differentiation compared with either one of the wild populations of the two parent plants.

This mathematical model also more supportive of a longer complex origin of plants through cross breeding of a number of attempts at domestication rather than a single plant type being selectively bred and from a single useful mutation that is selectively grown quickly out paces the benefits natural selection

Dr Robin Allaby says:

"This picture of protracted development of crops has major implications for the understanding of the biology of the domestication process and these strike chords with other areas of evolutionary biology."

"This lengthy development should favour the close linkage of domestication syndrome trait genes which may become much more important because linked genes will not be broken up by gene flow – and this makes trait selection and retention easier. Interestingly, as more crop genomes become mapped, the close linkage of two or more domestication syndrome genes has been reported on several occasions."

"This process has similarities to the evolution of 'supergenes' in which many genes cluster around a single locus to contribute to one overall purpose."

"We now need to move this research area to a new level. Domestication was a complex process and can now be viewed more legitimately as the paragon of evolutionary process that Darwin originally recognized. There are many interacting factors involved that we know about operating on a wide range of levels from the gene to the farmer and climate – the challenge is to integrate them into a single story."

Plastic-munching bugs turn waste bottles into cash

* 12:34 19 September 2008

* NewScientist.com news service

* **Colin Barras**

Newly discovered bacterial alchemists could help save billions of plastic bottles from landfill. The *Pseudomonas* strains can convert the low-grade PET plastic used in drinks bottles into a more valuable and biodegradable plastic called PHA.

PHA is already used in medical applications, from artery-supporting tubes called stents to wound dressings. The plastic can be processed to have a range of physical properties. However, one of the barriers to PHA reaching wider use is the absence of a way to make it in large quantities.

The new bacteria-driven process – termed upcycling – could address that, and make recycling PET bottles more economically attractive.

PET bugs

Although billions of plastic bottles are made each year, few are ultimately recycled. Just 23.5% of US bottles were recycled in 2006. This is because the recycling process simply converts the low value PET bottles into more PET, says Kevin O'Connor at University College Dublin, Ireland.

"We wanted to see if we could turn the plastic into something of higher value in an environmentally friendly way," he says.

O'Connor and colleagues knew that heating PET in the absence of oxygen – a process called pyrolysis – breaks it down into terephthalic acid (TA) and a small amount of oil and gas. They also knew that some bacteria can grow and thrive on TA, and that other bacteria produce a high-value plastic PHA when stressed. So they wondered whether any bacteria could both feed on TA and convert it into PHA.

Bacteria hunt

"It was a long shot to be honest," says O'Connor. His team studied cultures from around the world known to grow on TA, but none produced PHA. So they decided to look for undiscovered strains, in environments that naturally contain TA.

Analysing soil bacteria from a PET bottle processing plant, which are likely to be exposed to small quantities of TA, yielded 32 colonies that could survive in the lab using TA as their only energy source. After 48 hours they screened each culture for PHA. Three cultures, all similar to known strains of *Pseudomonas*, accumulated detectable quantities of the valuable plastic.

The next step is to improve the efficiency of the process, says O'Connor. "A quarter to a third of each cell is filled with plastic – we want to increase that to 50 to 60%."

Less landfill

Sudesh Kumar, a microbiologist at the University of Science, Malaysia, in Penang, is impressed with the study.

"There are many other systems that are economically more viable to produce PHA with better material properties," he says. "But Kevin's work offers an interesting novel approach to solve the problem of PET accumulation in landfill dumps."

But it is still unlikely that using the new approach alone will appeal to industry, O'Connor says.

"Working with this kind of environmental technology in isolation, the chances of success are reduced," he says. The best approach, he continues, would be to use the new bacteria as just one part of a bio-refinery capable of upcycling an array of waste products in an environmentally friendly way.

Journal reference: Environmental Science and Technology (DOI: 10.1021/es801010e)

Sweet smells lead to sweet dreams

* 16:30 21 September 2008

* NewScientist.com news service

* **Jessica Griggs**

Can smells sweeten your dreams? Certain aromas, such as lavender, are known to have soporific effects, but once you're asleep, can smells influence what you dream about?

To find out, Boris Stuck of University Hospital Mannheim, Germany, exposed 15 sleeping volunteers to chemicals that mimicked the smell of either rotten eggs or roses.

"Most everyday smells have two components: the actual smell and a component that irritates your nose," says Stuck. "By exposing the patients to chemicals chosen to only incorporate the smelly component, we were able to stimulate them with really high doses of the smell without them waking up."

Stuck's team waited until their subjects had entered the REM phase of sleep, the stage at which most dreams occur, and then exposed them to a high dose of smelly air for 10 seconds before waking them up one minute later. The volunteers were then quizzed about the content of their dreams and asked how it made them feel.

Rose-tinted dreams

All subjects reported a positive dream experience when stimulated by the rose smell, and most experienced the opposite when exposed to the rotten eggs. Stuck says the smells influence the "emotional colouration" of the dream.

The team are now looking to recruit people who suffer from nightmares to see if exposure to smells can help make their dreams more pleasant.

"The relationship between external stimuli and dreaming is something we are all at some level aware of," says Irshaad Ebrahim of The London Sleep Centre. "This initial research is a step in the direction towards clarifying these questions and may well lead to therapeutic benefits."

Stuck is presenting his work on Sunday at the American Academy of Otolaryngology's annual meeting in Chicago.

E.R. Patients Often Left Confused After Visits

By LAURIE TARKAN

A vast majority of emergency room patients are discharged without understanding the treatment they received or how to care for themselves once they get home, researchers say. And that can lead to medication errors and serious complications that can send them right back to the hospital.

In a new study, researchers followed 140 English-speaking patients discharged from emergency departments in two Michigan hospitals and measured their understanding in four areas — their diagnosis, their E.R. treatment, instructions for their at-home care and warning signs of when to return to the hospital.

The study, published online in July by the *Annals of Emergency Medicine*, found that 78 percent of patients did not understand at least one area and about half did not understand two or more areas. The greatest confusion surrounded home care — instructions about things like medications, rest, wound care and when to have a follow-up visit with a doctor.

"We're finding that people are just not prepared for self-care, and that's what is bringing them back," said Dr. Eric Coleman, director of the Care Transitions Program at the University of Colorado, who was not involved in the study.

The researchers described a woman in her 20s who went to the emergency room with abdominal pain. After extensive testing, doctors there diagnosed pelvic inflammatory disease, a sexually transmitted infection.

But when interviewed by a researcher, the woman said that she was not aware of any diagnosis, that she did not realize she had been sent home with an antibiotic (she took only the pain medication she was given), and that she did not know she should abstain from sex, tell her partner or have follow-up care.

"The risk is that she could become more seriously ill," said one of the authors, Dr. Kirsten G. Engel, a clinical instructor at Northwestern University. "It's a significant risk to her fertility, and she could pass it to her partner."

Dr. Paul M. Schyve, senior vice president of the Joint Commission, the main organization that accredits hospitals, said: "This study showed that this is much more common than you think. It's not the rare patient."

Similar results have been found for patients leaving hospitals, not just emergency rooms. And experts say they help explain why about 18 percent of Medicare patients discharged from a hospital are readmitted within 30 days.

Doctors and patients say that with hospitals pressed to see more patients faster, patients get less attention. “When I start my shift, I know what I’d like to accomplish, but by the end of the shift, my main concern is that nobody dies, and the other things become less important,” said Dr. Michael S. Radeos, research director in the department of emergency medicine at New York Hospital Medical Center of Queens.

Jaleh Teymourian Brahms of Millburn, N.J., ended up in the emergency room after falling face down on a street in Manhattan. “I had pavement embedded in my face and two chipped front teeth,” she said.

After being examined for broken bones (there were none), she waited four hours before she was discharged, with bits of pavement still embedded in her face. Ms. Teymourian Brahms said she received no instructions about how to care for her face. Her dentist had to pick the tar and gravel out with a dental tool, then instructed her on how to clean her face and to keep it moist with an antibacterial ointment.

“I risked a nasty infection had I not seen him,” she said.

Everything is exaggerated in the emergency department. Doctors are harried, they have little time to go over complicated information and they do not know the patients. Most patients are anxious, upset and not likely to be thinking clearly.

“These factors do not make for the best environment for someone to absorb information,” Dr. Engel said.

The problem is particularly acute when it comes to drugs. A patient-education program used in 130 health delivery systems across the country found that about 40 percent of patients 65 or older have a medication error after they leave the hospital. A 2006 report by the Institute of Medicine found that doctors and nurses were contributing to these errors by not providing information in an effective way.

“The physician’s ability to predict whether a patient understands isn’t as good as can be,” said Dr. Rade B. Vukmir, an emergency physician at the University of Pittsburgh and spokesman for the American College of Emergency Physicians.

In the past, patients who did not follow discharge instructions were often labeled noncompliant. “Now, it’s being called health illiteracy,” Dr. Coleman said, adding that as many as half of all patients are considered to lack the ability to process and understand basic health information that they need to make decisions.

But the patient is only part of the equation, he continued; doctors are notoriously inept at communicating to patients.

The new study found that people were not aware of what they did not understand, suggesting that simply asking a patient if he understands is not enough.

“We’re good at saying, ‘Here’s the information, any questions?’ ” Dr. Coleman said, “and the person nods his head, but they don’t get it.”

Older patients are particularly vulnerable. “They have the kinds of communication barriers we might expect, with vision and hearing problems,” said Dr. Susan N. Hastings, an instructor in geriatrics at Duke. The hectic environment of the emergency department can be particularly stressful for them.

Until recently, poor communication was largely ignored by hospitals. “Just a few years ago, there were subtle incentives for hospitals to not get involved in this area, because of financial gains when people come back,” Dr. Coleman said.

But hospitals are now being forced to face their communication inadequacies. “We’ve raised the bar of what’s expected of hospitals,” said Dr. Schyve, of the Joint Commission. At the same time, the Medicare Payment Advisory Commission, a government agency that advises Congress on Medicare issues, has recommended a policy change that would reduce payments to hospital with excessive readmission rates. It has also asked Medicare to allow hospitals to reward physicians who help lower readmission rates.

Experts in doctor-patient communication recommend a “teach back” approach, in which the patient, preferably accompanied by a relative, friend or caregiver, has to repeat the instructions back to the doctor.

“No matter what you put in writing, what diagrams you have, you really can’t be confident that patients understand what they should be doing unless you have them repeat it back to you,” Dr. Schyve said.

Dr. Vukmir, of the emergency physicians’ group, recommends a “dual discharge” approach: the physician talks to the patient about the results, treatment plan and follow-up care. Then a nurse follows up with computerized discharge instructions.

But Dr. Coleman believes this is not enough. “A third of people over 55 have impaired executive cognitive function,” he said, adding that such patients might understand their medications and know when to take them, but fail to follow through.

He recommends that hospitals coach patients on self-management skills before discharge. Patients need to ask questions, he said. Hospitals should make follow-up calls and visits to patients, a costly endeavor but potentially less expensive than getting reduced Medicare payments if readmission rates are high.

“Hospitals need to have some accountability for the no-care zone, the period between when you leave the emergency department or hospital and when you get into your primary care setting,” Dr. Coleman said. “They should be available for 72 hours.”

'Friendly' bacteria protect against type 1 diabetes, Yale researchers find

In a dramatic illustration of the potential for microbes to prevent disease, researchers at Yale University and the University of Chicago showed that mice exposed to common stomach bacteria were protected against the development of Type I diabetes.

The findings, reported in the journal *Nature*, support the so-called "hygiene hypothesis" – the theory that a lack of exposure to parasites, bacteria and viruses in the developed world may lead to increased risk of diseases like allergies, asthma, and other disorders of the immune system. The results also suggest that exposure to some forms of bacteria might actually help prevent onset of Type I diabetes, an autoimmune disease in which the patient's immune system launches an attack on cells in the pancreas that produce insulin.

The root causes of autoimmune disease have been the subject of intensive investigation by scientists around the world.

In the past decade, it has become evident that the environment plays a role in the development of some overly robust immune system responses. For instance, people in less-developed parts of the world have a low rate of allergy, but when they move to developed countries the rate increases dramatically. Scientists have also noted the same phenomenon in their labs. Non-obese diabetic (NOD) mice develop the disease at different rates after natural breeding, depending upon the environment where they are kept. Previous research has shown that NOD mice exposed to killed (i.e., non-active) strains of tuberculosis or other disease-causing bacteria are protected against the development of Type I diabetes. This suggests that the rapid "innate" immune response that normally protects us from infections can influence the onset of Type 1 diabetes.

In the *Nature* paper, teams led by Li Wen at Yale and Alexander V. Chervonsky at the University of Chicago showed that NOD mice deficient in innate immunity were protected from diabetes in normal conditions. However, if they were raised in a germ-free environment, lacking "friendly" gut bacteria, the mice developed severe diabetes. NOD mice exposed to harmless bacteria normally found in the human intestine were significantly less likely to develop diabetes, they reported.

"Understanding how gut bacteria work on the immune system to influence whether diabetes and other autoimmune diseases occurs is very important," Li said. "This understanding may allow us to design ways to target the immune system through altering the balance of friendly gut bacteria and protect against diabetes." *Changyun Hu from Yale also contributed to their research. Other institutions involved in the study were Washington University; The Jackson Laboratory, Bar Harbor, Me.; Bristol University, United Kingdom; and the University of California-San Francisco.*