

## **Many African-Americans have a gene that prolongs life after heart failure**

About 40 percent of African-Americans have a genetic variant that can protect them after heart failure and prolong their lives, according to research conducted at Washington University School of Medicine in St. Louis and collaborating institutions.

The genetic variant has an effect that resembles that of beta blockers, drugs widely prescribed for heart failure. The new study offers a reason why beta blockers don't appear to benefit some African-Americans.

"For several years a controversy has existed in the cardiovascular field because of conflicting reports about whether beta blockers helped African-American patients," says senior author Gerald W. Dorn II, M.D., professor of medicine, associate chairman for translational research and director of the Center for Pharmacogenomics at Washington University.

"By mimicking the effect of beta blockers, the genetic variant makes it appear as if beta blockers aren't effective in these patients," he explains. "But although beta blockers have no additional benefit in heart failure patients with the variant, they are equally effective in Caucasian and African-American patients without the variant."

Co-author Stephen B. Liggett, M.D., professor of medicine and physiology at the University of Maryland School of Medicine and director of its cardiopulmonary genomics program says the discovery adds to the accumulating evidence that genetic differences contribute to the way people respond to medications and should encourage the use of genetic testing in clinical trials to identify people who can benefit from therapy tailored to their genetic makeup.

About 5 million people in the United States have heart failure, and it results in about 300,000 deaths each year. Beta blockers slow heart rate and lower blood pressure to decrease the heart's workload and prevent lethal cardiac arrhythmias.

While Caucasians with heart failure participating in clinical studies of beta blockers have shown clear benefit from the drugs, the evidence for benefit in African-Americans has been ambiguous. The current study, reported online April 20, 2008, in *Nature Medicine*, identified one particular race-specific gene variant that seems to account mechanistically and biologically for these indeterminate results.

The gene codes for an enzyme called GRK5, which depresses the response to adrenaline and similar hormonal substances that increase how hard the heart works. Adrenaline is a hormone released from the adrenal glands that prompts the "fight-or-flight" response — it increases cardiac output to give a sudden burst of energy.

In heart failure, decreased blood flow from the struggling heart ramps up the body's secretion of adrenaline to compensate for a lower blood flow. Overproduction of the hormone makes the weakened heart pump harder, but eventually worsens heart failure.

Beta blockers alleviate this problem by blocking adrenaline at its receptor in the heart and blood vessels. GRK enzymes mimic this effect by serving as "speed governors" that work like the governor in an engine to prevent adrenaline from over-revving the heart, says Dorn.

The researchers — including three equally contributing co-authors: Liggett, Sharon Cresci, M.D., assistant professor of medicine in the Cardiovascular Division at Washington University and a cardiologist at Barnes-Jewish Hospital, and Reagan J. Kelly, Ph.D., at the University of Michigan — found that 41 percent of African-Americans have a variant GRK5 gene that more effectively suppresses the action of adrenaline than the more common version of the gene. People with the variant gene could be said to have a natural beta blocker, Dorn says. The variant is extremely rare in Caucasians, accounting for its predominant effects in African-Americans.

The researchers showed that African-American heart failure patients with this genetic variant have about the same survival rate even if they don't take beta blockers as Caucasian and African-American heart failure patients who do take beta blockers.

"That doesn't mean African-Americans with heart failure need to be tested for the genetic variant to decide whether to take beta blockers," Dorn says. "Under the supervision of a cardiologist, beta blockers have very low risk but huge benefits, and I am comfortable prescribing them to any heart failure patients who do not have a specific contraindication to the drug."

"This is a step toward individualized therapy," Cresci says. "Medical research is working to identify many genetic variants that someday can ensure that patients receive the medications that are most appropriate for them. Right now, we know one variant that influences beta blocker efficacy, and we are continuing our research into this and other relevant genetic variants."

The human heart has two forms of GRK: GRK2 and GRK5. The researchers meticulously searched the DNA sequence of these genes in 96 people of European-American, African-American or Chinese descent to look for differences. They found most people, no matter their race, had exactly the same DNA sequence in GRK2 or GRK5. But there was one common variation in the DNA sequence, a variation called GRK5-Leu41, the variant that more than 40 percent of African-Americans have.

To determine the effect of the GRK5-Leu41 variant, the team studied the course of progression of heart failure in 375 African-American patients. They looked for survival time or time to heart transplant, comparing people with the variant to those without. Some of these patients were taking beta blockers and some were not.

In patients who did not take beta blockers, the researchers found that those with the variant lived almost twice as long as those with the more common version of the GRK5 gene. Beta blockers prolonged life to the same degree as the protective GRK5 variant, but did not further increase the already improved survival of those with the variant.

"These results offer an explanation for the confusion that has occurred in this area since clinical trials of beta blockers began," Dorn says. "Our study demonstrates a mechanism that should lay to rest the question about whether beta blockers are effective in African-Americans — they absolutely are in those who don't have this genetic variant."

*Other institutions collaborating in the study are the University of Cincinnati, Thomas Jefferson University and the University of Missouri, Kansas City.*

*Liggett SB, Cresci S, Kelly RJ, Syed FM, Matkovich SJ, Hahn HS, Diwan A, Martini JS, Sparks L, Parekh RR, Spertus JA, Koch WJ, Kardia SLR, Dorn II GW. A GRK5 polymorphism that inhibits beta-adrenergic receptor signaling is protective in heart failure. Nature Medicine April 20, 2008 (advance online publishing).*

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### **Most lethal melanomas are on scalp and neck**

CHAPEL HILL – People with scalp or neck melanomas die at nearly twice the rate of people with melanoma elsewhere on the body, including the face or ears, researchers at the University of North Carolina at Chapel Hill have found.

The analysis of 51,704 melanoma cases in the U.S. confirms that survival rates differ depending on where skin cancer first appears. Those with scalp or neck melanomas die at a rate 1.84 times higher than those with melanomas on the extremities, after controlling for the possible influences of age, gender, tumor thickness and ulceration.

"Scalp and neck melanomas patients have a higher rate of death than patients with melanoma anywhere else on the body," said Nancy Thomas, M.D., Ph.D., associate professor of dermatology in the UNC School of Medicine, a member of the UNC Lineberger Comprehensive Cancer Center and the study's senior author. Anne Lachiewicz, a medical student in the UNC School of Medicine, is the lead author of the study.

Thomas recommends that physicians pay special attention to the scalp when examining patients for signs of skin cancer. "Only six percent of melanoma patients present with the disease on the scalp or neck, but those patients account for 10 percent of melanoma deaths. That's why we need to take extra time to look at the scalp during full-skin examinations," she said.

The results appear in the April issue of the journal Archives of Dermatology.

The study helps address a controversy among cancer researchers: whether scalp and neck skin cancer is more lethal primarily because it's diagnosed later than other melanomas. "That was the thinking of a lot of people in the field," Thomas said. But the analysis indicates that the presence of the melanoma on the scalp or neck, in itself, is an indicator of a poorer prognosis.

"We think there's something different about scalp and neck melanomas," Thomas said. "This gives us directions for research to look at tumor cell types in those areas at the molecular level and to see if there are differences. I'm interested in identifying the mutations that drive malignancy."

Thomas, Lachiewicz and their colleagues analyzed data from 13 National Cancer Institute Surveillance Epidemiology and End Results (SEER) Program registries in nine states. Each case represented the first invasive melanoma diagnosed among non-Hispanic white adults between 1992 and 2003.

Patients with scalp or neck melanomas were older (59 years) than patients with other melanomas (55 years), and more likely to be male (74 percent versus 54 percent, respectively). In addition, scalp and neck melanomas were thicker (0.8 millimeters) than melanomas at other sites (0.6 millimeters) and more likely to be ulcerated. Lymph node involvement was also more common in patients with scalp-neck melanomas.

Melanomas on the extremities or on the face or ears had the best prognosis. The five-year melanoma-specific survival rate for patients with scalp or neck melanomas was 83 percent, compared with 92 percent for patients with melanomas at other sites. The ten-year survival rate was 76 percent for scalp or neck melanomas and 89 percent for other melanomas.

*Study co-authors are Drs. Marianne Berwick and Charles Wiggins of the University of New Mexico.*

*Funding was provided by the National Cancer Institute and a Holderness Medical Foundation Fellowship to Lachiewicz.*

## **Life expectancy worsening or stagnating for large segment of the US population Diseases related to smoking, high blood pressure and obesity contributing to worsening health, particularly for women**

Boston, MA -- One of the major aims of the U.S. health system is improving the health of all people, particularly those segments of the population at greater risk of health disparities. In fact, overall life expectancy in the U.S. increased more than seven years for men and more than six years for women between 1960 and 2000.

Now, a new, long-term study of mortality trends in U.S. counties over the same four decades reports a troubling finding: These gains are not reaching many parts of the country; rather, the life expectancy of a significant segment of the population is declining or at best stagnating.

Researchers at the Harvard School of Public Health (HSPH) and the University of Washington found that 4% of the male population and 19% of the female population experienced either decline or stagnation in mortality beginning in the 1980s.

"There has always been a view in U.S. health policy that inequalities are more tolerable as long as everyone's health is improving. There is now evidence that there are large parts of the population in the United States whose health has been getting worse for about two decades," said Majid Ezzati, Associate Professor of International Health at HSPH and lead author of the study.

The majority of the counties that had the worst downward swings in life expectancy were in the Deep South, along the Mississippi River, and in Appalachia, extending into the southern portion of the Midwest and into Texas.

The researchers analyzed mortality data from the National Center for Health Statistics and population data from the U.S. Census Bureau between 1959 and 2001. The study is the first to look at mortality trends in the U.S. by county over such a long period of time. (County data is the smallest measurable unit for which mortality data is available.) The National Center for Health Statistics stopped providing data after 2001.

The results showed that, between 1961 and 1999, average life expectancy in the U.S. increased from 66.9 to 74.1 years for men and from 73.5 to 79.6 for women. Looking at individual counties, however, the researchers found that beginning in the 1980s, the best-off counties continued to improve but there was a stagnation or worsening of life expectancy in the worst-off counties--what the researchers refer to as "the reversal of fortunes." As a result, while men in the best-off counties lived 9.0 years longer than those in the worst-off counties in 1983, by 1999 that gap had increased to 11.0 years; for women the 1983 life expectancy gap of 6.7 years increased to 7.5 years by 1999. Over the past few decades, life expectancy in high-income countries around the world has gradually risen, with few exceptions.

Given the consistent trend of declining mortality rates in high-income countries, the results of this study, which show large segments of the American population experiencing stagnating or worsening health conditions, are particularly troubling. Ezzati said, "The finding that 4% of the male population and 19% of the female population experienced either decline or stagnation in mortality is a major public health concern." Christopher Murray, Director of the Institute for Health Metrics and Evaluation at the University of Washington and co-author of the study, added that "life expectancy decline is something that has traditionally been considered a sign that the health and social systems have failed, as has been the case in parts of Africa and Eastern Europe. The fact that is happening to a large number of Americans should be a sign that the U.S. health system needs serious rethinking."

The researchers also analyzed data on deaths from different diseases and showed that the stagnation and worsening mortality was primarily a result of an increase in diabetes, cancers and chronic obstructive pulmonary disease, combined with a slowdown or halt in improvements in cardiovascular mortality. An increase in HIV/AIDS and homicides also played a role for men, but not for women.

The diseases that are responsible for this troubling trend seem to be most related to smoking, high blood pressure, and obesity. "Smoking and blood pressure have a long history of being controlled through both personal and population strategies. There is good evidence on relatively low-cost and effective ways of dealing with these issues if one of the health system's imperatives becomes to close this widening life expectancy gap," said Ezzati.

*The study appears in the April 22, 2008, edition of the open-access journal PLoS Medicine. Journalists can preview the paper here: <http://www.plos.org/press/plme-05-04-ezzati.pdf>*

## **US sees decline in number of general surgeons**

The number of general surgeons per 100,000 Americans has declined by more than 25 percent during the past 25 years, according to a report in the April issue of Archives of Surgery, one of the JAMA/Archives journals.

"General surgeons play a pivotal role in the health care systems of the United States," according to background information in the article. Rural general surgeons provide surgical backup to primary care physicians and help keep small rural hospitals financially viable, while urban general surgeons provide

important surgical services, including emergency and trauma care that some surgical subspecialists may not offer. "There is some question as to whether there will be an adequate number of general surgeons to care for an increasingly elderly population, with its attendant increased demand for surgical care."

Dana Christian Lynge, M.D., and colleagues at the University of Washington, Seattle, analyzed the number of general surgeons per 100,000 population using the American Medical Association's Physician Masterfiles from 1981, 1991, 2001 and 2005. Surgeon's age, sex and locale were also noted.

The number of active general surgeons fluctuated from 17,394 in 1981 to 17,922 in 2001 to 16,662 in 2005. The ratio of general surgeons to the population declined from 7.68 surgeons per 100,000 people in 1981 to 5.69 surgeons per 100,000 people in 2005. With the U.S. population increasing from 226 million to 292 million, the national general surgeon to population ratio declined by 25.91 percent during those 25 years, with a greater decrease in urban areas (27.24 percent) and a 21.07 percent decline in rural areas.

The number of women general surgeons increased substantially from 1981 to 2005, but they were disproportionately concentrated in urban areas. The average age of rural surgeons increased compared with surgeons practicing in urban areas.

Although other medical practitioners and health care clinicians can help the U.S. medical system adjust to the decline in general surgeons, they cannot completely fill the role of general surgeons, the authors note. Ways to address this decline should be considered by surgeons, their professional organizations and organizations that control the number of general surgeons trained annually. "These might include increased funding of residency positions, and exploring and addressing the issues surrounding training, remuneration and lifestyle that seem to have made general surgery less attractive than other specialties to medical students, especially women," the authors conclude. Medical schools and surgical residencies should also "ensure that general surgical residents are sufficiently exposed to rural surgical practice through rural training tracks and rural-based residencies."

"A growing and aging population, especially in rural areas, will continue to require a workforce of well-trained general surgeons who can provide a wide spectrum of surgical services."

*(Arch Surg. 2008;143[4]:345-350. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)*

### **Chemotherapy causes delayed severe neural damage**

Cancer treatment with chemotherapeutic agents is often associated with delayed adverse neurological consequences - an occurrence often referred to as "chemobrain" - that may compromise the quality of life of a proportion of cancer survivors. Now, research published in the open access Journal of Biology demonstrates that treatment with a single chemotherapeutic agent, 5-fluorouracil (5-FU), by itself is sufficient to cause a syndrome of delayed degeneration in the central nervous system (CNS). 5-FU is a widely used chemotherapeutic agent that is employed, alone or in combination with other agents, in the treatment of cancers of the colon, rectum, breast, stomach, pancreas, ovaries and bladder.

Little is known about the side-effects of chemotherapy on the CNS, despite their obvious clinical importance. Until now researchers have not fully understood the underlying biology, including whether these effects require: exposure to multiple chemotherapeutic agents; chemotherapeutic agents plus the body's own response to cancer; blood-brain barrier damage; or inflammation. Clinicians have also lacked animal models to study this important problem.

Professor Mark Noble and colleagues of the University of Rochester Stem Cell and Regenerative Medicine Institute and the Harvard Medical School, Boston discovered that short-term systemic administration of 5-FU to mice caused both acute CNS damage and a syndrome of progressively worsening delayed damage. This damage was not self-repairing, and instead became worse over time. In addition, Noble and colleagues also demonstrated that treatment with chemotherapy also had delayed effects on the speed with which information is transferred from the ear to the brain.

Myelin sheaths are necessary for normal neuronal function. One key finding of the study was that clinically relevant concentrations of 5-FU were toxic not only for dividing cells of the CNS but also for the cells that produce the insulating myelin sheaths (non-dividing oligodendrocytes). The delayed damage the researchers measured was to the myelinated tracts of the CNS and associated with extensive myelin pathology. The findings regarding the speed of ear-to-brain information transfer may offer a non-invasive means of analyzing myelin damage associated with cancer treatment.

"Multiple clinical reports have identified neurotoxicity as a complication of treatment regimens in which chemotherapeutic agents such as 5-fluorouracil are components," says Noble. "As treatments with chemotherapeutic agents will clearly remain the standard of care for cancer patients for many years to come, the need to better understand such damage is great."

Professor Noble continues "These studies extend the field of stem cell medicine beyond the use of cell transplantation for tissue repair. It is our knowledge of stem cell biology that allows us to begin to understand some of the causes of this syndrome, as well as providing the means of preventing or repairing this damage."



This research provides the first demonstration that delayed CNS damage can be induced by a single chemotherapeutic agent and also generates the first animal model of such damage. These studies further demonstrate that this syndrome differs from that caused by irradiation and thus may represent a new class of delayed CNS degenerative damage.

**Notes to Editors:**

1. *Systemic 5-fluorouracil treatment causes a syndrome of delayed myelin destruction in the CNS.*  
Ruolan Han, Yin M. Yang, Joerg Dietrich, Anne Luebke, Margot Mayer-Pröschel and Mark Noble  
*Journal of Biology (in press)*

During embargo, article available here: <http://jbiol.com/press/noble.pdf>

After the embargo, article available at the journal website: <http://jbiol.com/>

**Vitamin D in brain function**

***Vitamin D supplementation for high risk groups may be warranted***

In a definitive critical review, scientists at Children's Hospital & Research Center Oakland ask whether there is convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction. Joyce C. McCann, Ph.D., assistant staff scientist and Bruce N. Ames, Ph.D., senior scientist at Children's Hospital Oakland Research Institute (CHORI) conclude that there is ample biological evidence to suggest an important role for vitamin D in brain development and function, and that supplementation for groups chronically low in vitamin D is warranted. Their conclusions will be published on April 22, 2008 in the Federation of American Societies for Experimental Biology (FASEB) Journal.

"This critical analysis of vitamin D function and the brain is a model of careful thinking about nutrition and behavior", says Gerald Weissmann, MD, Editor-in-Chief of the FASEB Journal "One wishes that all studies of nutritional supplements or requirements were this thoughtful. Drs. McCann and Ames deftly show that while vitamin D has an important role in the development and function of the brain, its exact effects on behavior remain unclear. Pointing to the need for further study, the authors argue for vitamin D supplementation in groups at risk."

Vitamin D has long been known to promote healthy bones by regulating calcium levels in the body. Lack of sufficient vitamin D in very young children results in rickets, which can be easily prevented by vitamin D supplements. Only recently the scientific community has become aware of a much broader role for vitamin D. For example, we now know that, in addition to its role in maintaining bone health, vitamin D is involved in differentiation of tissues during development and in proper functioning of the immune system. In fact, over 900 different genes are now known to be able to bind the vitamin D receptor, through which vitamin D mediates its effects. In addition to protecting against rickets, evidence now strongly indicates that a plentiful supply of vitamin D helps to protect against bone fractures in the elderly. Evidence also continues to accumulate suggesting a beneficial role for vitamin D in protecting against autoimmune diseases, including multiple sclerosis and type I diabetes, as well as some forms of cancer, particularly colorectal and breast.

Vitamin D is present in only a few foods (e.g., fatty fish), and is also added to fortified milk, but our supply typically comes mostly from exposure to ultraviolet rays (UV) in sunlight. UV from the sun converts a biochemical in the skin to vitamin D, which is then metabolized to calcitriol, its active form and an important hormone. Formation of vitamin D by UV can be 6 times more efficient in light skin than dark skin, which is an important cause of the known widespread vitamin D deficiency among African Americans living in northern latitudes. Dark skin has been selected during evolution because it protects against the burning UV rays of the sun in the tropics. White skin has been selected for allowing as much UV exposure to make sufficient vitamin D in Northern (high) latitudes. Thus, fair-skinned northerners are at risk in Australia or Arizona for sunburns and UV-induced cancer, while dark-skinned people in the Northern U.S. or European latitudes with little exposure to the sun are at risk for rickets, bone fractures and possibly other diseases including several types of cancer due to a lack of vitamin D. Fortunately sun-screens and vitamin D supplements are inexpensive.

McCann & Ames point out that evidence for vitamin D's involvement in brain function includes the wide distribution of vitamin D receptors throughout the brain. They also discuss vitamin D's ability to affect proteins in the brain known to be directly involved in learning and memory, motor control, and possibly even maternal and social behavior. The review also discusses studies in both humans and animals that present suggestive though not definitive evidence of cognitive or behavioral consequences of vitamin D inadequacy. The authors discuss possible reasons for the apparent discrepancy between the biological and behavioral evidence, and suggest new, possibly clarifying avenues of research.

Many vitamin D experts advise that the currently recommended level of vitamin D intake is much too low and should be raised to protect against bone fractures and possibly cancer in addition to rickets (2). Indeed, even using present guidelines, too many Americans have low vitamin D blood levels. McCann & Ames propose that, despite uncertainty regarding all of the deleterious effects of vitamin D inadequacy, the evidence overall

indicates that supplementation, which is both inexpensive and prudent, is warranted for groups whose vitamin D status is exceptionally low, particularly nursing infants, the elderly, and African Americans (e.g., see (3)).

This review is the fourth in a series by McCann & Ames that critically evaluate scientific evidence linking deficiencies in micronutrients (the approximately 40 vitamins, minerals, amino acids, and fatty acids required for the body to function) to brain function. Other reviews in the series discuss the long-chain polyunsaturated fatty acid docosahexaenoic acid (DHA) (4, 5), choline (6), and iron (7).

1. McCann, JC, Ames BN (2008) Review Article: Is there convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction" *FASEB J.* 22: 982-1001.
2. Vieth R, Bischoff-Ferrari H, Boucher BJ, et al. The urgent need to recommend an intake of vitamin D that is effective. *Am J Clin Nutr* 2007;85:649-50.
3. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr* 2007;137:447-52.
4. McCann JC, Ames BN. Is docosahexaenoic acid, an n-3 long chain polyunsaturated fatty acid, required for the development of normal brain function" An overview of evidence from cognitive and behavioral tests in humans and animals. *Am J Clin Nutr* 2005;82:281-95.
5. McCann JC, Ames BN. DHA and cognitive development: an update on the science. *Pediatric Basics* 2007;April.
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7. McCann JC, Ames BN. An overview of evidence for a causal relationship between iron deficiency during development and cognitive or behavioral function in children. *Am J Clin Nutr* 2007;85:931-45.

### **Computer scientists develop solutions for long-term storage of digital data**

SANTA CRUZ, CA--Although the digital age is well under way, one crucial detail remains to be worked out--how to store vast amounts of digital information in a way that allows future generations to recover it.

"The problem is how to build a large-scale data storage system to last 50 to 100 years," said Ethan Miller, associate professor of computer science in the Baskin School of Engineering at the University of California, Santa Cruz.

Tape libraries are widely used for data storage, but digital tape has many shortcomings as an archival medium. Miller's group has come up with a new approach, called Pergamum, which uses hard disk drives to provide energy-efficient, cost-effective storage. The declining cost of hard drives has made them more competitive with tape, and they offer numerous advantages for searching and retrieving data. "It's like the difference between a VCR and TiVo," Miller said.

Pergamum, named after the ancient Greek library that made the transition from fragile papyrus to more durable parchment, is a distributed network of intelligent, disk-based storage devices. The team that developed it includes UCSC graduate students Mark Storer and Kevin Greenan, along with researcher Kaladhar Voruganti of NetApp (formerly Network Appliance), a company that focuses on storage and data management solutions.

Archival storage is a big issue for businesses, partly due to legal requirements for the preservation of financial and business records, and also because data mining strategies can turn stored data into a valuable resource. Long-term storage is also a growing issue for individuals who are filling their personal computers with digital photos, movies, and documents.

"There is a risk that an entire generation's cultural history could be lost if people aren't able to retrieve that data," Storer said. "Everyone is switching to digital cameras, but we've never demonstrated that digital data can be reliably preserved for a long time."

Pergamum has attracted a lot of attention from industry since Storer presented it at a leading conference in the field, the USENIX Conference on File and Storage Technologies (FAST '08), held in San Jose in February. Robin Harris, an industry consultant who writes an influential blog called StorageMojo, called the Pergamum paper his "favorite FAST '08 paper" (see <http://storagemojo.com/2008/03/14/storagemojos-favorite-fast-08-paper/>).

The researchers designed the system to provide reliable, energy-efficient data storage using off-the-shelf components. It also has the ability to evolve over time as storage technologies change. "You want to avoid 'forklift upgrades,' where you have to get rid of the old system and transfer all your data to a whole new system," Miller said.

According to Storer, businesses are beginning to recognize that archival storage is very different from simply backing up their data. "A backup is a safety net--you hope you won't need it. Archival data you do want to use--it's a valuable resource and you want to be able to mine it for information," he said.

Tapes work well for backups, in which data are written once, rarely read, and not kept indefinitely. But archival data should be easy to read, query, browse, and search, and tape has inherent weaknesses in these areas. Existing disk-based systems offer excellent performance, but rely on power-hungry central controllers.

"Energy usage is a big issue, so a lot of our effort in designing Pergamum focused on dramatically reducing power use," Miller said.

Pergamum uses individual building blocks consisting of a hard drive; a small, low-power processor (like the chip in an iPhone); a flash memory card; and an ethernet port. These units, called "tomes," are connected using relatively inexpensive ethernet switches.

"Each tome is like a minicomputer, but with very low power demands," Miller said. "When not in use, it can shut down almost completely."

Even when active, the devices use very little power (less than 13 watts), which can be delivered over the network using Power over Ethernet technology. As a result, each unit is essentially a self-contained box with a network connection. The flash memory provides low-power, persistent storage so that many operations can be performed without activating the hard drive.

For reliability, Pergamum uses two levels of redundancy--within and between disks--to protect from both disk failures and errors in writing data to a disk (so-called "latent sector errors"). Tomes can be easily added to expand the system or to replace failed disks. And if hard disk drives become obsolete in 10 years, Pergamum won't suffer the same fate. The system doesn't care what the actual storage medium is, as long as the device can implement the simple protocol that will allow it to function as part of the network.

"In 50 years, the devices might use holographic storage," Storer said. "As long as you can wrap the new storage medium in this intelligent layer that speaks the protocol, it can participate in the network."

Pergamum is one of several related projects being developed by researchers in the Storage Systems Research Center (SSRC) at UCSC's Baskin School of Engineering. The center's other archival storage projects include Deep Store, which dramatically reduces the amount of space required to store data, and POTSHARDS, which provides long-term secure storage using "secret splitting" instead of traditional encryption. Both of these projects would be compatible with Pergamum, Miller said.

### **Brain reacts to fairness as it does to money and chocolate**

The human brain responds to being treated fairly the same way it responds to winning money and eating chocolate, UCLA scientists report. Being treated fairly turns on the brain's reward circuitry.

"We may be hard-wired to treat fairness as a reward," said study co-author Matthew D. Lieberman, UCLA associate professor of psychology and a founder of social cognitive neuroscience.

"Receiving a fair offer activates the same brain circuitry as when we eat craved food, win money or see a beautiful face," said Golnaz Tabibnia, a postdoctoral scholar at the Semel Institute for Neuroscience and Human Behavior at UCLA and lead author of the study, which appears in the April issue of the journal *Psychological Science*.

The activated brain regions include the ventral striatum and ventromedial prefrontal cortex. Humans share the ventral striatum with rats, mice and monkeys, Tabibnia said.

"Fairness is activating the same part of the brain that responds to food in rats," she said. This is consistent with the notion that being treated fairly satisfies a basic need, she added.

In the study, subjects were asked whether they would accept or decline another person's offer to divide money in a particular way. If they declined, neither they nor the person making the offer would receive anything. Some of the offers were fair, such as receiving \$5 out of \$10 or \$12, while others were unfair, such as receiving \$5 out of \$23.

"In both cases, they were being offered the same amount of money, but in one case it's fair and in the other case it's not," Tabibnia said.

Almost half the time, people agreed to accept offers of just 20 to 30 percent of the total money, but when they accepted these unfair offers, most of the brain's reward circuitry was not activated; those brain regions were activated only for the fair offers. Less than 2 percent accepted offers of 10 percent of the total money.

The study group consisted of 12 UCLA students, nine of them female, with an average age of 21. They had their brains scanned at UCLA's Ahmanson-Lovelace Brain Mapping Center. The subjects saw photographs of various people who were said to be making the offers.

"The brain's reward regions were more active when people were given a \$5 offer out of \$10 than when they received a \$5 offer out of \$23," Lieberman said. "We call this finding the 'sunny side of fairness' because it shows the rewarding experience of being treated fairly."

A region of the brain called the insula, associated with disgust, is more active when people are given insulting offers, Lieberman said.

When people accepted the insulting offers, they tended to turn on a region of the prefrontal cortex that is associated with emotion regulation, while the insula was less active.

"We're showing what happens in the brain when people swallow their pride," Tabibnia said. "The region of the brain most associated with self-control gets activated and the disgust-related region shows less of a response."

"If we can regulate our sense of insult, we can say yes to the insulting offer and accept the cash," Lieberman said. UCLA is California's largest university, with an enrollment of nearly 37,000 undergraduate and graduate students. The UCLA College of Letters and Science and the university's 11 professional schools feature renowned faculty and offer more than 300 degree programs and majors. UCLA is a national and international leader in the breadth and quality of its academic, research, health care, cultural, continuing education and athletic programs. Four alumni and five faculty have been awarded the Nobel Prize.

### **Complete 'cookbook' for running a genome published**

\* 14:00 21 April 2008

\* NewScientist.com news service

\* **Jason Palmer**

Get ready to start hearing "epigenomics" as often as you hear about genomics.

If the genome is like a list of genetic ingredients, then the rules for how those genes are used and when they are switched on and off is the business of epigenetics. The first full piece of this "cookbook" has now been sequenced – a plant's epigenome.

Life often modifies its genetic material without changing the letters of the genetic code. One of the main ways this is done is through the addition of a chemical unit called a methyl group to a gene.

This methylation effectively gums up a gene's copying machinery. It is thought to be an important factor in directing stem cells to develop into different tissues, and problems with methylation are implicated in a number of diseases including cancer and Huntington's.

Joseph Ecker of the Salk Institute in La Jolla, California and colleagues have used a new method to sequence the complete "methylome" of the cress *Arabidopsis* for every letter of its genetic code, giving a far more detailed recipe than prior efforts.

#### **Epic genetics**

The work is also an improvement on a technique demonstrated in March by Steven Jacobsen of the University of California, Los Angeles. By removing some of the steps that the method requires, Ecker's team have greatly speeded up the process of sequencing epigenetic data.

The method produces lots of data – the *Arabidopsis* genome comprises some 120 million DNA bases – so the team has developed open-source software to "browse" the genome and find where methylation is controlling gene expression. The program will be able to track more epigenetic data as it is produced, forming a global resource for collecting and analysing it.

"Capturing this kind of sequence-level information for entire genomes of individual plants or humans is now possible and will soon become routine," Ecker says. "In fact, we have already begun using these methods for sequencing of the human methylome."

Ecker says that the team will look into how methylation affects the development of human stem cells as they change into other types of cells.

Eric Selker, a molecular biologist at the University of Oregon, calls the work a tour de force. He says that the steep drop in the costs and of sequencing in recent years means that the floodgates are open for epigenomics.

"It's amazing what can be done in a small amount of time with this new technique," he says.

*Journal references: Cell, DOI: 10.1016/j.cell.2008.03.029; Science, DOI: 10.1126/science.1153069; Nature, DOI: 10.1038/nature06745*

### **Stephen Hawking calls for Moon and Mars colonies**

\* 23:56 21 April 2008

\* NewScientist.com news service

\* **David Shiga**

Stephen Hawking called for a massive investment in establishing colonies on the Moon and Mars in a lecture in honour of NASA's 50th anniversary. He argued that the world should devote about 10 times as much as NASA's current budget – or 0.25% of the world's financial resources – to space.

The renowned University of Cambridge physicist has previously spoken in favour of colonising space as an insurance policy against the possibility of humanity being wiped out by catastrophes like nuclear war and climate change. He argues that humanity should eventually expand to other solar systems.

***Hawking spoke at George Washington University in Washington, DC, US, in honour of NASA's 50th anniversary (Image: NASA)***





But in a speech in Washington, DC, US, delivered in honour of NASA's 50th anniversary in 2008, Hawking focused on near-term possibilities, backing the space agency's goals of returning astronauts to the Moon by 2020 and sending humans to Mars soon after that.

The Moon is a good place to start because it is "close by and relatively easy to reach", Hawking said. "The Moon could be a base for travel to the rest of the solar system," he added. Mars would be "the obvious next target", with its abundant supplies of frozen water, and the tantalising possibility that life may have been present there in the past.

Some space experts have recently called for NASA to send astronauts to a near-Earth asteroid instead of the Moon as a next step.

Hawking did not mention the idea, but said that any long-term site for a human base should have a significant gravity field. That's because long missions in microgravity lead to health issues such as bone loss.

### **Boldly go**

He also called for an acceleration of NASA's plans for human landings on Mars, which one NASA study suggested could be done in the early 2030s. "A goal of a base on the Moon by 2020 and of a manned landing on Mars by 2025 would reignite the space programme and give it a sense of purpose in the same way that President Kennedy's Moon target did in the 1960s," he said.

Hawking made a pitch for human space exploration, rather than just sending robots to explore space, a position taken by Nobel laureate Steven Weinberg, among others.

"Robotic missions are much cheaper and may provide more scientific information, but they don't catch the public imagination in the same way, and they don't spread the human race into space, which I'm arguing should be our long-term strategy," Hawking said. "If the human race is to continue for another million years, we will have to boldly go where no one has gone before."



***In 2007, Hawking experienced zero gravity aboard a modified Boeing 727 aircraft (Image: NASA/Jim Campbell/Aero-News Network)***

### **Interstellar travel**

Eventually, Hawking said, humanity should try to expand to Earth-like planets around other stars.

No such planets are known so far. But even if only 1% of the 1000 or so stars within 30 light years of Earth has an Earth-size planet at the right distance from its star for liquid water to exist, that would make for 10 such planets in our solar system's neighbourhood, he said.

"We cannot envision visiting them with current technology, but we should make interstellar travel a long-term aim," he said. "By long term, I mean over the next 200 to 500 years."

Humanity can afford to battle earthly problems like climate change and still have plenty of resources left over for colonising space, he said.

### **Intelligent life**

"Even if we were to increase the international [space exploration] budget 20 times to make a serious effort to go into space, it would only be a small fraction of world GDP," he said. GDP, or Gross Domestic Product, is a measure of a country's economic activity.

Hawking argued that the world can afford 0.25% of its collective GDP to devote to space colonisation. "Isn't our future worth a quarter of a percent?" he asked.

The physicist also speculated on the reasons that SETI (Search for Extra-Terrestrial Intelligence) projects have not yet detected any alien civilisations.

He offered three possibilities: that life of any kind is very rare in the universe; that simple life forms are common, but intelligent life rare; or that intelligent life tends to quickly destroy itself.

"Personally, I favour the second possibility – that primitive life is relatively common, but that intelligent life is very rare," he said. "Some would say it has yet to occur on Earth."

### **Turkish site a Neolithic 'supernova'**

By Nicholas Birch - URFA, Turkey - As a child, Klaus Schmidt used to grub around in caves in his native Germany in the hope of finding prehistoric paintings. Thirty years later, as a member of the German Archaeological Institute, he found something infinitely more important: a temple complex almost twice as old as anything comparable.

"This place is a supernova," said Mr. Schmidt, standing under a lone tree on a windswept hilltop 35 miles north of the Syrian border.

"Within a minute of first seeing it, I knew I had two choices: go away and tell nobody, or spend the rest of my life working here."

Behind him are the first folds of the Anatolian Plateau. Ahead, the Mesopotamian plain, like a dust-colored sea, stretches south hundreds of miles to Baghdad and beyond. The stone circles of Gobekli Tepe, his workplace since 1994, are just in front, hidden under the brow of the hill.

Compared with Stonehenge, they are humble affairs. None of the circles that have been excavated, four out of an estimated 20, is more than 100 feet across. Two of the slender, T-shaped pillars tower at least three feet above their peers.

What makes them remarkable are the carved reliefs of boars, foxes, lions, birds, snakes and scorpions that cover them, and their age. Dated at about 9500 B.C., these stones are 5,500 years older than the first cities of Mesopotamia and 7,000 years older than Stonehenge.

Nevermind wheels or writing, the people who erected them did not even have pottery or domesticated wheat. They lived in villages, but were hunters, not farmers.

"Everybody used to think only complex, hierarchical civilizations could build such monumental sites and that they only came about with the invention of agriculture," said Ian Hodder, a Stanford University anthropology professor who has directed digs at Catalhoyuk, Turkey's most-famous Neolithic site, since 1993.

"Gobekli changes everything. It's elaborate, it's complex, and it is pre-agricultural. That fact alone makes the site one of the most important archaeological finds in a very long time."

With only a fraction of the site opened after a decade of excavation, Gobekli Tepe's significance to the people who built it remains unclear. Some think it was the center of a fertility rite, with the two tall stones at the center of each circle representing a man and woman.

Urfa's tourist board has taken that theory up with alacrity; visit the Garden of Eden, its brochures trumpet, see Adam and Eve.

Mr. Schmidt, however, is skeptical. He agreed the site could well have been "the last flowering of a semi-nomadic world that farming was just about to destroy" and pointed out that if it is in near-perfect condition today, it is because those who built it buried it soon after under tons of soil, as though its wild animal-rich world had lost all meaning.

However, the site is devoid of the fertility symbols that have been found at other Neolithic sites, and the T-shaped columns, while clearly semi-human, are sexless.

"I think here we are face to face with the earliest representation of gods," according to Mr. Schmidt.

"They have no eyes, no mouths, no faces. But they have arms, and they have hands. They are makers."

"In my opinion, the people who carved them were asking themselves the biggest questions of all. What is this universe? Why are we here?"

With no evidence of houses or graves near the stones, Mr. Schmidt thinks the hilltop was a site of pilgrimage for communities within a radius of roughly 100 miles. He notes how the tallest stones all face southeast, as if scanning plains that are scattered with contemporary sites in many ways no less remarkable than Gobekli Tepe.

Last year, for instance, French archaeologists working at Jade al-Mughara in northern Syria uncovered the oldest mural ever found — "two square meters of geometric shapes, in red, black and white — a bit like a Paul Klee painting," according to Eric Coqueugniot, the University of Lyon archaeologist who is leading the excavation.

Mr. Coqueugniot describes Mr. Schmidt's hypothesis that Gobekli Tepe was a meeting point for feasts, rituals and sharing ideas as "tempting," given the site's spectacular position. He warned, though, that surveys of the region are still in their infancy and that "tomorrow, somebody might find somewhere even more dramatic."

Vecihi Ozkaya, the director of a dig at Korpiktepe, on the Tigris River 120 miles east of Urfa, doubts that the thousands of stone pots he has found since 2001, in hundreds of 11,500-year-old graves, qualify as such.

Nevertheless, his excitement fills his austere office at Dicle University in Diyarbakir.

"Look at this," he said, pointing at a photo of an exquisitely carved sculpture showing an animal, half-human and half-lion. "It's a sphinx, thousands of years before Egypt. Southeastern Turkey, northern Syria — this region saw the wedding night of our civilization."

### **Terracotta army has egg on its face**

Monday, 21 April 2008 **Jennifer Viegas** Discovery News

China's terracotta army, a collection of 7000 soldier and horse figures in the mausoleum of the country's first emperor, was covered with beaten egg when it was made, scientists say.

According to German and Italian chemists who have analysed samples from several figurines, the egg was as a binder for colourful paints, which went over a layer of lacquer.

"Egg paint is normally very stable, and not soluble in water ... This makes it less sensitive to humidity and moisture," says German co-author Catharina Blaensdorf, a scientist at the Technical University of Munich.

Egg proteins would have also ensured the adhesion of the paint to the lacquer, while also giving the paint thickness and texture, says Blaensdorf's Italian colleague Ilaria Bonaduce, of the University of Pisa.

For the study, which is published in the latest issue of the *Journal of Cultural Heritage*, the researchers took samples from warrior figurine faces, kneeling archers, swans and paint fragments found on the ground inside the 210 BC mausoleum.

They separated the flakes chemically to isolate the ingredients and then inserted them into a machine to determine their composition.

The researchers thought animal glue might have served as a binder, but all of the data pointed to egg instead.

The pigments, they found, were bone white, lead white, cerussite (which sparkles), quartz, cinnabar, malachite, charcoal black, copper salts, Chinese purple and azurite.

Bright hues were important "because colour was precious and a colourful army was the best, and an emperor could demand the best", says Blaensdorf.

### **Built to last**

The sturdy terracotta and thick, eggy paint add to the conclusion that the army was also built to last.

The mausoleum was even booby-trapped, with rigged crossbows to stop would-be thieves.

Eighty master potters left their signatures on the terracotta figures. These names show some individuals came from the imperial court, while other artists appear to have been respected local craftsmen.

Some official names overlap with those found on sewage pipes and floor tiles found in other locations.

"So it seems there was an office for making pottery [within] the imperial court," says Blaensdorf.

### **Historical significance**

Erika Ribechini, a scientist in the Department of Chemistry and Industrial Chemistry at the University of Pisa, who did not work on the project, says the new findings "are very well presented".

"Even though the terracotta army is very famous," she says, not much is known about it.

"[The egg discovery] is particularly fascinating in terms of its historical significance, because roughly in the same period, in the Roman Empire and in ancient Greece, the artists used to utilise egg as a binder in creating mural and stone paintings."

The research is likely to help art restorers to repair and preserve the terracotta army.

### **Synchrotron light unveils oil in ancient Buddhist paintings from Bamiyan**

The world was in shock when in 2001 the Taliban destroyed two ancient colossal Buddha statues in the Afghan region of Bamiyan. Behind those statues, there are caves decorated with precious paintings from 5th to 9th century A.D. The caves also suffered from Taliban destruction, as well as from a severe natural environment, but today they have become the source of a major discovery. Scientists have proved, thanks to experiments performed at the European Synchrotron Radiation Facility (ESRF), that the paintings were made of oil, hundreds of years before the technique was "invented" in Europe. Results are published today in the peer-reviewed *Journal of Analytical Atomic Spectrometry*.

In many European history and art books, oil painting is said to have started in the 15th century in Europe. But scientists from the National Research Institute for Cultural Properties in Tokyo (Japan), the Centre of Research and Restoration of the French Museums-CNRS (France), the Getty Conservation Institute (United States) and the ESRF have recently identified drying oils in some of the samples they studied from the Bamiyan caves. Painted in the mid-7th century A.D., the murals show scenes with Buddhas in vermilion robes sitting cross-legged amid palm leaves and mythical creatures. The scientists discovered that 12 out of the 50 caves were painted with oil painting technique, using perhaps walnut and poppy seed drying oils.



***A cross-section of the sample, where the different layers are visible. National Research Institute for Cultural Properties, Tokyo (Japan)***

A combination of synchrotron techniques such as infrared micro-spectroscopy, micro X-ray fluorescence, micro X-ray absorption spectroscopy or micro X-ray diffraction was crucial for the outcome of the work. "On one hand, the paintings are arranged as superposition of multiple layers, which can be very thin. The micrometric beam provided by synchrotron sources was hence essential to analyze separately each of these layers. On the other hand, these paintings are made with inorganic pigments mixed in organic binders, so we



needed different techniques to get the full picture" Marine Cotte, a research scientist at CNRS and an ESRF scientific collaborator explains.

The results showed a high diversity of pigments as well as binders and the scientists identified original ingredients and alteration compounds. Apart from oil-based paint layers, some of the layers were made of natural resins, proteins, gums, and, in some cases, a resinous, varnish-like layer. Protein-based material can indicate the use of hide glue or egg. Within the various pigments, the scientists found a high use of lead whites. These lead carbonates were often used, since Antiquity up to modern times, not only in paintings but also in cosmetics as face whiteners.



***A detail of a painting in the cave. National Research Institute for Cultural Properties, Tokyo (Japan)***

"This is the earliest clear example of oil paintings in the world, although drying oils were already used by ancient Romans and Egyptians, but only as medicines and cosmetics", explains Yoko Taniguchi, leader of the team.

The paintings are probably the work of artists who traveled on the Silk Road, the ancient trade route between China, across Central Asia's desert to the West. However, there are very few studies about this region. "Due to political reasons research on paintings in Central Asia is scarce. We were fortunate to get the opportunity from UNESCO, as a part of conservation project for the World Heritage site Bamiyan, to study these samples and we hope that future research may provide deeper understanding of the painting techniques along the Silk Road and the Eurasian area", says Taniguchi.

The results were presented in a scientific conference in Japan last January, but are only published today in a peer-reviewed journal.

**A simplified method of giving rabies vaccine**

A simplified economical method of giving rabies vaccine is just as effective as the expensive standard vaccine regimen at stimulating anti-rabies antibodies.

A clinical trial in healthy volunteers has found that a simpler and cheaper way of using rabies vaccines proved to be just as effective as the current most widely used method at stimulating antibodies against rabies. The trial is published in this week's PLoS Neglected Tropical Diseases.

Dr Mary Warrell (Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, United Kingdom) and colleagues, who conducted the trial with a vaccine in routine use, say that the simplified method has the advantages of requiring fewer clinic visits, being more practicable, and acceptable, and having a wider margin of safety, especially in inexperienced hands. It would therefore, they say, be "suitable for use anywhere in the world where there are financial constraints, and especially where two or more patients are likely to be treated on the same day."

All human deaths from rabies result from failure to give adequate prophylaxis. After a rabid animal bite, immediate wound cleaning, rabies vaccine and injections of anti-rabies antibody (immunoglobulin) effectively prevent fatal infection. But anti-rabies immunoglobulin is very rarely available in developing countries, and so prevention relies on giving people bitten by rabid animals effective vaccine treatment.

The vaccines that are currently approved by the World Health Organization, which are usually injected into the muscle, are prohibitively expensive, and so are unaffordable in developing countries. In Africa, for example, the average cost of an intramuscular course of vaccine is \$US 39.6, equivalent to 50 days' wages.

Two economical regimens, involving injecting small amounts of vaccine into the skin (intradermally) at 2 or 8 sites on the first day of the course, with subsequent booster doses are available in a few places. With the 8-site method, a large dose of vaccine is given on the first day only, whereas with the 2-site method the same dose is divided between the first and third days, entailing an extra visit to the clinic. However, practical or perceived difficulties have restricted widespread uptake of these economical methods. Dr Warrell and colleagues therefore set out to test a new, similar simplified regimen, involving injections at 4 sites on the first day.

They vaccinated healthy volunteers to compare the antibody levels induced by the 4-site intradermal regimen with those induced by the current 2-site and 8-site intradermal regimens and the "gold standard" intramuscular regimen favored internationally. All of the economical intradermal regimens worked just as well as the intramuscular method at stimulating anti-rabies antibodies.



The authors conclude that the results provide sufficient evidence that the simplified 4-site regimen now meets all the criteria necessary for its recommendation for use wherever the cost of vaccine is prohibitive.

### **Link Between Ozone Air Pollution and Premature Death Confirmed**

WASHINGTON -- Short-term exposure to current levels of ozone in many areas is likely to contribute to premature deaths, says a new National Research Council report, which adds that the evidence is strong enough that the U.S. Environmental Protection Agency should include ozone-related mortality in health-benefit analyses related to future ozone standards. The committee that wrote the report was not asked to consider how evidence has been used by EPA to set ozone standards, including the new public health standard set by the agency last month.

Ozone, a key component of smog, can cause respiratory problems and other health effects. In addition, evidence of a relationship between short-term -- less than 24 hours -- exposure to ozone and mortality has been mounting, but interpretations of the evidence have differed, prompting EPA to request the Research Council report. In particular, the agency asked the committee to analyze the ozone-mortality link and assess methods for assigning a monetary value to lives saved for the health-benefits assessments.

Based on a review of recent research, the committee found that deaths related to ozone exposure are more likely among individuals with pre-existing diseases and other factors that could increase their susceptibility. However, premature deaths are not limited to people who are already within a few days of dying.

In addition, the committee examined research based on large population groups to find how changes in ozone air concentration could affect mortality, specifically to determine the existence of a threshold -- a concentration of ozone below which exposure poses no risk of death. The committee concluded that if a threshold exists, it is probably at a concentration below the current public health standard. As people have individual susceptibilities to ozone exposure, not everyone may experience an altered risk of death if ozone air concentration also changes. Further research should explore how personal thresholds may vary and the extent to which they depend on a person's frailty, the committee said.

The research on short-term exposure does not account for all ozone-related mortality, and the estimated risk of death may be greater than if based solely on these studies, the committee noted. To better understand all the possible connections between ozone and mortality, future research should address whether exposure for more than 24 hours and long-term exposure -- weeks to years -- are associated with mortality, including how ozone exposure could impact life expectancy. For example, deaths related to short-term exposure may not occur until several days afterward or may be associated with multiple short-term exposures.

Additionally, EPA should monitor ozone during the winter months when it is low and in communities with warmer and cooler winters to better understand seasonal and regional differences in risk. More research could also look at how other pollutants, such as airborne particulate matter, may affect ozone and mortality risk.

EPA, like other federal agencies, is required to carry out a cost-benefit analysis on mitigation actions that cost more than \$100 million per year. EPA recently used the results of population studies to estimate the number of premature deaths that would be avoided by expected ozone reductions for different policy choices, and then assigned a monetary value to the avoided deaths by using the value of a statistical life (VSL).

The VSL is derived from studies of adults who indicate the "price" that they would be willing to pay -- i.e. what benefits or conveniences someone would be willing to forgo -- to change their risk of death in a given period by a small amount. The monetary value of the improved health outcome is based on the value the group places on receiving the health benefit; it is not the value selected by policymakers or experts.

EPA applies the VSL to all lives saved regardless of the age or health status. For instance, a person who is 80 years old in poor health is estimated to have the same VSL as a healthy 2-year-old. To determine if an approach that accounts for differences in remaining life expectancy could be supported scientifically, EPA asked the committee to examine the value of extending life. For example, EPA could calculate VSL to estimate the value of remaining life, so a 2-year-old would have a higher VSL than an 80-year-old. It is plausible that people with shorter remaining life expectancy would be willing to devote fewer resources to reducing their risk of premature death than those with longer remaining life expectancy. In contrast, if the condition causing the shortened life expectancy could be improved and an acceptable quality of life can be preserved or restored, people may put a high value on extending life, even if they have other health impairments or are quite elderly.

The committee concluded that EPA should not adjust the VSL because current evidence is not sufficient to determine how the value might change according to differences in remaining life expectancy and health status. However, the committee did not reject the idea that such adjustments may be appropriate in the future. To move toward determining a value of remaining life, alternative approaches should be explored in sensitivity analyses, and further research should be conducted to answer the questions raised about the validity of EPA's current approach.

*The study was sponsored by the U.S. Environmental Protection Agency. The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council make up the National Academies. They are private, nonprofit institutions that provide science, technology, and health policy advice under a congressional charter. The Research Council is the principal operating agency of the National Academy of Sciences and the National Academy of Engineering. A committee roster follows.*

*Copies of Estimating Mortality Risk Reduction and Economic Benefits from Controlling Ozone Air Pollution are available from the National Academies Press; tel. 202-334-3313 or 1-800-624-6242 or on the Internet at <http://www.nap.edu>. Reporters may obtain a copy from the Office of News and Public Information (contacts listed above).*

### **Why fruit-eating bats eat dirt**

“Don’t eat the green parts of tomatoes, cut the green off the potatoes.” Any child would know that eating these parts of vegetables is a bad idea. The reason behind this is that they contain secondary plant compounds which may have detrimental effects on the consumer.

Each night, tropical fruit-eating bats ingest large amounts of secondary plant compounds with their food. This may become particularly problematic for pregnant or lactating bat mothers, since secondary plant compounds may damage the embryo or the juvenile. Now, a scientific study describes for the first time how female fruit-eating bats deal with this situation. In a study published in the online journal PLoS ONE, researchers from the Berlin Leibniz Institute for Zoo and Wildlife Research (IZW), Boston University and Cornell University, found evidence that fruit-eating bats take up large amounts of mineral rich water and clay from so-called mineral licks to detoxify the secondary plant compounds they ingest in fruits.

Bats include more than 1200 species, represent the second most species rich mammalian group and are important seed dispersers in tropical rain forests. Dr. Christian Voigt and his colleagues captured pregnant and lactating bats at mineral licks in the Amazonian rainforest of Ecuador.

“At first glance it seemed that bats visit these sites for the same purpose as other animals such as large tapirs or birds, i.e. to meet their daily mineral requirements,” Voigt describes their initial thoughts when they started the study. Bat mothers have particularly high mineral demands, because their juveniles cannot be weaned before they have reached almost adult size.

“To our amazement, we found fruits to be relatively rich in minerals compared to insects,” states Dr. Voigt. In the present study, the researchers focused on one bat species that feeds on both fruits and insects.

The study demonstrates that although insects and not fruits had a low mineral content insufficient for bat reproduction, only bats with a fruit-dominated diet visited mineral licks. The researchers assume that female bats ingest more fruits than usual during pregnancy and lactation. Therefore, they are directly exposed to the detrimental effects of secondary plant compounds. Female bats seem to be able to compensate the toxicity of secondary plant compounds by consuming mineral rich clay or water. Local people in Africa and South America or Africa are also familiar with the detoxifying qualities of mineral-rich clay and consume it during pregnancy and lactation. It seems as if humans and bats have found a similar solution for a shared problem. Scientists Clarify a Mechanism of Epigenetic Inheritance

### **“Silent” DNA stays that way as a result of RNA interference during chromosome replication**

Cold Spring Harbor, NY – Although letters representing the three billion pairs of molecules that form the “rungs” of the helical DNA “ladder” are routinely called the human “genetic code,” the DNA they comprise transmits traits across generations in a variety of ways, not all of which depend on the sequence of letters in the code.

In some cases, rather than the sequence of “letters,” it is the physical manner in which DNA is spun around protein spools called histones and tightly packed into chromosomes that determines whether or with what intensity specific genes are expressed. A team of scientists at Cold Spring Harbor Laboratory (CSHL) has solved another in a series of mysteries about this critical mechanism of gene expression, described in a paper in the April 8 issue of Current Biology.

#### **Inherited Clumping**

According to CSHL professor Rob Martienssen, Ph.D., who led the research team, about a tenth of our DNA stands aloof, spending its time in tightly packed clumps called heterochromatin, and unwinding only to replicate when a cell divides. After copying, both of the resulting DNA molecules — to the surprise of many — have been observed to form reclusive clumps in the same places as the original one did.

This inherited clumping of DNA, which causes genes to be expressed in distinctive ways, is one of a series of phenomena that scientists call epigenetic. The same sequence of nucleotides in two people can produce different patterns of gene expression if the way the DNA is clumped happens to be different.

#### **Probing Epigenetics in Yeast**

“We have not understood epigenetic inheritance very well,” says Dr. Martienssen, a plant geneticist and one of the pioneers in the study of epigenetics. To explore this process, he and his team are studying the way

DNA is packed in yeast, and how this packing can be transmitted across generations. The single-cell yeast organism is easy to study, in part because it lacks other epigenetic inheritance mechanisms, such as chemical modifications of DNA, that complicate the study of more complex animals and plants.

Long DNA molecules almost miraculously cram into cell nuclei that are almost a million times smaller than they are. They do so by wrapping around proteins called histones, which array themselves along the length of the DNA molecule like beads on a string. These DNA-wrapped histones then form larger arrays. The densely packed mass is then modified chemically by other proteins to form heterochromatin.

The dense packing of heterochromatin hides the DNA sequence from the cellular machinery that reads its genetic information, so the DNA in heterochromatin is "silenced." The genes it contains are effectively turned off.

Surprisingly, the clumping persists even after cells divide, although, says Dr. Martienssen, "it's always been a mystery how modifications of histones could be inherited." A few years ago, however, his group and others solved this mystery. They found that histone modification is controlled by complicated cellular mechanisms broadly known as RNA interference, or RNAi.

In RNAi, RNA that is copied from particular regions of DNA interacts with various proteins to modify histones in the same regions. Because the RNA matches only the section of DNA that produced it, it "provides the specificity that you need to make sure that only that part of the chromosome gets these histone modifications," Dr. Martienssen says. "If the whole chromosome were to get those histone modifications, you'd be dead."

### All in the Timing

These results raised a new puzzle, though: Since genes contained within heterochromatin are silenced, how can they give rise to the RNA molecules that help to modify histones? In new research, Martienssen's team has now solved this puzzle by tracking the cells through their cycle of growth and division.

They found that the interfering RNA molecules appear only during the brief part of the cell cycle when DNA is replicating. This result, Martienssen says, "neatly accounts for the paradox about how 'silent' heterochromatin can be transcribed [into interfering RNA], because it's transcribed only in a narrow window of the cell cycle."

The researchers also found that RNAi varies strongly with temperature. They speculate that this variation is responsible for inherited traits such as vernalization, the well-known process by which certain plants must be exposed to low temperatures before they will flower. Indeed, Martienssen says, there is "a whole slew of epigenetic phenomena that are sensitive to temperature."

"RNA Interference Guides Histone Modification during the S Phase of Chromosomal Replication" appears in the April 8, 2008, edition of *Current Biology*. The complete citation is as follows: Anna Kloc, Mikel Zaratiegui, Elphege Nora and Rob Martienssen. The paper is available online at: <http://www.current-biology.com/content/article/abstract?uid=PIIS0960982208003163>.

### Really?

## The Claim: During a Seizure, You Can Swallow Your Tongue

By ANAHAD O'CONNOR

**THE FACTS** One problem with old wives' tales and medical myths is that they can sometimes lead well-meaning people to do ill-advised things. Armed with the adage that people having seizures can swallow their tongue, Good Samaritans will sometimes try to force an object into the victim's mouth to keep that from happening.

A persistent belief, experts say, but a wrong and potentially injurious one.

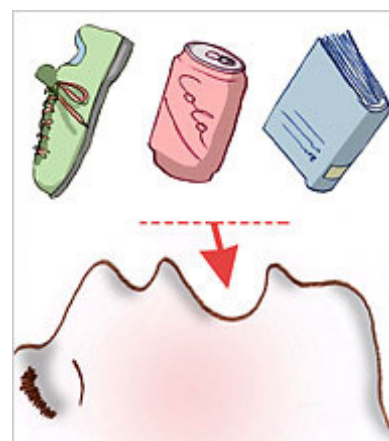
Swallowing the tongue is virtually impossible. In the human mouth, a small piece of tissue called the frenulum linguae, which sits behind the teeth and under the tongue, keeps the tongue in place, even during a seizure.

Ryan Brett, the director of education for the Epilepsy Institute in New York, said people who witness a seizure often reach for a wallet, a spoon, or a dirty object to stick in the person's mouth, much to the chagrin of epilepsy patients. He said he frequently conducted first-aid workshops in which he had to disabuse people of the myth.

"The only thing that happens when something is put in the mouth is you end up cutting someone's gums or injuring the teeth," he said. "We get complaints all the time."

The best way to help, instead, is to roll the person on one side to drain fluids from the mouth, cushion the head to prevent cranial injuries, and seek medical help if necessary.

**THE BOTTOM LINE** Never place an object in a person's mouth during a seizure.



## Personal Health

### **Hypertension: In Retreat, but Hardly Vanquished**

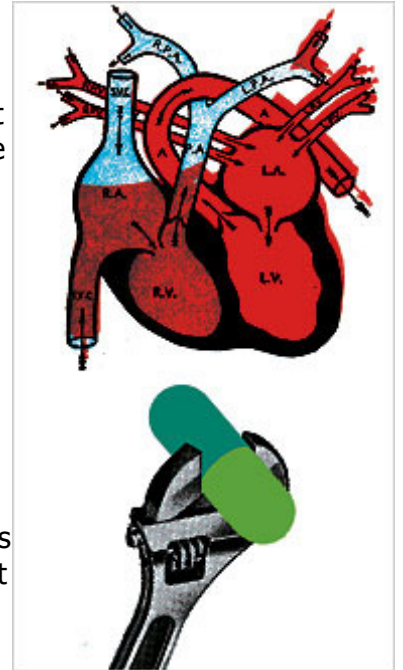
By JANE E. BRODY

As with cholesterol levels, the concept of a normal blood pressure has fallen strikingly as doctors learn what it takes to preserve good health. Decades ago, for example, my brother, Jeff, who had high blood pressure that hovered between 160/80 and 170/90, would have been considered normal.

Lacking good treatments for hypertension, no doctor was concerned when, at age 57, President Franklin D. Roosevelt's blood pressure was 170/90. And so the president's blood pressure rose inexorably over the next six years, and on April 12, 1945, at age 63 and with a pressure of 200/110, he died of a brain hemorrhage caused by severe hypertension.

But in 2000, when Jeff was 54, his cardiologist knew better. Now with excellent treatments, most often used in combination, an elevated pressure can be lowered to normal in most people. His doctor said that, with our family's medical history of three coronaries on our father's side occurring at ages 56 and 58, something should be done to protect Jeff's health.

Jeff's treatment "evolved" until he was taking a daily three-pill cocktail — Diovan HCT, a combination of a diuretic and angiotensin II receptor blocker; Norvasc, a calcium channel blocker; and Toprol XL, a beta blocker. He also works out on a treadmill several times a week, runs up and down stairs at home and at work all day, and eats a mostly heart-healthy diet, including five to 10 servings of fruits and vegetables a day, whole grain breads, nonfat milk and no added salt.



**Andy Martin**

With his blood pressure now at 106/66, the low end of normal, my brother has thus far escaped a premature coronary death.

Hypertension, once known as the "silent killer," is now not so silent. Through campaigns urging doctors to check patients' pressure at every visit, most cases have been detected. Although treatment has been prescribed for nearly all people known to have blood pressures consistently above 140/90, now called the high end of normal, up to half of patients still have elevated pressures.

#### **Still a Common Problem**

Why? Because doctors are not aggressive and creative in treating the problem; because unlike my brother, many patients do not follow doctor's orders and fail to fill prescriptions or neglect to take medicine daily; and because the rising weight of Americans and the passion for high-salt processed and restaurant-prepared foods have raised the once-normal pressures of many people to levels that experts say should be treated.

A new report from the American Heart Association describes untreated hypertension as now particularly serious among women. Midsection obesity, an important risk factor for hypertension, is found in 79 percent of hypertensive women as against 64 percent of hypertensive men. About a third of hypertensive women have blood pressure controlled at optimal levels, 120/80 or below.

The problem is particularly common among women taking oral contraceptives, whose risk of hypertension is two to three times as high as that of women their age who use some other form of contraception or none at all.

Hypertension is one of the nation's most common life-threatening diseases, with an overall incidence among adults of nearly 30 percent, a survey of 14,600 people in 2003 and 2004 found. And as many as 66 percent of people 60 and older have elevated pressures that warrant treatment, the survey showed. An increase in blood pressure with age is common only in developed countries, largely a result of a rich and salty diet, overweight and inadequate exercise.

In the United States, the high incidence of hypertension and its inadequate treatment has helped level off a decades-long decline in coronary mortality. In addition to heart attacks, untreated or inadequately treated hypertension can cause strokes, congestive heart failure, kidney failure and diabetes.

According to a report last May in *The Journal of Clinical Hypertension*, myths persist. Last year, a national online survey of 1,245 adults with high blood pressure found that many people still thought that hypertension meant being tense or anxious and that about 30 percent of people thought that it could be cured by losing weight, Dr. Marvin Moser of the Hypertension Education Foundation in Scarsdale, N.Y., and Dr. Stanley S. Franklin of the University of California, Irvine, reported.

While weight loss and improvements in diet and exercise habits can indeed help people lower an elevated pressure, "most people can't adjust their lifestyles enough to normalize their blood pressure," Dr. Moser said



in an interview. "Most people need help from medication, notably a diuretic in combination with one or two other drugs. The majority of patients don't get their pressures to normal without such a combination."

Doctors have more than 100 drugs to choose from. If one or two do not lower pressure to normal or cause unpleasant side effects, patients should insist on trying others, Dr. Moser said. Side effects of blood pressure medications are no longer the problem they once were, the doctor said. "In doses now used, more than 90 percent of people experience very few side effects."

### **Difficulties of Following a Diet**

One problem with a drug-free approach is the difficulty many patients have in adopting and sticking with a diet and exercise program that can significantly lower their pressure. Data from the latest national nutrition survey, described in the Feb. 11 issue of *The Archives of Internal Medicine*, said that a diet called DASH that effectively lowered blood pressure was poorly followed by people with hypertension. This diet is rich in fruits, vegetables and low-fat dairy products, a mix that provides excellent sources of fiber, potassium, magnesium and calcium. The diet is most effective if it is low in salt, with a sodium intake of about 1,500 milligrams a day.

The widely publicized value of the DASH diet was demonstrated in a major government-sponsored study published in 1997. But the new report found that in the years since, instead of improving, the dietary quality of people with hypertension has diminished.

Still, as my brother's case showed, even with a good diet, regular exercise and a healthy weight, most hypertensive patients need medication to achieve an optimal blood pressure. And that includes the elderly, who generally do not respond as well as younger people to blood pressure drugs.

"Studies have shown that even a modest reduction in blood pressure is beneficial to the elderly, reducing their risk of strokes, heart attacks, heart failure and death," Dr. Moser said. "And a new study in the very elderly, people 80 and older, showed that treating hypertension also reduces the overall risk of death."

In all age groups, "physician inertia is a major problem," he said, adding, "In 30 percent of patients whose blood pressure remains high despite treatment, nothing is done about changing the medication."

He urged people whose blood pressure is higher than 140/90 to ask their doctors, "Shouldn't we be doing something else?"

## **PETA's Latest Tactic: \$1 Million for Fake Meat**

**By JOHN SCHWARTZ**

People for the Ethical Treatment of Animals wants to pay a million dollars for fake meat — even if it has caused a "near civil war" within the organization.

The organization said it would announce plans on Monday for a \$1 million prize to the "first person to come up with a method to produce commercially viable quantities of in vitro meat at competitive prices by 2012."

The idea of getting the next Chicken McNugget out of a test tube is not new. For several years, scientists have worked to develop technologies to grow tissue cultures that could be consumed like meat without the expense of land or feed and the disease potential of real meat. An [international symposium](#) on the topic was held this month in Norway. The tissue, once grown, could be shaped and given texture with the kinds of additives and structural agents that are now used to give products like soy burgers a more meaty texture.

[A pdf is downloadable here.](#)

New Harvest, a nonprofit organization formed to promote the field, says on its Web site, "Because meat substitutes are produced under controlled conditions impossible to maintain in traditional animal farms, they can be safer, more nutritious, less polluting and more humane than conventional meat."

Jason Matheny, a doctoral student at Johns Hopkins University who formed New Harvest, said the idea of a prize for researchers was promising. Citing the example of the Ansari X Prize, a competition that produced the first privately financed human spacecraft, Mr. Matheny said, "they inspire more dollars spent on a research problem than the prize represents."

A founder of PETA, Ingrid Newkirk, said she had been hoping to get the organization involved in advancing in vitro meat technology for at least a decade.

But, Ms. Newkirk said, the decision to sponsor a prize caused "a near civil war in our office," since so many PETA members are repulsed by the thought of eating animal tissue, even if no animals are killed.

Lisa Lange, a vice president of the organization, said she was part of the heated exchange. "My main concern is, as the largest animal rights organization in the world, it's our job to introduce the philosophy and hammer it home that animals are not ours to eat." Ms. Lange added, "I remember saying I would be much more comfortable promoting eating roadkill."

Ms. Newkirk said the disagreement was natural, adding, "We will have members leave us over this."

"People say animal rights people can't agree," she said. "Well, human beings can't agree. In any social cause community, there are people who strive for purity."

Her goal, she said, was more pragmatic. "We don't mind taking uncomfortable positions if it means that fewer animals suffer." In that way, she said, "in vitro meat is a godsend."

For some already working in the field, the news was greeted with a wary welcome.

Henk P. Haagsman, a professor at Utrecht University in the Netherlands and an in vitro meat research pioneer, said he welcomed the prize competition.

"It will hopefully spark more interest to invest in the technology," Professor Haagsman said.

But he said he would not like to see the field dominated by the animal welfare issue, since environmental and public health issues are such important "drivers for this research." The Netherlands has put \$5 million into in vitro meat studies.

Another scientist at Utrecht, Bernard Roelen, said via e-mail that he was "rather surprised" by news of the competition, but said that even with strong financing, it would be extremely difficult to produce commercially viable quantities of in vitro meat before 2012. Professor Roelen added, "For me as a researcher, the announcement does not mean so much."

Why not? "I do research because I want to understand fundamental mechanisms," he said, "not to gain fortune."

### **Vital Signs**

## **Nostrums: Testosterone and Sex Drive in Women**

**By ERIC NAGOURNEY**

Women who spray testosterone on their stomach to raise their sex drive may not see much benefit — unless they also want to grow hair on their belly.

Writing in *Annals of Internal Medicine*, researchers said it was possible that the treatment held promise for premenopausal women experiencing a loss of sexual interest and satisfaction. But the study found only limited improvements, and the researchers said even these might have been caused by a placebo effect. Treatments containing testosterone are given for women whose sex drive diminishes after menopause; none are approved for those still menstruating, the study said.

For this study, 261 women who reported a decrease in sexual activity and had low testosterone levels were given one of four sprays and told to put it on their stomach for four months. Three sprays held varying levels of testosterone, and one was a placebo.

At the start the study, the women reported having four to five sexual encounters a month, with an average of 1.4 described as satisfactory. After 16 weeks, the women in all the groups reported a somewhat better sex life, although the increase was statistically meaningful only for the group that received the middle dose of testosterone. Unwanted hair growth where the spray was placed was fairly common.

The results, the researchers said, justify more research, but they cautioned against the widespread use of testosterone in premenopausal women for now.

## **At 60, He Learned to Sing So He Could Learn to Talk**

**By KAREN BARROW**

Few people over the age of 10 would list "Happy Birthday" among their favorite songs. But Harvey Alter, now 62, has a special fondness for it. It helped teach him how to talk.

One morning in June 2003, Mr. Alter, then a self-employed criminologist, was putting a leash on his dog, Sam, in preparation for a walk around Greenwich Village, where he has lived for 30 years. Suddenly he felt dizzy and disoriented.

"My thoughts were intertwined, not making sense," he said in a recent interview. "I knew I was having a stroke."

At St. Vincent's Hospital, doctors diagnosed an ischemic stroke, caused by a blockage in blood flow to part of the left half of his brain. As a result, the right side of his body was temporarily paralyzed, the right side of his face drooped, and he had trouble coming up with the right words and stringing them into sentences — a condition called aphasia.

Within hours of his stroke, Mr. Alter met with Loni Burke, a speech therapist who now works at Lenox Hill Hospital. At first he was completely nonverbal; within a few days he could say small words.

"Mostly, he said, 'No,'" Ms. Burke recalled, "because he was frustrated that he couldn't speak."

After three weeks in the hospital and two years of painstaking therapy, Mr. Alter's paralysis had mostly disappeared and his smile was back to normal. But while he could communicate through small words and the help of a chalkboard, complex verbal communication remained elusive.

Using standard speech therapy techniques like reviewing lists of numbers and the days of the week, Ms. Burke helped her patient piece together short phrases. But they came slowly and sounded robotic.

Then one day, she asked him to sing.



**Interactive Feature**  
**[Patient Voices: Stroke](#)**

"How can I ever sing? I can't talk," Mr. Alter recalled thinking. But as soon as Ms. Burke began to sing "Happy Birthday," he chimed in.

"It sounded good," he said. "Almost like I didn't have anything wrong."

The technique, called melodic intonation therapy, was developed in 1973 by Dr. Martin Albert and colleagues at the Boston Veterans Affairs Hospital. The aim was to help patients with damage to Broca's area — the speaking center of the brain, located in its left hemisphere.

These patients still had relatively healthy right hemispheres. And while the left hemisphere is largely responsible for speaking, the right hemisphere is used in understanding language, as well as processing melodies and rhythms.

"You ask yourself, 'What specifically engages the right hemisphere?'" said Dr. Gottfried Schlaug, a neurologist at Beth Israel Deaconess Medical Center in Boston, who studies music's effect on the brain.

Melodic intonation therapy seems to engage the right hemisphere by asking patients to tap out rhythms and repeat simple melodies. Therapists first work with patients to create sing-song sentences that can be set to familiar tunes, then work on removing the melody to leave behind a more normal speaking pattern.

But relatively little research has been done to understand how this type of therapy affects the brain of a stroke patient.

In a study completed in 2006, Dr. Schlaug and colleagues at Harvard tracked the progress of eight patients with Broca's aphasia as they underwent 75 sessions of melodic intonation therapy. M.R.I. scans taken when the patients were speaking simple words and phrases showed that activity in the right hemisphere had changed significantly over the course of treatment.

"The combination of melodic intonation and hand-tapping activates a system of the right side of the brain that is always there, but is not typically used for speech," Dr. Schlaug said.

He recommends melodic intonation therapy for patients who have no meaningful form of speech, but can understand language and have the patience for therapy sessions.

Before music came back into his life, Mr. Alter had difficulty thinking of the words he wanted to use and forming them. For him, it seems, melodic intonation therapy was the key to retraining his brain to speak with tone and rhythm.

"After a stroke, the brain is learning to adapt," said Dr. Albert Favate, stroke director at St. Vincent's Hospital in New York. "For someone with Broca's aphasia, melodic intonation therapy can allow them to get back their speaking patterns, which may improve speech spontaneity."

Mr. Alter still speaks somewhat haltingly, with a noticeable lilt, but he no longer struggles so mightily to find the right word, and he will happily serenade anyone with conversation about his condition. While he attributes most of his success to melodic intonation therapy, Ms. Burke says it was only one tool she used among a host of others.

Still, she agrees that the therapy was crucial. "It may have caused an initial reaction of, 'Wow, maybe I can speak,'" she said.

As he has recovered, Mr. Alter has devoted his life to increasing awareness about aphasia. He created the International Aphasia Movement two years ago and spends much of his time leading support groups for stroke survivors and their families and touring the world to speak for those who can't speak for themselves.

And he is always happy to sing "Happy Birthday" with anyone who cares to join in. "But I don't mind Christmastime either," he said. "Because I know all of the carols."

## **The Body in Depth**

**By JOHN SCHWARTZ**

Roberta Corson recalled her father's dissection lab as a happy place.

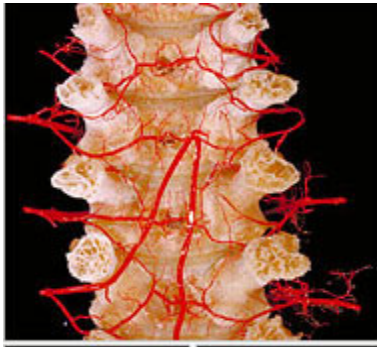
Her father, David L. Bassett, was an expert in anatomy and dissection at the University of Washington. For more than 17 years, he was engaged in creating what has been called the most painstaking and detailed set of images of the human body, inside and out, ever produced. In 3-D.

Working closely with William Gruber, the inventor of the View-Master, the three-dimensional viewing system that GAF Corporation popularized as a toy in the 1960s, Dr. Bassett created the 25-volume "Stereoscopic Atlas of Human Anatomy" in 1962. It included some 1,500 pairs of slides, along with line drawings that made the details more discernible. The paired slides could be examined with a View-Master, making the chest cavity look cavernous, and making details of structure and tissue stand out unforgettably.

The atlas was an immediate success and the images became an important resource for medical students, even more so as schools have de-emphasized gross anatomy and cadaver work. But the atlas eventually went out of publication in the 1960s.

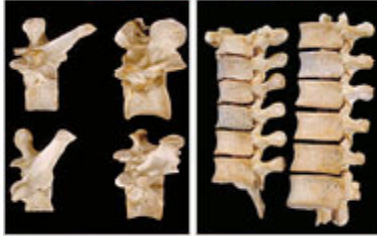


Thanks to Stanford University's school of medicine, however, the work will soon be available to the world. The school is bringing the images online, (See a sampling.). The school has also worked with eHuman, a

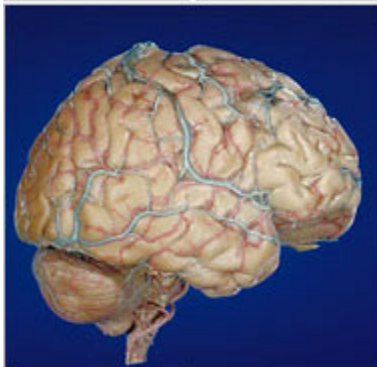


company in Silicon Valley that hopes to charge students and the curious for access to the trove. Rolling a computer mouse over an image at the eHuman site will highlight anatomical details, and bring up the line drawings from the atlas. So far access to the head and neck collection is \$8 a month. Nothing else is online yet.

Even without the stereoscopic boost, the images are stunning, though perhaps not best examined over breakfast. Blood vessels cluster in a cobwebby tangle along a spinal column, and pelvic bones stand out like butterflies against a stark black field. The back of a man's head, its layers of flesh and bone sliced away, shows the excavation from the scalp down to the brain as if looking at a stratified canyon wall. The original Kodachrome slides, carefully preserved, still provide images of tremendous clarity.



Looking at the images today is a little like viewing the "Body Worlds" exhibition but without unsettling concerns about the exact provenance of the bodies. Critics and the exhibitors give different accounts of where the bodies came from. It is quite clear that Dr. Bassett's cadavers were people who had willed their bodies to science.



Robert Chase, the Emile Holman Professor of Surgery, Emeritus, at Stanford University and curator of the Bassett collection, said, "It's never going to be duplicated" because the work was so precise and arduous few institutions could afford to recreate it. "And they're in stereo — that's really a double whammy," Dr. Chase said. Dr. Bassett's widow, Lucille Bassett, gave the collection to Stanford in her will.

Eventually, it will be possible to see the images online in stereo for anyone who owns the increasingly popular eyeglasses that provide a sense of three-dimensional depth in video games, said Robert Austrian, eHuman's chief executive. The devices have rapid electronic shutters that provide the optical illusion of three dimensions when each eye is fed a different perspective.



It was the close collaboration of two very different men that made possible the creation of the collection. Dr. Bassett was an academic and an anatomist, a gregarious man with a great talent for dissection. His daughter recalls that his fingers were so nimble and precise that he once caught a fish with his bare hands.



Mr. Gruber was a former pipe organ maker from Germany; his interest in photography and stereography had led him to create the View-Master, an invention that made him wealthy enough to take on projects simply because they fascinated him. And he chose corpses, formaldehyde and the dissecting skills of Dr. Bassett.



Mrs. Corson provided notes from her mother's unpublished memoir, in which she said that before Mr. Gruber approached her husband about creating a stereoscopic atlas, a similar project intended just to produce two-dimensional images had been attempted at the University of California. An anatomist "tried to work on unembalmed bodies of prisoners who had been executed." The result, she wrote, "was a crude and bloody mess."

By using embalmed bodies, Dr. Bassett and Mr. Gruber reasoned, they could work with better preserved tissues. Dr. Bassett had devised his own embalming fluid that would retain "near normal color" of the tissue, Mrs. Bassett wrote.

Her husband began the great work of his life with the head and neck; Mrs. Corson was 3 years old at the time. "I certainly grew up around bodies, and his dissections," she said — along with her three brothers. "We would go over there to pick up the mail," and "I grew up with a sense of comfort with the anatomy

labs, and with the corpses."

***Images of the human body made in the 1960s***  
***by David L. Bassett and William Gruber. [More Photos »](#)***

She recalled: "There was nothing gross or ugly about it. It was beautiful."



Dr. Bassett would come home to eat dinner, Mrs. Corson said, and "my mother would scratch his back, and then he would go back to the lab." Often, she recalled, "my mother would go over to the lab and talk to him while he dissected."

Mr. Gruber's visits were frequent; Dr. Bassett would prepare the specimens, and Mr. Gruber would arrive for a three-day visit, staying at the Bassett home. Dr. Bassett would perform the dissections, and Mr. Gruber would shoot from the slightly different angles that provided stereoscopic viewing. They worked into the night. "Bill would take the shots, and my dad would dissect deeper into the area," exposing layer upon layer of anatomical detail. "He was a craftsman," she said.

The images, when presented to the medical profession, were a sensation. In an essay that Dr. Chase wrote in a scientific journal in 1992, he recalled that when Dr. Bassett took three test booklets and six View-Masters to the American Association of Anatomists annual meeting in Detroit in 1951, a line "through the door and down the hall formed to get a glimpse of the unusual anatomical views."

The work was completed by 1962, with the 25 volumes packed with thousands of pictures and diagrams, and hundreds of View-Master reels. That year, Mr. Gruber wrote to Dr. Bassett to congratulate him on having finished the project, saying: "No one outside of Lucile and myself will ever know what torturous 10 years of slavery you went through to reach the top. Let me add my prayer and hope that you will not have to die to earn your just recognition."

He added, "Things should really begin to pop from now on."

But things don't always work out the way people hope. Dr. Bassett died in 1966, at just 52. He had planned to create a less expensive student edition that could get the anatomical knowledge out to a broader audience, but "he was never able to finish that," said Mrs. Corson, 64, a retired United Methodist minister and clinical psychologist in Saratoga, Calif.

Mrs. Corson said she hoped the Stanford project and its commercial counterpart would bring her father the recognition he deserved, and "finally our dad's atlas will be a valuable contribution to science and the understanding of the human body."

She said she believed the formaldehyde that was such a large part of her father's work contributed to his death, from a combination of rare biochemical diseases that caused his heart, lungs and other organs to thicken. "I always wondered," she said.

Still, the work survives. For all his knowledge, Mrs. Corson said, her father retained a sense of "amazement and wonder" at the complexity of the bodies he deconstructed.

Once, she recalled, he held up his hand and turned it over before her. "I know every muscle," he told her. "I know every nerve and every vessel in the hand. But there's so much I will never know."

### **Breakfast cereals boost chances of conceiving boys**

\* 00:01 23 April 2008

\* NewScientist.com news service

\* **Andy Coghlan**

Some people put a hammer under the pillow. Others try to ensure they conceive on the day of ovulation. Still others drink coffee, as this supposedly makes Y-chromosome carrying sperm swim faster. Now we can reveal a method that apparently really does affect the chances of having a boy: eat cereal for breakfast.

A survey of 740 pregnant women found that boys were slightly more likely if a woman had high energy intake prior to conception, and that the individual food with most impact was breakfast cereal.

"If you want a boy, eat a healthy diet with a high calorie intake, including breakfast," says Fiona Mathews of the University of Exeter in the UK, and lead researcher of the study.

She said it follows that the reverse is true for women who want girls, but on ethical grounds would not advise women to risk their health by skipping breakfast.

Intake of sodium, potassium and calcium was also a factor, providing partial support to the old wives' tale that salty diets help women conceive sons.

#### **Heavier boys**

The insights came from detailed records of diets reported by the women before and during pregnancy.

When the researchers divided the women into groups with high, medium and low intake of energy, they found that 56% of women in the high-energy group had boys, compared with 45% in lowest group.

Cereal intake had a bigger effect. "Of women eating cereals daily, 59% had boys, compared with only 43% who bore boys in the group eating less than a bowlful per week," says Mathews.

The team's results echo those in animals such as horses and cows, which are statistically more likely to bear males if well-fed.

The findings make evolutionary sense because baby boys are typically 100 grams heavier than baby girls, so female mammals may have evolved ways to favour production of boys when resources are plentiful.

## Rich kids

One possible mechanism is that high glucose levels in the body of a well-fed woman favour survival of male rather than female embryos.

"It's well known in IVF clinics that if you have high glucose concentrations in cell culture, it favours survival of male blastocysts," says Mathews.

As for the finding that salt intake favours boys, one theory is that salt alters the acidity of the vagina to favour male sperm, but Mathew says there is scant evidence for this.

The researchers say that their findings might help explain slight reductions in male births in richer countries. In the UK, for example, the number of boys born is falling by 1 per 1000 births per year.

## Eating habits

Mathews says that the findings might seem at odds with the obesity epidemic sweeping richer countries, but stressed that there were also problems with under-eating as well as over-eating. In the US, for example, the proportion of adults eating breakfast fell from 86 to 75% between 1965 and 1991. The fall for adolescent girls was steeper still, from 85 to 65%.

Mathews says that her findings provide hints of a cheap, "natural" way to select the sex of a child, although she stresses that much more research is needed to corroborate the results.

Lucilla Poston, who studies the impact of maternal nutrition on infant health at King's College London, says that if there is an effect at all, it could be down to folate in cereals.

"Excess folate prevents defects in DNA through methylation, a chemical process of silencing some genes but not others," she says. Maybe it plays a role in determining gender, but there's no evidence for it, she says. *Journal reference: Proceedings of the Royal Society B: Biological Sciences (DOI: 10.1098/rspb.2008.0105)*

## 'Flammable ice' could be mined for fuel

They call it flammable ice, and it could be the world's last great source of carbon-based fuel - assuming we can mine methane hydrates, crystal lattices of ice that trap methane beneath ocean beds and permafrost.

One problem with extracting this methane is that you have to melt the ice to bring the gas to the surface. In 2002, a team of geologists from Canada and Japan tried injecting hot water into the ice beneath the delta of the McKenzie river in northern Canada. While this released some hydrates, it used a lot of energy.

Now the same group has extracted methane much more efficiently, and without hot water, by pumping air out of drill holes in the frozen structures. This reduced the pressure, and so raised the melting temperature of the ice so the methane could be removed.

The state-owned Japan Oil, Gas and Metals National Corporation, which announced the test results, wants to extract the 7 trillion tonnes of methane thought to be trapped in hydrates in Japanese coastal waters. It hopes this will be the answer to Japan's century-long search for an indigenous source of fuel. Last month, the government approved a plan to commercialise the extraction of the fuel within a decade.

Mining methane may be easier said than done, however. There are fears that disturbing the hydrates could trigger blowouts that might release huge volumes of gas. Around 8000 years ago, a sudden natural release from the North Sea bed near Norway triggered a tsunami that flooded much of Scotland.

## Early parents didn't stand for weighty kids

### *Infant carrying ruled out as reason why humans walk upright*

Scientists investigating the reasons why early humans – the so-called hominins – began walking upright say it's unlikely that the need to carry children was a factor, as has previously been suggested.

Carrying babies that could no longer use their feet to cling to their parents in the way that young apes can has long been thought to be at least one explanation as to why humans became bipedal.

But University of Manchester researchers investigating the energy involved in carrying a child say the physical expense to the mother does not support the idea that walking upright was an evolutionary response to child transportation.

"Walking upright is one of the major characteristics that separates humans from their primate relatives," said Dr Jo Watson, who carried out the research in the University's Faculty of Life Sciences.

"Scientists have long hypothesised as to the reasons why hominins became bipedal in a relatively short space of time but the truth is we still don't know for sure.

"One of the more popular explanations is that walking upright freed our forelimbs allowing us to carry objects, including children; apes have no need to carry their young as they are able to grip using both hands and feet.

"Our study focused on the amount of energy required to carry 10kg loads, including a mannequin child. Importantly, the distribution of the weight varied in each instance."

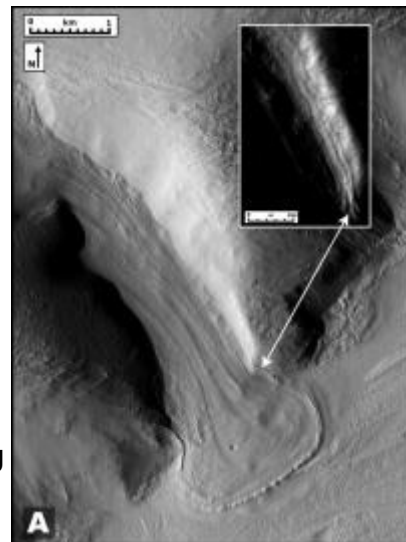
The team monitored the oxygen consumption of seven women, all healthy individuals under the age of 30, carrying either a symmetric load, in the form of a weighted vest or a 5kg dumbbell in each hand, or an asymmetric load, which was a single 10kg weight carried in one hand or a mannequin infant on one hip.

"Carrying an awkward asymmetric load, such as the infant on one side of the body, is the most energetically expensive way of transporting the weight," said Dr Watson, whose research is published in the Journal of Human Evolution.

"Unless infant carrying resulted in significant benefits elsewhere, the high cost of carrying an asymmetrical weight suggests that infant carrying was unlikely to have been the evolutionary driving force behind bipedalism."

The study, carried out with colleagues at the Universities of Sheffield and Salford and funded by the Natural Environment Research Council (NERC), is part of a larger project, run by Dr Bill Sellers at The University of Manchester, which uses computer simulations to understand evolutionary processes, particularly the way in which we and other animals move.

Future plans are to extend this work to assess the energy cost of carrying in great apes. Computer models of early hominins carrying loads will also be built to try and evaluate whether their body shape and posture – long arms and short legs – would have made them noticeably better or worse at carrying than present-day humans. The research team hopes this will help build up a picture of how humans evolved to walk on two legs.

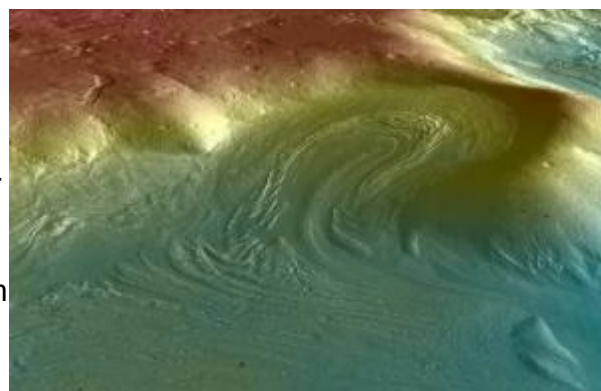


### **Glaciers Reveal Martian Climate Has Been Recently Active**

***Brown University researchers have found compelling evidence of thick, recurring glaciers on Mars, a discovery that suggests that the Red Planet's climate was much more dynamic than previously believed – and could change again. Results are published on the cover of Geology magazine.***

PROVIDENCE, R.I. [Brown University] - The prevailing thinking is that Mars is a planet whose active climate has been confined to the distant past. About 3.5 billion years ago, the Red Planet had extensive flowing water and then fell quiet - deadly quiet. It didn't seem the climate had changed much since.

Now, in a research article that graces the May cover of Geology, scientists at Brown University think Mars' climate has been much more dynamic than previously believed. After examining stunning high-resolution images taken last year by the Mars Reconnaissance Orbiter, the researchers have documented for the first time that ice packs at least 1 kilometer (0.6 miles) thick and perhaps 2.5 kilometers (1.6 miles) thick existed along Mars' mid-latitude belt as recently as 100 million years ago. In addition, the team believes other images tell them that glaciers flowed in localized areas in the last 10 to 100 million years - akin to the day before yesterday in Mars' geological timeline.



***Moraine on a Martian Box Canyon This high-resolution image, taken by the Mars Reconnaissance Orbiter, shows the rock debris that Brown scientists believe was left by a glacier that rose at least one kilometer from the surrounding plain and flowed downward onto the canyon. The image is on the cover of May's issue of Geology magazine. Credit: NASA***

This evidence of recent activity means the Martian climate may change again and could bolster speculation about whether the Red Planet can, or did, support life.

"We've gone from seeing Mars as a dead planet for three-plus billion years to one that has been alive in recent times," said Jay Dickson, a research analyst in the Department of Geological Sciences at Brown and lead author of the Geology paper. "[The finding] has changed our perspective from a planet that has been dry and dead to one that is icy and active."

In fact, Dickson and his co-authors, James Head, a planetary geologist and the Louis and Elizabeth Scherck Distinguished Professor at Brown, and David Marchant, an associate professor in the Department of Earth Sciences at Boston University, believe the images show that Mars has gone through multiple Ice Ages - episodes in its recent past in which the planet's mid-latitudes were covered by glaciers that disappeared with changes in the Red Planet's obliquity, which changes the climate by altering the amount of sunlight falling on different areas.

Dickson and the other researchers focused on an area called Protonilus Mensae-Coloe Fossae. The region is located in Mars's mid-latitude and is marked by splotches of mesas, massifs and steep-walled valleys that separate the lowlands in the north from the highlands in the south.

The team looked in particular at a box canyon set in a low-lying plain. Images show the canyon has moraines - deposits of rocks that mark the limits of a glacier's advance or the path of its retreat. The rock

deposit lines appear to show a glacier that flowed up the box canyon, which "physically cannot happen," Dickson said.

Instead, the team deduced the ice in the surrounding plain grew higher than the canyon's walls and then flowed downward onto the top of the canyon, which had become the lowest point on the ice-laden terrain. The team calculated the ice pack must have been one kilometer thick by past measurements of height between the plain and the lip of the canyon. Based on the ice flow patterns, the ice pack could have reached 2.5 kilometers at peak thickness during a period known as the late Amazonian, the authors said. The finding could have implications for the life-on-Mars argument by strengthening the case for liquid water. Ice can melt two ways: by temperature or by pressure. As currently understood, the Martian climate is dominated by sublimation, the process by which solid substances are transformed directly to vapor. But ice packs can exert such strong pressure at the base to produce liquid water, which makes the thickness of past glaciers on its surface so intriguing.

***Ancient Martian Tributary This image taken by the Mars Reconnaissance Orbiter shows a glacier-like lobe that had spilled from an ancient tributary on to the surrounding plain. Brown scientists report in May's issue of Geology that the lobe is superimposed on a past ice deposit and appears to be evidence of more recent glaciation. Credit: NASA***

Dickson also looked at a lobe across the valley from the box canyon site. There, he saw a clear, semi-circular moraine that had spilled from an ancient tributary on to the surrounding plain. The lobe is superimposed on a past ice deposit and appears to be evidence of more recent glaciation. Although geologists can't date either event, the landscape appears to show at least two periods in which glaciation occurred, bolstering their theory that the Martian climate has undergone past Ice Ages.

[Read an online version of the paper.](#)

### **Medical College researchers find dinosaur clues in fat**

VALHALLA, April 23, 2008—A team of researchers at New York Medical College has discovered why birds, unlike mammals, lack a tissue that is specialized to generate heat. A paper published April 21, 2008 in the online peer-reviewed journal BMC Biology contains the surprising implication that the same lack of heat-generating tissue may have contributed to the extinction of dinosaurs.

The paper, "The brown adipocyte differentiation pathway in birds: an evolutionary road not taken," was written by Stuart A. Newman, Ph.D., professor of cell biology and anatomy, Nadejda Mezentseva, a Ph.D. candidate at New York Medical College, and Jaliya Kumaratilake, Ph.D., University of Adelaide, Australia.

Humans, like all mammals, have two kinds of adipose tissue, white fat and brown fat. White fat is used for storing energy-rich fuels, while brown fat generates heat. Hibernating bears have a lot of brown fat, as do human infants, who have much more than adults, relative to their body size. Infants' brown fat protects them from hypothermia. Clinicians would like to find ways of making adult white fat behave more like brown fat so that we could burn, rather than store, energy.

While most mammals have a key gene called UCP1, which is responsible for the heat-generation function of brown fat, birds do not. The researchers found they could induce a specific type of stem cell in chicken embryos to produce differentiated cells that are structured and behave like brown fat. These chicken cells can even activate a UCP1 gene if presented with one from a mouse.

The ability to produce brown fat evolved in a common ancestor of birds and mammals, but the ability to generate heat was lost in the group that gave rise to birds and lizards after it separated from the mammalian lineage (the researchers found the lizard genome similarly lacks a UCP1 gene). This strongly implies that dinosaurs, which diverged from birds even later than lizards, also lacked brown fat.

### **MU psychologists demonstrate simplicity of working memory**

***Study could help with ADD and other attention difficulties***

COLUMBIA, Mo. – A mind is a terrible thing to waste, but humans may have even less to work with than previously thought. University of Missouri researchers found that the average person can keep just three or four things in their "working memory" or conscious mind at one time. This finding may lead to better ways to assess and help people with attention-deficit and focus difficulties, improve classroom performance and enhance test scores.

"Most people believe the human mind is incredibly complex," said Jeff Rouder, associate professor of psychology in the MU College of Arts and Science. "We were able to use a relatively simple experiment and look at how many objects can be in maintained in the human conscious mind at any one time. We found that every person has the capacity to hold a certain number of objects in his or her mind. Working memory is like the number of memory registers in a computer. Every object takes one register and each individual has a fixed number of registers. Limits in working memory are important because working memory is the mental process of holding information in a short-term, readily accessible, easily manipulated form where it can be combined, rearranged and stored more productively."



"We know that this kind of memory is really important in daily life," said co-author Nelson Cowan, psychology professor at Mizzou and an expert in working memory theory. "If a person is trying to do a math problem, there are partial results to keep in mind as that person solves the problem. When people are going to do any tasks in the house—like remembering the location of keys, turning off the stove, combining ingredients for a cake or recalling a phone number—they use working memory to keep in mind all the different aspects of the tasks."

Rouder said that to remember a series of items, people will use "chunking," or grouping, to put together different items. It can be difficult for someone to remember nine random letters. But if that same person is asked to remember nine letters organized in acronyms, IBM-CIA-FBI, for example, the person only has to use three slots in working memory. The difficulty in measuring working memory capacity is assuring that each item presented cannot be grouped together with others to form a larger chunk.

The researchers conducted a simple experiment involving an array of small, scattered, different-colored squares, to test their theory of working memory. The participant saw two, five or eight squares in the array, depending on the trial. The array was then "wiped out" by another display consisting of the same squares, minus the colors. Finally, the participant was shown a single color in one location and was asked to indicate whether the color in that spot had changed from the original array.

"How an individual does this test depends on working memory," Cowan said. "The results indicating that people have a fixed capacity provide evidence of simplicity in the mind. Many other theorists have suggested that the amount of working memory is circumstance-dependent, depends on a particular test, that there is nothing general we can get out of it, and that it's complex. We found the mind to be less complex in this case and that should be of great use in the future."

Working memory is closely related to attention because it requires attention to hold a number of items in mind at once. People with high working memory capacity have more focus. Those with a lower attention span are more easily distracted. This fact may help researchers help people with attention deficit disorders.

The researchers emphasized that the unique result of their study was that "the data were explained to surprising accuracy by a very simple mental model in which participants either used a register of working memory or, if all registers were full, guessed randomly."

*Rouder and Cowan's study, "An assessment of fixed-capacity models of visual working memory," was published this month in the Proceedings of the National Academy of Sciences. Other members of the research team are Richard Morey, Christopher Zwillung, Candice Morey and Michael Pratte.*

### **China down to 12 days of coal stocks**

\* 18:18 23 April 2008

\* NewScientist.com news service

\* **Fred Pearce**

China's booming economy could be running out of steam – literally.

At the end of a cold and stormy winter, the country has just 12 days of coal reserves at most power stations. Some provinces, including Hebei, bordering Beijing, have less than a week's coal left. This is a record low, the state electricity regulatory commission revealed on Tuesday.

China relies on burning coal for 70% of its electricity. Even though Chinese coal production in the first quarter of this year was up almost 15% on the same period last year, it has apparently not been enough to meet rapidly growing demand.

Coal imports, which started last year, have also failed to meet the difference between supply and demand. Such is the demand for power from an economy that has been growing by 10% a year for more than two decades.

#### **Coal-fired growth**

The International Energy Agency says China increased capacity at coal-fired power stations by 100 gigawatts in 2006, the most recent year for which figures are available.

It is often claimed that China builds a new coal-fired power plant once a week but the IEA figure suggests that it in fact builds two, assuming a typical plant size of one gigawatt.

Even that is not enough to meet soaring demand. The deputy head of the Chinese electricity regulatory commission, Wang Yeping, said the country is likely to be short of 10 gigawatts of electricity generating capacity by this summer.

#### **Power shortages**

That will cause brownouts and power shortages, particularly in southern provinces such as Guangdong, where the spread of air conditioning systems is competing with industry for power.

The coal mining industry, and the rail network needed to bring the coal to the power plants, are both struggling to keep up with the drive to build ever more generating capacity. The strains raise questions about how much longer China's breakneck industrialisation can continue.

Last year, by most calculations, China exceeded the US to become the world's largest carbon dioxide emitter – though its emissions per head of population remain far lower. Both countries are heavily reliant on coal for their power, which produces more CO2 per unit of energy than other major fossil fuels.

### **New nanotech products hitting the market at the rate of 3-4 per week**

#### ***Nanotechnology consumer products are in your mouth and on your face***

WASHINGTON — New nanotechnology consumer products are coming on the market at the rate of 3-4 per week, a finding based on the latest update to the nanotechnology consumer product inventory maintained by the Project on Emerging Nanotechnologies (PEN).

One of the new items among the more than 600 products now in the inventory is Swissdent Nanowhiting Toothpaste with “calcium peroxides, in the form of nano-particles.” Today, in testimony before the Senate Commerce Committee, PEN Project Director David Rejeski cited Ace Silver Plus—another of the nine nano toothpastes in the inventory—as an example of the upsurge in nanotechnology consumer products in stores. The hearing marks the start of U.S. Senate debate on the future direction of the annual \$1.5 billion federal investment in nanotechnology research and development (R&D).

The number of consumer products using nanotechnology has grown from 212 to 609 since PEN launched the world’s first online inventory of manufacturer-identified nanotech goods in March 2006. Health and fitness items, which includes cosmetics and sunscreens, represent 60 percent of inventory products. The colorful and searchable list of nanotechnology merchandise—containing everything from nanotech diamonds and cooking oil, to golf clubs and iPhones—is available free at

[www.nanotechproject.org/consumerproducts](http://www.nanotechproject.org/consumerproducts).

#### ***Washington, DC: Nano Silver Toothpaste, purchased in local market.***

There are 35 automotive products in the PEN inventory, including the Hummer H2. General Motors Corporation bills the H2 as having a cargo bed that “uses about seven pounds of molded in color nanocomposite parts for its trim, center bridge, sail panel and box rail protector.”

Nanoscale silver is the most cited nanomaterial used. It is found in 143 products or over 20 percent of the inventory. Carbon, including carbon nanotubes and fullerenes, is the second highest nanoscale material cited. Other nanoscale materials explicitly referenced in products are zinc (including zinc oxide) and titanium (including titanium dioxide), silica and gold.

While polls show most Americans know little or nothing about nanotechnology, in 2006 nanotechnology was incorporated into more than \$50 billion in manufactured goods. By 2014, Lux Research estimates \$2.6 trillion in manufactured goods will incorporate nanotechnology—or about 15 percent of total global output. Despite a 2006 worldwide investment of \$12.4 billion in nanotech R&D, comparatively little was spent on examining nanotechnology’s potential environmental, health and safety risks.

“Public trust is the ‘dark horse’ in nanotechnology’s future,” says Rejeski in his testimony. “If government and industry do not work to build public confidence in nanotechnology, consumers may reach for the ‘No-Nano’ label in the future and investors will put their money elsewhere.”

According to Rejeski, “The use of nanotechnology in consumer products and industrial applications is growing rapidly, with the products listed in the PEN inventory showing just the tip of the iceberg. Public perceptions about risks—real and perceived—can have large economic consequences. How consumers respond to these early products—in food, electronics, health care, clothing and cars—is a litmus test for broader market acceptance of nanotechnologies in the future.”

*Nanotechnology is the ability to measure, see, manipulate and manufacture things usually between 1 and 100 nanometers (nm). A nanometer is one billionth of a meter. A human hair is roughly 100,000 nanometers wide. The limit of the human eye’s capacity to see without a microscope is about 10,000 nm.*

*The Project on Emerging Nanotechnologies is an initiative launched by the Woodrow Wilson International Center for Scholars and The Pew Charitable Trusts in 2005. It is dedicated to helping business, government and the public anticipate and manage possible health and environmental implications of nanotechnology.*



## Does the Earth's magnetic field cause suicides?

\* 13:39 24 April 2008

\* NewScientist.com news service

\* **Catherine Brahic**

Many animals can sense the Earth's magnetic field, so why not people, asks Oleg Shumilov of the Institute of North Industrial Ecology Problems in Russia.

Shumilov looked at activity in the Earth's geomagnetic field from 1948 to 1997 and found that it grouped into three seasonal peaks every year: one from March to May, another in July and the last in October.

Surprisingly, he also found that the geomagnetism peaks matched up with peaks in the number of suicides in the northern Russian city of Kirovsk over the same period.

Shumilov acknowledges that a correlation like this does not necessarily mean there is a causal link, but he points out that there have been several other studies suggesting a link between human health and geomagnetism.

For example, a 2006 review of research on cardiovascular health and disturbances in the geomagnetic field in the journal *Surveys in Geophysics* (DOI: 10.1007/s10712-006-9010-7) concluded that a link was possible and that the effects seemed to be more pronounced at high latitudes.

### Twinned peaks

The review's author, Michael Rycroft, formerly head of the European Geosciences Society, says that geomagnetic health problems affect 10 to 15% of the population.

"Others have found similar things [to Shumilov's results] in independent sets of data," says Rycroft. "It suggests something may be linking the two factors."

A 2006 Australian study, for example, also found a correlation between peaks in suicide numbers and geomagnetic activity (*Bioelectromagnetics*, vol. 27 p 155).

### Brain storms

Psychiatrists too have noticed a correlation between geomagnetic activity and suicide rates. A review of 13 years of South African data on suicides and magnetic storms in *South African Psychiatry Review*, vol. 6 p. 24) suggested a link.

Geomagnetic storms – periods of high geomagnetic activity caused by large solar flares – have also been linked to clinical depression.

In 1994, a study was published suggesting a 36.2% increase in the number of men admitted into hospital for depression in the second week after geomagnetic storms (*British Journal of Psychiatry* vol 164, p 403).

What may be the cause of the link, if there is one, remains unknown. "The intriguing correlation between geomagnetism and suicide justifies more research into its mechanism," says Rycroft.

### Environmental cue?

"The most plausible explanation for the association between geomagnetic activity and depression and suicide is that geomagnetic storms can desynchronise circadian rhythms and melatonin production," says Kelly Posner, a psychiatrist at Columbia University in the US.

The pineal gland, which regulates circadian rhythm and melatonin production, is sensitive to magnetic fields. "The circadian regulatory system depends upon repeated environmental cues to [synchronise] internal clocks," says Posner. "Magnetic fields may be one of these environmental cues."

Geomagnetic storms could disrupt body clocks, precipitating seasonal affective disorder and therefore increase suicide risk, Posner told *New Scientist*.

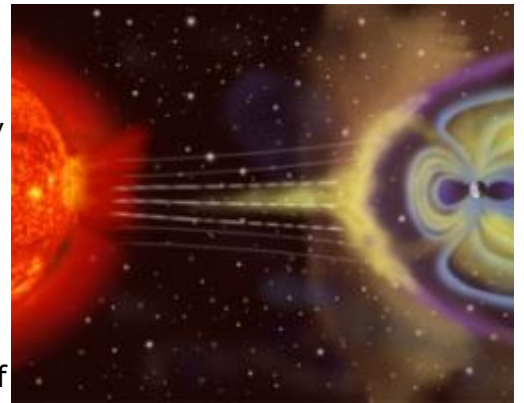
There seems little doubt that the brain responds to electromagnetic fields – coils that generate electromagnetic fields can trigger muscular twitches when placed over a person's skull.

However, Shumilov, who was presenting his data at the European Geoscience Union (EGU) annual meeting in Vienna, Austria, last week, does not believe geomagnetic activity influences everyone equally.

### Suicide statistics

He also presented hospital data from 6000 pregnant women who had routine scans of their fetus's heart rates between 1995 and 2003. In 15% of the fetuses, periods of disturbances in their heart rates coincided with periods of high geomagnetic activity.

Shumilov accepts that light levels in northern countries can influence depression, but believes that geomagnetism may be another factor, and one that is under-appreciated.



The trouble with studying the causes of suicide is that it is a rare condition, says Klaus Ebmeier, a psychiatrist at the University of Oxford. "You are bound to get spurious effects. A study of the causes would have to enrol a country's entire population."

Cosmo Hallstrom, a member of the Royal College of Psychiatrists, agrees. "You have to be very careful with suicide statistics," he says. "Countries report them differently. Catholic countries are very reluctant to diagnose suicide. Scandinavian countries consider it a social injustice not to."

### **Dull jobs really do numb the mind**

Boring jobs switch our minds to autopilot, say scientists - and it means we can seriously mess up some simple tasks.

Monotonous duties switch our brain to "rest mode", whether we like it or not, the researchers report in Proceedings of National Academy of Sciences.

They found mistakes can be predicted up to 30 seconds before we make them, by patterns in our brain activity.

The team hopes to design an early-warning brain monitor for pilots and others in "critical situations".

The scientists say the device would be particularly suitable for monotonous jobs where focus is hard to maintain - such as passport and immigration control.

#### **Mistakes 'foreshadowed'**

"We might be able to build a device (that could be placed) on the heads of people that makes these easy decisions," said Dr Eichele, of the University of Bergen, Norway.

"We can measure the signal and give feedback to the user that your brain is in the state where your decisions are not going to be the right one."



#### ***Mistakes can be predicted by patterns of brain activity***

In the study, Dr Eichele and his colleagues asked participants to repeatedly perform a "flanker task" - an experiment in which individuals must quickly respond to visual clues.

As they did so, brain scans were performed using functional magnetic resonance imaging (fMRI).

They found the participants' mistakes were "foreshadowed" by a particular pattern of brain activity.

"To our surprise, up to 30 seconds before the mistake we could detect a distinct shift in activity," said Dr Stefan Debener, of Southampton University, UK.

"The brain begins to economise, by investing less effort to complete the same task.

"We see a reduction in activity in the prefrontal cortex. At the same time, we see an increase in activity in an area which is more active in states of rest, known as the Default Mode Network (DMN)."

#### **Workplace safety**

This is not a sign of the brain going to sleep, says Debener.

"Autopilot would be a better metaphor," he explains. "We can assume that the tendency to economise task performance leads to an inappropriate reduction of effort, thus causing errors."

Since this state begins about 30 seconds prior to a mistake being made, it could be possible to design an early-warning system that alerts people to be more focused or more careful, said the researchers.

That could significantly improve workplace safety and also improve performance in key tasks, such as driving, analysis of X-rays, or airport security screening.

But MRI scanners are neither portable enough nor fast enough to be practical for these real life scenarios, so the next step is to see if more mobile EEG devices are able to detect the phenomenon.

A prototype of a wireless, mobile, and lightweight EEG amplifier is currently in development and could be ready for the market in "10 to 15 years", says Dr Debener, who is based at the MRC Institute of Hearing Research, at Royal South Hants Hospital.

"But first, we must establish what is causing these mistakes," he adds.

"We do not know whether the change in brain activity we see has a causal link to the mistakes. After we establish that, we can try to develop monitoring devices."

### **Genetic Sequencing of Protein from T. rex Bone Confirms Dinosaurs' Link to Birds** ***Study also shows mastodon link to modern elephants***

Scientists have put more meat on the theory that dinosaurs' closest living relatives are modern-day birds.

Molecular analysis, or genetic sequencing, of a 68-million-year-old Tyrannosaurus rex protein from the dinosaur's femur confirms that T. rex shares a common ancestry with chickens, ostriches, and to a lesser extent, alligators.

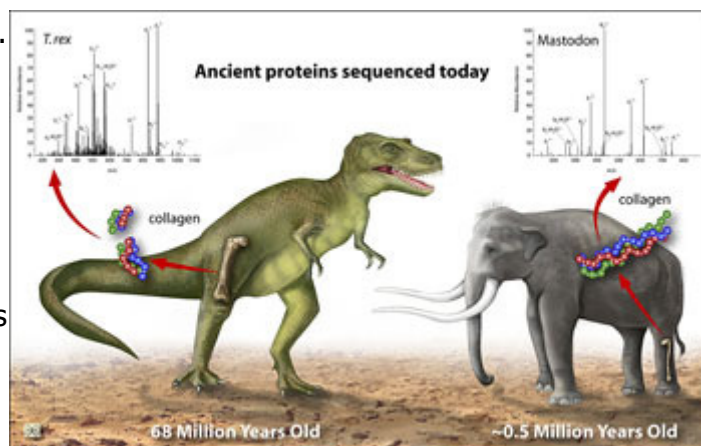


The dinosaur protein was wrested from a fossil T. rex femur discovered in 2003 by paleontologist John Horner of the Museum of the Rockies; the bone was found in a fossil-rich stretch of land in Wyoming and Montana.

The new research results, published this week in the journal Science, represent the first use of molecular data to place a non-avian dinosaur in a phylogenetic tree, a "tree of life," that traces the evolution of species.

"These results match predictions made from skeletal anatomy, providing the first molecular evidence for the evolutionary relationships of a non-avian dinosaur," says Science paper co-author Chris Organ, a researcher at Harvard University. "Even though we only had six peptides--just 89 amino acids--from T. rex, we were able to establish these relationships."

"Tests of the peptide sequences in T. rex bone fossils have confirmed that newer methods of molecular systematics agree with more traditional methods of taxonomic classification based on morphology, or shapes," says Paul Filmer, program director in the National Science Foundation (NSF)'s Division of Earth Sciences, which funded the research.



### **Genetic sequencing show link of T. rex with birds and mastodons with elephants.**

Paper co-author Mary Schweitzer of North Carolina State University (NCSU) and the North Carolina Museum of Natural Sciences first discovered the soft-tissue preservation in the T. rex bone in 2005.

The current paper builds on work reported in Science last year. In that paper, a team headed by John Asara and Lewis Cantley, both of Beth Israel Deaconess Medical Center (BIDMC) and Harvard Medical School (HMS), first captured and sequenced tiny pieces of collagen protein from T. rex.

Asara became involved in analysis of the collagen protein because of his expertise in mass spectrometry techniques capable of sequencing minute amounts of protein from human tumors.

For the current work, Organ, Asara and colleagues compared collagen protein from several dozen species. The goal: placing T. rex on the animal kingdom's family tree using molecular evidence.

"Most of the collagen sequence was obtained from protein and genome databases, but we also needed to sequence some critical organisms, including modern alligator and modern ostrich, by mass spectrometry," says Asara.

"We determined that T. rex, in fact, grouped with birds--ostrich and chicken--better than any other organism that we studied," he says. "We also showed that it groups better with birds than modern reptiles, such as alligators and green anole lizards."

While scientists have long suspected that birds, and not more basal reptiles, are dinosaurs' closest living relatives, for years that hypothesis rested largely on morphological similarities in bird and dinosaur skeletons.

The scientists also report that a similar analysis of 160,000- to 600,000-year-old collagen protein sequences derived from a mastodon bone establishes a close phylogenetic relationship between that extinct species and modern elephants.

*Organ, Asara, Schweitzer and Cantley's co-authors on the current Science paper are Wenxia Zheng of NCSU and Lisa Freimark of BIDMC.*

*The research also was funded by the National Institutes of Health, the Paul F. Glenn Foundation and the David and Lucile Packard Foundation. -NSF-*

### **Research: Early man near vanished in Africa**

**Judy Siegel-Itzkovich**, THE JERUSALEM POST Apr. 25, 2008

For a large part of its history the early human race was split into two separate species, and was so small that it likely verged on extinction, an Israeli-led genetic study has shown.

The research shows that two separate populations may have formed in the East and South of Africa, and perhaps dropped to as few as 2,000.

The study also demonstrates that DNA samples from people alive today - and not only studies of bones, archeological evidence and wall drawings - can be used to determine how the human race evolved.

The analysis - just published in the American Journal of Human Genetics and led by Dr. Doron Behar at Rambam Medical Center's laboratory of molecular medicine in Haifa and Dr. Saharon Rosset of IBM's T.J. Watson Research Center in New York and Tel Aviv University - is said to be the most extensive survey to date of African mitochondrial DNA handed down by mothers since the beginning of the human race.

"The migrations 60,000 years ago that led modern humans on their epic journeys to populate the world have been the primary focus of anthropological genetic research, but relatively little is known about the

demographic history of our species over the previous 140,000 years in Africa," Behar said. "The new study returned the focus to Africa, and in doing so refines our understanding of early modern Homo sapiens history."

"This study illustrates the extraordinary power of genetics to reveal insights into some of the key events in our species, history. Tiny bands of early humans, forced apart by harsh environmental conditions, coming back from the brink to reunite and populate the world. It was truly an epic drama, written in our DNA," said Dr. Spencer Wells, a National Geographic explorer-in-residence and director of the Genographic Project.

For the article called "The Dawn of Human Matrilineal Diversity," the researchers used blood or cheek epithelial cell samples stored in labs around the world - that included mitochondrial DNA - from some 600 people who originated in Africa. The researchers put a special focus on the Himla Soodyall indigenous people, who number in the thousands to tens of thousands and whose native language consists of clicks.

Various studies in other disciplines showed these people had many things in common, including their features and the fact that they were hunter-gatherers rather than farmers.

The 600 unrelated participants, including 38 Himla Soodyall and people from all of North Africa - including Chad, Egypt, Guinea-Bissau, Cameroon, Morocco, Tunisia and even Israeli Jews, Beduin and Druse - gave their informed consent for taking part in the research.

The researchers' analyses of the extensive genotyped data provided surprising insights into the early demographic history of human populations before they moved out of Africa. Research shows that early human populations were small and isolated both geographically and socially from each other for tens of thousands of years.

"Our aim was to document if these people descend from the oldest in the human species. It seems that their ancestors split off from other Africans between 90,000 and 150,000 years ago and were isolated due to topographical and other reasons," Behar told The Jerusalem Post on Thursday. "Small groups of hunter-gatherers looked for a good place to live in a difficult environment."

Recent paleoclimatological data suggest that eastern Africa went through a series of massive droughts between 90,000 and 135,000 years ago. It is possible, the researchers suggest, that this climatological shift contributed to the population splits. What is surprising is the length of time the populations were separate - as much as half of our entire history as a species.

The genetic split in Africa resulted in distinct populations that lived in isolation for as much as 100,000 years, the scientists say. At the time of the split - some 150,000 years ago - our species, Homo sapiens, was still confined to the African continent.

On one side of this divide were the mitochondrial lineages now found predominantly in East and West Africa, and all maternal lineages found outside Africa.

On the other side of the divide are lineages predominantly found in the Khoi and San (Khoisan) hunter-gatherer people of southern Africa.

This could have been caused by arid conditions driving a wedge between humans in eastern and southern Africa.

It would be the longest period for which modern human populations have been isolated from one another.

The isolated African groups started to meet up again with each other about 40,000 years ago, during the African Late Stone Age, and then grew in numbers and moved to an expanding area. Many archeologists believe this era heralded the beginning of fully modern human behavior, including abstract thought and complex spoken language.

Other researchers have hypothesized that during the initial isolation, about 70,000 years ago, Homo sapiens was almost wiped out, with the world population numbering as low as 2,000 people. But they banded together and survived.

The researchers were members of the Genographic Project launched in 2005 by National Geographic and IBM, with field research supported by the Waitt Family Foundation and laboratory research supported by Applied Biosystems. The aim was to use genetics as a tool to address anthropological questions on a global scale. A consortium of 10 regional scientific teams took DNA samples and analyzed them in their respective regions.

Mitochondrial DNA, inherited down the maternal line, was used to discover the age of the famous "mitochondrial Eve" in 1987, said Behar. This work has since been extended to show unequivocally that the most recent common female ancestor of everyone alive today was an African woman who lived in the past 200,000 years. Paleontology provides corroborating evidence that our species originated in Africa approximately 200,000 years ago.

"We see strong evidence of ancient population splits beginning as early as 150,000 years ago, probably giving rise to separate populations localized to eastern and southern Africa," Behar said.

While human populations had been quite small prior to the Late Stone Age, the expansion after this time led to the occupation of many previously uninhabited areas, including the world beyond Africa.

"It was only around 40,000 years ago that they became part of a single pan-African population, reunited after as much as 100,000 years apart."

Rosset said that "the analysis of such a massive dataset presents statistical and computational challenges as well as great opportunities for discovery of the events that shaped our history and genetic landscape. For example, we can see evidence of a population expansion period starting around 70,000 years ago, perhaps leading to the out-of-Africa dispersal shortly afterward."

Paleontologist Meave Leakey, a Genographic advisory board member, National Geographic explorer-in-residence and research professor at Stony Brook University in New York, said: "Who would have thought that as recently as 70,000 years ago, extremes of climate had reduced our population to such small numbers that we were on the very edge of extinction?"

### **Alexander the Great's "Crown," Shield Discovered?**

**Sara Goudarzi** for National Geographic News April 23, 2008

An ancient Greek tomb thought to have held the body of Alexander the Great's father is actually that of Alexander's half brother, researchers say.

This may mean that some of the artifacts found in the tomb—including a helmet, shield, and silver "crown"—originally belonged to Alexander the Great himself. Alexander's half brother is thought to have claimed these royal trappings after Alexander's death.

The tomb was one of three royal Macedonian burials excavated in 1977 by archaeologists working in the northern Greek village of Vergina (see map of Greece).

Excavators at the time found richly appointed graves with artifacts including a unique silver headband, an iron helmet, and a ceremonial shield, along with a panoply of weapons and an object initially identified as a scepter.

"[Archaeologists] announced that the burial in the main chamber of the large rich [tomb] was that of Philip II, father of Alexander the Great, who was assassinated in 336 B.C.," said Eugene N. Borza, professor emeritus of ancient history at Pennsylvania State University.

But recent analyses of the tombs and the paintings, pottery, and other artifacts found there, suggest that the burials are in fact one generation more recent than had previously been thought, Borza said.

"Regarding the paraphernalia we attribute to Alexander, no single item constitutes proof, but the quality of the argument increases with the quantity of information," he said.

"We believe that it is likely that this material was Alexander's. As for the dating of the tombs themselves, this is virtually certain."

#### **Tomb Mystery**

The original excavation at Vergina was led by Manolis Andronikos, an archaeologist at Greece's Aristotle University of Thessaloniki who died in 1992.

His team found the first tomb to be a simple stone box containing human remains identified as a mature male, a somewhat younger female, and a newborn.

Tomb II, a large vaulted tomb with two chambers, contained the remains of a young woman and a mature male.

Tomb III, with two vaulted chambers, was the resting place of a young teenager, most likely a male.

Both of the larger tombs contained gold, silver, and ivory ornaments, as well as ceramic and metal vessels.

"[Andronikos] presented his theories [that the tombs were those of Alexander's father and his family] with great skill, and the Greek nation responded with fervent enthusiasm," Borza said.

"Indeed I was one of those who, in two early articles in the late 1970s, accepted Andronikos' view that the remains were those of Philip II."

Borza started to doubt Andronikos' conclusions, however, as he studied the evidence.

He contacted Olga Palagia, an art historian at the University of Athens, to evaluate the tombs' construction, pottery, and paintings.

Soon the duo realized the significance of the fact that Tomb II and Tomb III were built using a curved ceilings called barrel vaults.

"The earliest securely dated barrel vault in Greece dates to the late 320s [B.C.], nearly a generation after the death of Philip II," Borza told National Geographic News.

Palagia also found that paintings on the exterior frieze of the tomb reflected themes that were likely from the age of Alexander the Great, rather than that of his father.

The paintings depict a ritual hunt scene with Asian themes, suggesting influences resulting from Alexander's extensive campaigns to the east.

## Treasures

The six-foot (two-meter) scepter found at the burial site is another clue, Borza added.

"We have several surviving coins issued in his own lifetime showing Alexander holding what appears to be a scepter of about that height," he said.

Additionally, a number of silver vessels discovered in Tomb II and Tomb III are inscribed with their ancient weights, which use a measurement system introduced by Alexander the Great a generation after Philip II's death.

"Once we have determined on archaeological grounds that Tomb II is a generation later than Philip II's death, we can then ask, Whose tomb is it?" Borza said.

"We have a double royal burial from this era attested in the ancient literature. Thus the tomb is that of [Alexander's half brother] Philip III Arrhidaeus and his queen, Adea Eurydice."

Borza and Palagia discussed their new analysis at the meeting of the Archaeological Institute of America in January. Their findings will be published in a forthcoming study from the German Archaeological Institute.

Most of the ancient artifacts found at Vergina are on display today at a museum at the site of the tombs.

## Death of Alexander

Alexander died of disease in ancient Babylon, near modern-day Baghdad, Iraq, in 323 B.C.

His generals appointed Philip III to take his place, and the half brother claimed Alexander's royal objects as public symbols to solidify his power, historians suggest.

Alexander's son, Alexander IV, who was appointed joint king along with Philip III, was assassinated around 310 B.C. He is likely buried in Vergina's Tomb III, which contains the remains of a young teenager, Borza said.

Historically, the only known Macedonian royal teenage burial is that of Alexander IV, he explained.

Alexander's father, Phillip II, is buried in Tomb I, along with his wife and their infant, according to Borza.

"Tomb I is from the age of Philip II—unlike the big chamber tombs, which are later—and the human remains of the three burials accord well with the assassinations of these individuals."

Winthrop Lindsay Adams, a professor of history at the University of Utah who was not involved with the study, said Borza's work builds on what other specialists have thought about the various aspects of the Vergina tombs.

The work of Borza and his colleagues convincingly make the case that Tomb II is the final resting place of Alexander's half brother, Adams explained.

"Indeed for most scholars working in fourth-century Macedonia, the original attribution by Andronikos now seems doubtful," he said. "This case is convincing."

## Autistic mannerisms reduced by sensory treatment

Parents of children with autism are increasingly turning to sensory integration treatment to help their children deal with the disorder, and they're seeing good results. In 2007, 71 percent of parents who pursued alternatives to traditional treatment used sensory integration methods, and 91 percent found these methods helpful.

A new study from Temple University researchers, presented this month at the American Occupational Therapy Association's 2008 conference, found that children with autistic spectrum disorders who underwent sensory integration therapy exhibited fewer autistic mannerisms compared to children who received standard treatments. Such mannerisms, including repetitive hand movements or actions, making noises, jumping or having highly restricted interests, often interfere with paying attention and learning.

The children assigned to the sensory integration intervention group also reached more goals specified by their parents and therapists, said study authors Beth Pfeiffer, Ph.D., OTR/L, BCP, and Moya Kinnealey, Ph.D., OTR/L, from the Occupational Therapy Department in Temple University's College of Health Professions. The children made progress toward goals in the areas of sensory processing/regulation, social-emotional and functional motor tasks.

Sensory integration is the ability of the brain to properly integrate and adapt to the onslaught of information coming in through the senses. Dysfunction in this area makes it difficult for people with autism to adapt to and function like others in their environment. They may be hypersensitive to sound or touch, or unable to screen out distracting noise or clothing textures. Their response might be impulsive motor acts, making noises or running away.

Pfeiffer and Kinnealey are part of a group of researchers seeking to bring more scientific understanding to occupational therapy using a sensory integration approach.

"It's been heavily documented that children on the autistic spectrum have differences in the way they process sensory information and respond motorically," Pfeiffer said. "While more families are seeking out the sensory integration approach because of its positive results, more research is needed to scientifically establish its effectiveness."



Children receiving sensory integration therapy typically participate in sensory-based activities to enable them to better regulate their behavioral responses to sensations and situations that they find disturbing or painful. A child who is oversensitive to light touch may enjoy rolling and playing in a giant foam pillow, after which he might be more able to calmly explore, touch and play with other textures. This in turn makes self-care such as dressing and washing and classroom activities that require touch more manageable.

Interpreting the child's behavior as intentional and controllable and not recognizing the underlying cause and hypersensitivities is common in educational and home settings, but is an approach that Kinnealey discourages as stressful for the child.

The study took place this past summer at a camp near Allentown, Pa., for children with autism. Participants were between the ages of 6 and 12 years old and diagnosed with autism or Pervasive Developmental Disorder–Not Otherwise Specified (PDD-NOS).

One group (17) received traditional fine motor therapy and the other group (20) received sensory integration therapy. Each child received 18 treatment sessions over a period of six weeks.

A statistician randomly assigned the participants to groups; this information was provided to the project coordinator at the site. The primary researchers were blinded to group assignment and served as evaluators before and after the study.

Parents were also blinded to the interventions that their children were assigned to and were not on site. However, there was the potential for the verbal children to talk about the activities that they participated in, which may have influenced the blinding for the parents.

For their outcome data, researchers used a series of scales that measure behavior. While both groups showed significant improvements, the children in the sensory integration group showed more progress in specific areas at the end of the study.

"This pilot study provided a foundation for how we should design randomized control trials for sensory integration interventions with larger sample sizes," Pfeiffer said. "Specifically, it identified issues with measurement such as the sensitivity of evaluation tools to measure changes in this population.

"Sensory integration treatment is a widely used intervention in occupational therapy. There is a real need for research such as randomized control trials to validate what we are doing with sensory integration in the profession," she added.

*The other presenter was Kristie Koenig, Ph.D., OTR/L, Steinhardt School of Culture, Education and Human Development, New York University. Funding was provided by Autism Speaks, which is dedicated to funding global biomedical research into the causes, prevention, treatments, and cure for autism and raising public awareness about autism and its effects on individuals, families, and society.*

### **Study shows common vitamin and other micronutrient supplements reduce risks of TB recurrence**

New findings show a link between micronutrient supplementation and reduced risk of recurrence during tuberculosis chemotherapy, according to a study published in the June 1 issue of *The Journal of Infectious Diseases*, now available online.

Nutritional assessment and support in tuberculosis therapy, once common before the advent of anti-TB drugs, is no longer an integral part of clinical therapy in most low-income countries even though poor nutrition impairs the immune system and leads to risk of further infection and relapse.

In Tanzania, Eduardo Villamor, MD, DrPH, of the Harvard School of Public Health, and a team of researchers conducted a randomized trial of micronutrients using doses of vitamins A, B-complex, C, E, and selenium or placebo in 887 patients receiving tuberculosis therapy, who were then followed for a medium of 43 months; 471 were HIV-coinfected and not receiving antiretroviral therapy and 416 were HIV-uninfected.

The study showed that micronutrient supplementation was associated with reduced rates of TB recurrence. In the study, both HIV-infected and uninfected patients with pulmonary TB who were receiving the supplements had a decreased risk of TB recurrence during the next few months after the TB culture had become negative: 45 percent overall and 63 percent in HIV-infected patients. Supplementation also reduced the incidence of peripheral neuropathy by 57 percent, irrespective of HIV status, and increased the levels of certain cells (CD3 and CD4) important in immune response in HIV-uninfected patients.

As Villamor noted, "We found that providing micronutrients to patients with tuberculosis who were undergoing anti-TB treatment appeared to decrease the risk of recurrences. This effect was stronger in patients infected with HIV than in those who were HIV-negative. This could be relevant because TB reactivation is common among HIV-infected persons." Villamor further noted, "that it will be important to find out whether micronutrients improve the outcome of TB treatment in TB-HIV co-infected patients who are undergoing antiretroviral therapy."

Christine Stabell Benn, MD, and colleagues in Copenhagen noted in their accompanying editorial that results to date relating to TB recurrence and mortality are inconsistent, with previous studies using different

dosages and combinations of micronutrients. Dr. Stabell pointed out that the promising results of the Villamor study show that further investigations are needed to develop optimal combinations of micronutrients that can be provided inexpensively in TB therapy to reduce relapses and increase survival.

**Fast Facts:**

- 1) *Supplements of common vitamins and other micronutrients may reduce the risk of recurrence in patients receiving tuberculosis treatment.*
- 2) *Further studies of micronutrient supplementation offer the potential for an inexpensive treatment strategy for vitamin-deficient tuberculosis patients in low-income countries.*
- 3) *The effects of micronutrient supplementation in TB-HIV co-infected patients undergoing antiretroviral therapy have yet to be studied.*

## Happy spamiversary! Spam reaches 30

\* 15:00 25 April 2008

\* NewScientist.com news service

\* **Kurt Kleiner**

Thirty years ago next week, Gary Thuerk, a marketer at the now-defunct computer firm Digital Equipment Corporation, sent an email to 393 users of Arpanet, the US government-run computer network that eventually became the internet. It was the first spam email ever.

That commercial message, sent on 3 May 1978, drew a swift and negative reaction. Recipients complained directly to Thuerk, who had made no attempt to hide his identity, and DEC was reprimanded by the Arpanet administrators.

Nevertheless, the email was a portent of things to come. Today, spam makes up 80 to 90% of all emails sent – around 120 billion messages per day – and is a multi-billion dollar industry.

### Spam wars

Today spammers target not just email, but also websites, blogs, social networking sites, and cellphones.

And there seems to be no end in sight, as spam-fighters struggle to keep the junk from overwhelming useful communications. Spammers and anti-spammers seem locked in an arms race. No one expects that the fight against spam will be won anytime soon, despite Bill Gates promise in 2004 that the world would be spam-free by 2006.

The first spam message was the product of a more innocent time. Thuerk sent the ad for a new computer model from his own email address, and had a co-worker type in all of the addresses by hand, says Brad Templeton, an internet pioneer, now chairman of the Electronic Frontier Foundation.

Templeton has documented the first spam on his website.

"Almost everybody who is involved in net issues got pretty interested in spam," he says. "It was the first really bad thing that people started doing on the internet, in terms of letting the small town rules break down and start abusing people."

### Spam for dummies

Spam grabbed mainstream attention in 1994, when Arizona lawyers Laurence A Canter and Martha S Siegel posted a commercial spam to 6000 Usenet discussion groups advertising their services as immigration lawyers.

The two lawyers went on to write books about how to spam, helping others start spamming too.

The first wave of spammers saw their email inboxes flooded with angry responses, and were often kicked off of their accounts by their ISPs. Canter and Siegel's book also prompted the development of the first software that aimed to detect and delete spam messages.

Spamming went underground as people quickly learned to hide their identities and locations. A cat and mouse game has ensued. Organizations like the Spamhaus Project publish lists of IP addresses known to produce spam. ISPs use the information to block email to their users from those addresses.

The latest spam filters use Bayesian filters that learn to distinguish spam using the content of emails, or systems that identify new spam through digital "fingerprints".

### Spam gets clever

Spammers have fought against these countermeasures with countermeasures of their own. To avoid being tracked down, spammers have created large "botnets" of millions of "zombie" computers – under outside control, unbeknownst to their owners.

These botnets are used to send out huge volumes of spam, which can be hard to identify and block because they are decentralized.

Spammers also tweak the contents of their spams to defeat filtering techniques. Many spams contain "word salad" – for example, extracts culled from free online books – to disguise spam messages. Other spammers constantly mutate their spam so that it can't be easily recognized using fingerprinting.

Nevertheless, spam defences do work, to an extent, says Adam O'Donnell, senior research scientist at Cloudmark, an anti-spam company based in San Francisco, California, US.

One reason so much spam is sent is that such a small proportion of it beats ISP's defenses and makes it into inboxes, he says. Spammers have to send out more just to make sure some of it gets through.

The price of spam

But while the cost to spammers remains low, ISPs and their customers pay a higher price because of the bandwidth wasted, and the cost of the filtering technology. Ferris Research, another San Francisco-based firm, estimates that the cost of fighting spam will be \$140 billion globally in 2008.

"You can buy your way out of the problem. But once you start paying money to buy your way out, it ups the ante for the spammer," O'Donnell says.

John Aycock, a computer scientist at the University of Calgary, Canada, worries that email spammers will eventually use their zombie computers to write better spam.

Programs could customize spam, he predicts, writing it in the same style, and about the same subjects, as the owner of the computer. When sent to the owner's personal contacts this technique could make spam even more difficult to detect and block.

### **New flavours of spam**

In the meantime, spammers have moved beyond email. In Asia, where internet access using cellphones is more common, phone spam is becoming more common.

On the web, automated software creates spam blogs, or "splogs," that exist entirely to host advertising. On social networking sites like Facebook or MySpace, spammers send phony "friend" requests simply so they can flood their new friends with spam messages.

The bad news is that no one thinks spam is going away anytime soon – and that new ways to communicate will always lead to new types of spam. The good news is that early predictions that spam would bring the internet grinding to a halt have not been borne out.

"So long as email is still usable, I think spam is just going to be some of the necessary background noise. I think there are enough methods that bad guys could use to continue to pump out spam for years to come that we're still going to be stuck with it for awhile," Aycock says.

### **Surprising language abilities in children with autism**

What began as an informal presentation by a clinical linguist to a group of philosophers, has led to some surprising discoveries about the communicative language abilities of people with autism.

Several years back, Robert Stainton, now a philosophy professor at The University of Western Ontario, attended a presentation by his long-time friend Jessica de Villiers, a clinical linguist now at the University of British Columbia. The topic was Autism Spectrum Disorder (ASD). De Villiers explained that many individuals with ASD have significant difficulties with what linguists call "pragmatics." That is, people with ASD often have difficulty using language appropriately in social situations. They do not make appropriate use of context or knowledge of what it would be "reasonable to say." Most glaringly, many speakers with ASD have immense trouble understanding metaphor, irony, sarcasm, and what might be intimated or presumed, but not stated.

Drawing on his philosophical training, however, Stainton noticed less-than-obvious pragmatic abilities at work in de Villiers' examples, which were drawn from transcripts of conversations with 42 speakers with ASD – abilities that had been missed by clinicians.

Thus began research to more clearly understand and define the conversational abilities and challenges of people with Autism Spectrum Disorder (ASD). Stainton and de Villiers' research, in collaboration with Peter Szatmari, a clinical psychiatrist at McMaster University, has shown that indeed, many individuals with ASD do have "a rich array of pragmatic abilities."

These researchers do not contest the well-established claim that people with ASD have difficulty with non-literal pragmatics, such as metaphors ("Juliet is the sun") or irony/sarcasm ("Boy, is that a good idea"). They have, however, found that many speakers with ASD do not show the same difficulty with literal pragmatics. An example is the phrase, "I took the subway north" from a transcript of a conversation with a research participant with ASD. The use of the word "the" could indicate there is only one subway in existence going north. "The subway" could also be referring to a subway car, a subway system or a subway tunnel. Taking account of the context and the listener's expectations, however, the individual using the phrase was able to convey the specific meaning he intended. That is, he used pragmatics effectively.

In short, Stainton and his colleagues produced surprising evidence to show that speakers with ASD use and understand pragmatics in cases of literal talk, as in the subway example.

Stainton, who is also Acting Associate Dean of Research in the Faculty of Arts and Humanities at Western, says, "It is especially gratifying and encouraging, because this is an Arts and Humanities contribution to clinical research. Without a philosophical perspective, this discovery might not have been made."

Related research allowed de Villiers and Szatmari to develop a rating scale of pragmatic abilities that can be used in the clinical assessment of people with ASD. Stainton says, "In the short term, their new tool will help identify where an individual fits on that spectrum. In the longer term, however, by making use of recent

results in philosophy of language, it may contribute to our theoretical understanding of the boundary between knowledge of the meanings of words, and non-linguistic abilities – specifically pragmatics.”

Stainton believes that both clinicians who work with people with ASD, and language theorists who are interested in pragmatics for philosophical reasons, will find these results striking.

*ASD affects approximately one in 165 people. The results of the research, conducted from a study of 42 children with autism and Asperger's Syndrome, has been published in the journal, Midwest Studies in Philosophy.*

### **Nitric oxide regulates plants as well as people**

Nitric oxide has emerged as an important signaling molecule in plants - as in mammals including people. In studies of a tropical medicinal herb as a model plant, researchers have found that nitric oxide targets a number of proteins and enzymes in plants.

In collaborative work with the research group of Renu Deswal, a faculty member, and her doctoral student at the Botany Department, University of Delhi, India, Agricultural Research Service (ARS) scientist Autar Mattoo has identified 19 such targeted proteins and enzymes in *Kalanchoe pinnata*, also known as "miracle leaf."

These proteins and enzymes are involved in regulating processes from seed germination to cell development to plant death. Notably, they also regulate many other important processes including photosynthesis, sugar metabolism, disease- and stress tolerance in plants.

Mattoo is a plant physiologist with the ARS Sustainable Agricultural Systems Laboratory at Beltsville, Md.

The collaborative research suggests that the effects of nitric oxide, a sometimes toxic byproduct of nitrogen oxidation in soil, may have broader implications in plant processes than realized. Its modification of proteins, a process called S-nitrosylation, is increasingly recognized as an ubiquitous regulatory reaction in plants and mammals.

Mattoo and Deswal have shown for the first time that nitric oxide inactivates Rubisco, a major enzyme involved in carbon dioxide fixation and photosynthesis in plants.

*Kalanchoe* represents plants that have a unique method of carbon dioxide fixation that is shared by succulent plants. *Kalanchoe* has diverse possible medicinal benefits suggesting the presence of interesting processes at work. Mattoo hopes to do similar studies with major crops grown in different production systems, with an eye toward improving both crop yields and quality, including nutritional benefits.

Other scientists have studied nitric oxide targets in the most common model plant, *Arabidopsis*. Mattoo and collaborators found that *Kalanchoe* had some nitric oxide targets in common with *Arabidopsis*, such as Rubisco and drought-protective proteins. They also found new protein targets in *Kalanchoe* that have not been reported previously.

### **Gene therapy improves vision in patients with congenital retinal disease**

#### ***Patients' vision improved from detecting hand movements to reading lines on eye chart***

In a clinical trial at The Children's Hospital of Philadelphia, researchers from The University of Pennsylvania have used gene therapy to safely restore vision in three young adults with a rare form of congenital blindness. Although the patients have not achieved normal eyesight, the preliminary results set the stage for further studies of an innovative treatment for this and possibly other retinal diseases.

An international team led by The University of Pennsylvania, The Children's Hospital of Philadelphia, the Second University of Naples and the Telethon Institute of Genetics and Medicine (both in Italy), and several other American institutions reported their findings today in an online article in the *New England Journal of Medicine*.

"This is the first gene therapy trial for a nonlethal pediatric condition," said Albert M. Maguire, M.D., Associate Professor, Department of Ophthalmology, University of Pennsylvania School of Medicine and a physician at The Children's Hospital of Philadelphia. Maguire, together with his wife, Jean Bennett, M.D., Ph.D., Professor of Ophthalmology at Penn and Senior Investigator at the F.M. Kirby Center for Molecular Ophthalmology at Penn's Scheie Eye Institute, have been researching inherited retinal degenerations such as Leber congenital amaurosis (LCA), for 18 years. LCA is a group of inherited blinding diseases that damages light receptors in the retina. It usually begins stealing sight in early childhood and causes total blindness during a patient's twenties or thirties. Currently, there is no treatment for LCA.

"Patients' vision improved from detecting hand movements to reading lines on an eye chart," Maguire added. In 2001, Bennett and Maguire were part of a team which reported successfully reversing blindness using gene therapy on dogs affected by the same naturally occurring form of congenital blindness.

The current study is sponsored by the Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia, directed by Katherine A. High, M.D. High, a study leader and an Investigator of the Howard Hughes Medical Institute, has been a pioneer in translational and clinical studies of gene therapy for genetic disease, and in 2005 initiated a collaboration with Bennett and her group to translate their exciting animal findings into a clinical study.



The scientists used a vector, a genetically engineered adeno-associated virus, to carry a normal version of the gene, called RPE65, that is mutated in one form of LCA. Three patients, ages 19, 26 and 26, received the gene therapy via a surgical procedure performed by Maguire between October 2007 and January 2008 at The Children's Hospital of Philadelphia, where the gene vector was manufactured at the hospital's Center for Cellular and Molecular Therapeutics (CCMT).

Starting two weeks after the injections, all three patients reported improved vision in the injected eye. "Standard vision tests showed significantly improved vision in the patients," said Alberto Auricchio, M.D., a study leader from the Telethon Institute of Genetics and Medicine and University of Naples Federico II. The researchers also reported that each injected eye became approximately three times more sensitive to light, and each was improved compared to the uninjected, previously better functioning eye.

The LCA gene therapy vector showed no signs of causing inflammation in the retina or other toxic side effects. One of the three patients had an adverse event, a hole in the retina that did not affect eyesight and may have been surgery-related, rather than related to biological effects of the therapeutic gene or the vector used to carry it.

The patients enrolled in the study to date were identified at the Department of Ophthalmology at the Second University of Naples, an institution with long-standing experience in collecting and studying patients with inherited retinal diseases, under the supervision of Francesca Simonelli, M.D.

Testing continued over a period of six months following the gene therapy vector administration. One patient was better able to navigate an obstacle course compared to before the injection. The patients also had less nystagmus, an involuntary movement of the eyes that is common in LCA. In the patient who experienced better vision even in the uninjected eye, the researchers suggest that the reduced nystagmus benefited both eyes.

"The current clinical trial will continue with more patients and with ongoing follow-up to monitor results," said Bennett. "We expect improvements to be more pronounced if treatment occurs in childhood, before the disease progresses."

"This result is important for the entire field of gene therapy," notes High, a past president of the American Society of Gene Therapy. "Gene transfer has been in clinical trials for over 15 years now, and although it has an excellent safety record, examples of therapeutic effect are still relatively few. The results in this study provide objective evidence of improvement in the ability to perceive light, and thus lay the groundwork for future studies in this and other retinal disorders," said High.

The pace of moving from pre-clinical discoveries into clinical trials has typically been slow in the field of gene therapy due to the breadth of expertise required, ranging from in-depth knowledge of the disorder to detailed understanding of vector design, manufacture, and pre-clinical evaluation. The complexities of regulatory oversight at both the federal and local levels also present challenges. Through the Center for Cellular and Molecular Therapeutics, The Children's Hospital of Philadelphia has developed concentrated expertise and substantial resources to facilitate the "bench to bedside" translation of gene therapy.

### **The Archimedes Codex unpeeled by modern technological sleuthing**

#### ***Deciphering latent script on ancient parchment makes curator Will Noel's job an Indiana Jones-style adventure***

**By Richard O'Mara** | Correspondent of The Christian Science Monitor

Baltimore, Md. - This is about an ancient book called The Archimedes Codex, bought for \$2.2 million in October, 1998, at an auction in New York City by an anonymous collector who sent it to the Walters Art Museum, here to be restored, conserved, and probed for its content. It was thought to contain mathematical theses conceived by the genius of Syracuse (287-212 BC), whose name it bears, ideas not found anywhere else in the world.

The Walters faced a daunting task: what arrived was a clump of folios, crushed, torn, punctured by worm holes, in the inflexible grip of old carpenter's glue, charred at its edges, and covered with mold and water stains.

It's a miracle it still exists.

It took four years just to remove the glue, and open the book sufficiently to allow experts on ancient Greek texts to access much of its content and, with the help of ultra sophisticated imaging systems, to read it.

"It was an extraordinary adventure to read the thoughts of a guy who lived over 2,000 years ago," says Will Noel, the young curator of ancient books at the Walters and leader of the nine-year restoration effort. Mr. Noel – tall, thin, buoyant, and bespectacled in a Harry Potterish way – adds: "In the field of old books nothing gets more romantic than that."

The Archimedes texts were copied in the 10th century by an unknown scribe in Constantinople, then a major center of the Christian world eventually to become a center of the Islamic world. Three centuries later, another scribe washed, scraped, and otherwise tried to remove the text from the book's parchment. This

person undid the book, rebound it in the opposite direction, then, on the imperfectly cleared pages, wrote his Christian prayers in Greek over the original text, which was also in Greek, and still discernible in a faint rust-colored thread running beneath. This procedure was common in medieval times: Parchment was scarce. Thus, the Archimedes Codex became a palimpsest, a twice-used book.

The findings gleaned from it have raised Archimedes's status as a thinker higher than anyone might have expected. Noel describes him as "the most important scientist who ever lived."

Most significant among the discoveries was the knowledge that "Archimedes was the first to calculate with actual infinity in the mathematics of the West." That is to say, he was operating at an intellectual level that didn't become common in the mathematical world until the 17th century, nearly 2,000 years after his time. The Archimedean texts, Noel writes, make the mathematics of Leonardo da Vinci "look like child's play."

"The method," the thesis of premier importance, writes Noel, "survives in the Palimpsest alone ... the Palimpsest is the only physical object in the universe to bear witness to this achievement of Archimedes."

Also found in the palimpsest, and there only, was an Archimedes treatise about an ancient game involving 14 flat pieces of various shapes that fit into a square in an uncountable number of combinations. This game, the Stomachion, possibly invented by Archimedes, reveals the beginnings of the science of combinatorics, which eventually evolved into the science of probability. Noel also regards the treatise on the Stomachion as "a major discovery."

Everyone knows Archimedes was ahead of his time. How far, no one could've imagined. He devised the mathematics for locating the center of gravity of plane figures, like triangles, then in more complicated three-dimensional shapes. He discovered the law of balance: two objects are placed on a plane, one weighing 10 pounds is placed one foot to the right of the fulcrum; the other object, weighing 2 pounds, is placed five feet to the left of the fulcrum. They balance. Why? Because their distances from the fulcrum are reciprocal to the differences in their weight, 5 to 1.

He discovered the law of the lever, based on the same principle, and allegedly boasted that with a lever long enough and a place to stand he could move the earth. No one ever proved him wrong. His mathematics had practical purposes: Engineers have been using Archimedean principles since time immemorial.

**Recently** a new book came out, also named *The Archimedes Codex*. It's a history of the palimpsest and a narration of the work done on it so far, written by Noel, and Reviel Netz, of Stanford University, among the many scholars, technicians, and curators who helped rescue the codex.

The new book recounts how the old book survived wars, floods, fires, and who knows what other cataclysms its thousand years of history exposed it to. It also describes the abuse and mutilation it suffered, mostly during modern times, sometimes for benign but wrong-headed purposes, like the glue; other times for nefarious reasons, like the four forged images of ancient scribes, painted in gold over the Archimedean text within the past 70 years in an attempt to lure buyers.

The codex dodged extinction, abiding in safe collections or languishing in parlous circumstances. In fact, Noel, and film maker John Dean traced its fateful itinerary. They started where the ideas contained in it were conceived, Syracuse, Archimedes's home in Sicily. From there they went to Istanbul (Constantinople), where Archimedes's thoughts were transcribed, certainly not for the first time. They went to St. Sabas Monastery in the Judean Desert, where the codex was kept for 300 years and where 60 folios – a third of its content – disappeared.

It eventually wound up back in Istanbul, then disappeared during the turmoil in Turkey following World War I. World War II found it in Paris, and from there its private owner brought it to New York.

Noel's essays about his pursuit of the palimpsest through the centuries reads like a mix of *Indiana Jones* (without the punch-ups) and *Casablanca* (without Ingrid Bergman).

Archimedes was a lonely genius with few contemporaries who understood his ideas. In his letters, Noel finds "a faint note of exasperation. There was no one to write to, no reader good enough." They were yet to be born: "Archimedes would eventually be read by Omar Khayyam, Leonardo da Vinci, Galileo, and Newton. He must have known he was writing for posterity."

Noel readily says that the main discovery in the palimpsest, that of Archimedes's stratospheric levels of calculation, produced in him "a fantastic sense of relief: It meant that all we had been doing here was worth it."

Noel was later staggered by the discovery of materials in the codex unconnected to Archimedes. These include commentaries about Aristotle and new information about the naval battle at Salamis in 480 BC, when the Greeks defeated the Persians and won the freedom to pursue their democratic course. The book also contains text about another of the more prominent ancients, the Greek orator Hyperides ("I'd never even heard of him before," Noel admits). He spoke out against the occupation of Athens by the Macedonians, who cut out his tongue before executing him.

And, of course, there are the Christian texts from Byzantine times, which were written over the more ancient texts. The Christian texts included "a blessing for loaves at Easter ... a prayer for repentance ... a prayer of marriage ... a prayer recited at the foundation of a church ... a prayer for the dead."

From the beginning of his experience with the codex, Noel has cultivated a simmering animosity toward the long-dead scribe who defaced the work of the great Archimedes. That changed as the perilous history of the codex was revealed, and Noel began to see the mysterious scribe's work as the very thing that shielded the texts it concealed: "I just grew up, I guess. I realized that had it not been put into this Christian disguise, it would likely have been lost."

On April 14, 1229, the day before Easter Sunday, this "unwitting savior" of the secrets of Archimedes, put down his pen and presented his work to a church in Constantinople.

On April 13, 2002, his identity was retrieved from the chaos and damage of the palimpsest's first page by ultraviolet imaging that enabled scholars to see and read the ancient characters of his name: Ionnes Myronas, a presbyter. He became one of the five people to whom Noel and Netz dedicated their book.

*Find this article at: <http://www.csmonitor.com/2008/0415/p20s01-ussc.html>*

### **Emperor Nero's gate discovered in Cologne**

The gate, found complete with 11 meters of wall, was a goods-delivery entrance to the Roman town from its river port outside on the Rhine.

Cologne, Germany -- A town gate that was probably built with a grant from Roman Emperor Nero has been discovered in Cologne, Germany during work on a new underground train line, archaeologists said.

"This is finest Roman handiwork," said Hansgerd Hellenkemper, director of the Roman museum in the city.

The gate, found complete with 11 meters of wall, was a goods-delivery entrance to the Roman town from its river port outside on the Rhine. The sturdy Roman wall protected Cologne for 1,000 years.

The city fathers have appropriated 3 million euros to preserve the site with a train line underneath and a road deck overhead.

"I'm delighted it's going to stay in the ground where it has always been," said Hellenkemper.

Recently diggers also found the bottom of a Roman wooden barge in Cologne.

The assumed Nero connection is based on the fact that the wall was built in the second half of the 1st century AD and that the city itself could not have afforded the cost. Nero's mother had been born in Cologne, so the emperor is thought to have fortified the town.

In the late Roman period, the inhabitants walled up the gate for fear of attack by the warlike Frankish tribe, using any rocks at hand including tombstones. Hellenkemper said the closure would not be undone and the gate would be left as is. DPA