

A lethal cancer knocked down by one-two drug punch

Bar Harbor, Maine – In the battle against cancer, allies can come from unexpected sources. Research at The Jackson Laboratory has yielded a new approach to treating leukemia, one that targets leukemia-proliferating cells with drugs that are already on the market.

Jackson Adjunct Professor Shaoguang Li, M.D., Ph.D., who now has a laboratory at the University of Massachusetts Medical School in Worcester, led a research team that identified a gene involved with the inflammatory response that could hold the key to treating or even preventing chronic myeloid leukemia (CML), a lethal cancer.

In research published in the journal *Nature Genetics*, the researchers also showed that an asthma medication for human patients is an effective treatment for CML in mice. The gene, *Alox5*, processes essential fatty acids to leukotrienes, which are important agents in the inflammatory response. But according to the researchers, *Alox5* has a more sinister side. It is vital to the development and maintenance of cancer stem cells.

Cancer stem cells are slow-dividing cells that are thought to give rise to a variety of cancers, including leukemia, and to be critical for maintaining them. Researchers theorize that cancer stem cells must be targeted for effective treatment of many cancers, but direct evidence is still lacking.

The researchers found that CML did not develop in mice without *Alox5* because of impaired function of leukemia stem cells. Also, *Alox5* deficiency did not affect normal stem cell function, providing the first clear differentiation between normal and cancer stem cells.

Li also treated mice with CML with Zileuton, an asthma medication that inhibits the *Alox5* inflammation pathway, as well imatinib, commonly known as Gleevec, the most effective current leukemia medication. Imatinib effectively treated CML, but Zileuton was more effective. The two drugs combined provided an even better therapeutic effect. The Jackson Laboratory is seeking patent protection on the novel approach to treat CML that Li and colleagues have demonstrated.

The exact mechanism for the *Alox5* gene in regulating the function of leukemia stem cells but not normal stem cells needs further study, but it appears that the two types of stem cells employ different pathways for self-renewal and differentiation. The findings provide a new focus of study into how leukemia stem cells are distinct from normal stem cells and how they can be targeted in cancer therapies. A future clinical trial targeting *Alox5* will provide the first anti-stem cell strategy in cancer therapy. It is likely that other cancer stem cells will have specific pathways that also differentiate them from their normal stem cell counterparts.

Li conducted the research primarily at The Jackson Laboratory, with collaborators at UMass Medical Center and the Dana-Farber Cancer Institute at Harvard in Boston.

Mobile DNA elements in woolly mammoth genome give new clues to mammalian evolution

The woolly mammoth died out several thousand years ago, but the genetic material they left behind is yielding new clues about the evolution of mammals. In a study published online in *Genome Research* (www.genome.org), scientists have analyzed the mammoth genome looking for mobile DNA elements, revealing new insights into how some of these elements arose in mammals and shaped the genome of an animal headed for extinction.

Interspersed repeats, also known as transposable elements, are DNA sequences that can "jump" around the genome, causing mutations in the host and contributing to expansion of the genome. Interspersed repeats account for a significant fraction of mammalian genomes, and some of these elements are still actively mobile. In humans, interspersed repeats account for approximately 44% of the entire genome sequence. Even more extreme is the opossum genome, where more than half of the sequence is composed of repetitive elements.

Scientists recently sequenced the woolly mammoth genome, using DNA samples obtained from preserved specimens. Dr. Stephan Schuster and his research group at Penn State University, who were involved in the sequencing and analysis of the mammoth genome, are now looking deeper into the sequence for interspersed repeats. The mammoth genome is an excellent candidate for comparative analysis of interspersed repeats in mammals, as it had a remarkably large genome of approximately 4.7 billion bases, 1.5 times larger than the human genome. Using the mammoth genome sequence and sequences of other mammals for comparison, Schuster's group found that the mammoth genome contained the largest proportion of interspersed repeats of any other mammal studied. In fact, a single class of elements, known as the BovB long interspersed repeat, accounted for nearly 12% of the mammoth genome alone.

Dr. Fangqing Zhao, a postdoctoral researcher in Schuster's group and primary author of the work, emphasized that the BovB family of repeats is particularly interesting, because while this family has been identified in other mammalian genomes, such as ruminants, snakes, opossum, and now the mammoth, its distribution in the mammalian lineage is inconsistent. Zhao explained that this finding in mammoth further

supports the hypothesis that BovB may have been acquired "horizontally," meaning that vertebrate genomes attained the element from another organism, rather than inherited from ancestors.

Many species within the Afrotheria group of mammals, which includes the woolly mammoth, are at high risk for extinction or are already extinct. "Further analyses examining if the genomes of extinct and endangered Afrotherians contain more repetitive elements than non-endangered mammals may elucidate whether there is an interplay between repetitive elements and extinction," Zhao noted, underscoring the need to study genomes of species on the brink of extinction. *Scientists from Penn State University (University Park, PA) contributed to this study. Stephan C. Schuster, Ph.D. is supported by the Gordon and Betty Moore Foundation.*

Let me sleep on it: Creative problem solving enhanced by REM sleep

Research led by a leading expert on the positive benefits of napping at the University of California, San Diego School of Medicine suggests that Rapid Eye Movement (REM) sleep enhances creative problem-solving. The findings may have important implications for how sleep, specifically REM sleep, fosters the formation of associative networks in the brain.

The study by Sara Mednick, PhD, assistant professor of psychiatry at UC San Diego and the VA San Diego Healthcare System, and first author Denise Cai, graduate student in the UC San Diego Department of Psychology, shows that REM directly enhances creative processing more than any other sleep or wake state. Their findings will be published in the June 8th online edition of the Proceedings of the National Academy of Sciences (PNAS).

"We found that – for creative problems that you've already been working on – the passage of time is enough to find solutions," said Mednick. "However, for new problems, only REM sleep enhances creativity."

Mednick added that it appears REM sleep helps achieve such solutions by stimulating associative networks, allowing the brain to make new and useful associations between unrelated ideas. Importantly, the study showed that these improvements are not due to selective memory enhancements.

A critical issue in sleep and cognition is whether improvements in behavioral performance are the result of sleep-specific enhancement or simply reduction of interference – since experiences while awake have been shown to interfere with memory consolidation. The researchers controlled for such interference effects by comparing sleep periods to quiet rest periods without any verbal input.

While evidence for the role of sleep in creative problem-solving has been looked at by prior research, underlying mechanisms such as different stages of sleep had not been explored. Using a creativity task called a Remote Associates Test (RAT), study participants were shown multiple groups of three words (for example: cookie, heart, sixteen) and asked to find a fourth word that can be associated to all three words (sweet, in this instance). Participants were tested in the morning, and again in the afternoon, after either a nap with REM sleep, one without REM or a quiet rest period. The researchers manipulated various conditions of prior exposure to elements of the creative problem, and controlled for memory.

"Participants grouped by REM sleep, non-REM sleep and quiet rest were indistinguishable on measures of memory," said Cai. "Although the quiet rest and non-REM sleep groups received the same prior exposure to the task, they displayed no improvement on the RAT test. Strikingly, however, the REM sleep group improved by almost 40 percent over their morning performances."

The authors hypothesize that the formation of associative networks from previously unassociated information in the brain, leading to creative problem-solving, is facilitated by changes to neurotransmitter systems during REM sleep.

Additional contributors to the study include Sarnoff A. Mednick, University of Southern California, Department of Psychology; Elizabeth M. Harrison, UCSD Department of Psychology; and Jennifer Kanady, UCSD Department of Psychiatry and Veterans Affairs San Diego Healthcare System, Research Service. Funding was provided by the National Institutes of Health.

Unexpected discovery can open a new chapter in the fight against tuberculosis

A close relative of the microorganism that causes tuberculosis in humans has been found to form spores. This is a sensational finding because researchers have long been convinced that these kinds of bacteria—the mycobacteria—were incapable of forming spores. Leif Kirsebom's research group at Uppsala University now has photographic proof, obtained while working with the bacteria that causes tuberculosis in fish, to challenge this long-held belief. Their discovery, which has attracted much attention from other scientists, might constitute a new turn in the fight against human tuberculosis.

"This opens a completely new chapter in mycobacteriology. Now we can perhaps understand how mycobacteria 'hibernate' and cause latent infections," says Leif Kirsebom.

To "hibernate", many types of bacteria generate spores. Anthrax bacteria are a well-known example of this. Spores are stable and can remain inactive for many years. Bacteria will often form spores when faced with harsh conditions, such as a drastic decrease in nutrition. However, the discovery that mycobacteria can produce

spores means that even this group of microorganisms has the ability to "hibernate". The Uppsala research group's pioneering discovery was completely unexpected. In fact, it was the result of a sidetrack in a study on something entirely different, RNA.

"In our studies we noticed something strange that we wondered about, but it wasn't until I received funding to take up a completely new line of research that we took the opportunity to examine more closely the strange finding that we were seeing," says Leif Kirsebom.

The microorganism that causes human tuberculosis, *Mycobacterium tuberculosis*, was identified in 1882 by the German microbiologist, Robert Koch. Every year ten million new cases of tuberculosis are diagnosed and two to three million people die of the disease. Treatment is difficult because the microorganism is becoming increasingly resistant to antibiotics. It is estimated that a third of the world's population carries the microorganism latently, without any symptoms of the disease.

"This means that the disease can break out much later, even decades after the initial infection," explains Leif Kirsebom.

Little is known about tuberculosis bacteria during this latent stage of the disease. It has been suggested that they are somehow "sleeping" or that their growth is retarded by the infected host's immune system. This lack of knowledge about how they "hibernate" applies to the other kinds mycobacteria as well. Mycobacteria are found everywhere in our environment—in groundwater and tap water, in humans and animals. Besides tuberculosis, they cause many other serious diseases, for example Buruli ulcer and leprosy in humans and Johne's disease in cattle. Even the intestinal disease, Crohn's, is believed to be linked to mycobacteria. The discovery that mycobacteria can form spores opens entirely new avenues to understanding how they "hibernate" and spread.

Scholarship on Ancient Middle East Becomes Free Digitally

A wealth of material that documents the ancient Middle East has become available through a new, free online service at the Oriental Institute of the University of Chicago. The material comes from the extensive collection at the institute, which is a major publisher of important academic books on the languages, history and cultures of the ancient Middle East.

Newswise - A wealth of material that documents the ancient Middle East has become available through a new, free online service at the Oriental Institute.

The material comes from the extensive collection at the institute, which is a major publisher of important academic books on the languages, history and cultures of the ancient Middle East. The effort began in 1906, when the University started issuing publications that have been essential for studying the past.

Since that time, more than 272 books have been published, ranging from dictionaries of the Assyrian and Hittite languages, to historical and archaeological studies and oversized folio volumes that document Egyptian temples and tombs.

Gil Stein, Director of the Oriental Institute, said, "Our publications are the lasting record of our excavations and research. They are fundamental tools for scholars of the ancient Middle East throughout the world. Making these books available to our colleagues, to educators and the public reflects our mission to share knowledge."

Books and other publications produced on the ancient Middle East by the University of Chicago are now available free on-line.

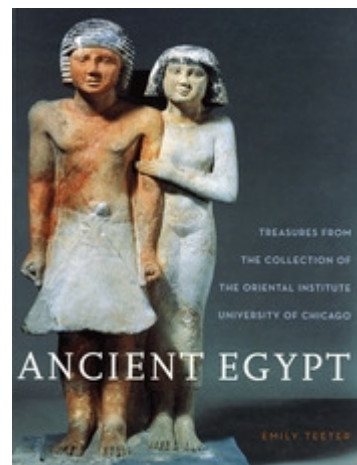
Publication of its research is a central tenet of the mission of the Oriental Institute. Equally important is making that research accessible to scholars and individuals throughout the world.

Toward that end, in October 2004, the Oriental Institute announced the Electronic Publications Initiative, which stated that all publications of the Oriental Institute would be simultaneously published in print and electronically.

New titles are made available for free download at the same time they are issued in print. Individuals, libraries and institutions may download one complimentary copy for personal use from the Oriental Institute's Web site: <https://oi.uchicago.edu/research/pubs/catalog/>.

More than a thousand copies of the Chicago Assyrian Dictionary have been downloaded since May 2008. To date, 147 Adobe PDFs (portable document files), each containing an entire book, can be accessed at the site. Many of those titles are older publications that have long been out of print. An additional 125 older titles, which comprise the institute's Egyptological collection published since the 1920s, such as the Epigraphic Survey, are being scanned in preparation for free Internet distribution.

Another 138 older titles, which document the institute's research on Anatolian, Arabic, Iranian, Mesopotamian, Syro/Palestinian cultures, among others, will continue to be scanned and distributed as time and funds permit.



Response to the EPI has been overwhelming, with positive comments received from all over the world. Complimentary Web distribution ensures that publications of the Oriental Institute, whether new or old, are made available to everyone with access to the Internet, especially in countries where the institute conducts research.

Thomas Urban, manager of the Publications Department at the Oriental Institute, said, "Technology now makes it possible for us to make these works widely available. So much effort goes into each volume - the author's original research, editorial work, artwork and photography. It is rewarding that these books, many of which are long out of print, can be consulted."

Statistics on downloads of electronic files and sales of printed books have been carefully tracked, and the Publication Sales office has noted that the availability of free downloads has not adversely impacted the sale of the printed volumes. In fact, the availability of free PDFs of titles has increased print sales. After the complimentary distribution of 21 titles - books that had not been accessible via the Internet before 2008 - print sales of those same titles increased by 7 percent compared to the previous two years.

"It seemed counterintuitive that making the electronic files available without charge would actually stimulate the sale of hard copies, but that is what we are seeing," Urban said. "We suspect that people are sampling the book through the download, then they decide they want a hard copy. This is an important message to others who are contemplating making their books available on the Internet," he added.

Print copies of the publications are available through the Oriental Institute's distributor, David Brown Books:

<http://www.oxbowbooks.com/>.

Siberian jays use complex communication to mob predators

When mobbing predators, Siberian jays use over a dozen different calls to communicate the level of danger and predator category to other members of their own group. A Swedish study from Uppsala University, published in the Proceedings of the Royal Society Biological Sciences, shows birds have evolved call systems that are as sophisticated as those of primates and meerkats.

Most prey immediately escape upon detecting a predator. However, when encountering resting predators, many prey approach and mob predators despite the associated risk. While mobbing predators, prey utter mobbing calls, which have been suggested to vary depending on risk or predator category. The new study from the Department of Ecology and Evolution, Uppsala University, shows that Siberian jays adjust their mobbing calls depending on both these factors simultaneously. According to the study, both factors matter since they determine the risk posed by the resting predator.

"The chatter of mobbing jays is rather complex. The birds use over a dozen different calls, some of which are specific for owls and other for hawks, the two main predator categories of jays," says researcher Michael Griesser.

Moreover, jays adjust their calling depending on group composition. Family groups utter much more calls than groups that only consist of unrelated individuals. The only other animal species with a comparably rich vocabulary when mobbing predators are meerkats, a small mammal that lives in large family groups.

Together with earlier published findings, this study demonstrates that Siberian jays can possess an extraordinary large "vocabulary" of over 25 different vocalisations, some of which are specific for a situation while others are uttered in various contexts.

"My study supports the idea that the need to survive encounters with predators might have played an important role for the evolution of complex animal communication," says Michael Griesser.

Not only our ancestors but also other family group living animals outwit their predators with the help of their cognitive abilities. Lowering the risk of relative of being killed benefits the propagation of the own genes through kin selection. In contrast, animals that live in anonymous groups rather rely on the selfish notion that other group members could become the target in the next predator attack, and therefore have no such communication systems.

Download and listen to the different mobbing calls at http://www.uu.se/news/news_item.php?typ=pm&id=663

Concussion experts: For kids -- no sports, no schoolwork, no text messages

International consensus defines important differences in treatment for child and adolescent concussions

WASHINGTON, DC - When it comes to concussions, children and teens require different treatment, according to international experts who recently published consensus recommendations. The British Journal of Sports Medicine's new guidelines say children and teens must be strictly monitored and activities restricted until fully healed. These restrictions include no return to the field of play, no return to school, and no cognitive activity.

The new consensus is from the International Conference on Concussion in Sports. Children's pediatric concussion expert and neuropsychologist Gerard Gioia, PhD, participated in the panel, and played a key role in delineating the differences between children, adolescents and teens, and adult athletes.

"These consensus recommendations mark the first time that international experts have focused on specialized treatment for kids," said Dr. Gioia, chief of Neuropsychology at Children's National. "This conference of experts has led the way in developing protocols for adult athletes, and now international protocols take into consideration that the developing brain of the child and adolescent requires special consideration. The guidelines also point to the important role parents, coaches, and teachers play in assessing and treating young athletes."

For children and adolescents, the guidance strongly reiterates several key points for coaches, parents, and physicians:

- * Injury to the developing brain, especially repeat concussions, may increase the risk of long term effects in children, so no return-to-play until completely symptom free.

- * No child or adolescent athlete should ever return to play on the same day of an injury - regardless of level of athletic performance.

- * Children and adolescents may need a longer period of full rest and then gradual return to normal activities than adults.

- * For children, "cognitive rest" is a key to recovery. While restrictions on physical activity restrictions are also important, cognitive rest must be carefully adhered to, including limits on cognitive stressors such as academic activities and at-home/social activities including text messaging, video games, and television watching.

The group's recommendations for children and adolescents were based on the fact that though 80 to 90 percent of adult concussions resolve in seven to 10 days, for children and adolescents, the recovery time is often longer. In all cases, the decision to "return-to-play" should be made based on the individual's progress, not a standard time period. Careful post-injury evaluation of the injured student-athlete is essential.

Bone bed tells of life along California's ancient coastline

By Robert Sanders, Media Relations | 08 June 2009

BERKELEY — In the famed Sharktooth Hill Bone Bed near Bakersfield, Calif., shark teeth as big as a hand and weighing a pound each, intermixed with copious bones from extinct seals and whales, seem to tell of a 15-million-year-old killing ground.

Yet, new research by a team of paleontologists from the University of California, Berkeley, the University of British Columbia in Vancouver, Canada, and the University of Utah paints a less catastrophic picture. Instead of a sudden die-off, the researchers say that the bone bed is a 700,000-year record of normal life and death, kept free of sediment by unusual climatic conditions between 15 million and 16 million years ago.

The team's interpretation of the fossils and the geology to establish the origins of the bone bed, the richest and most extensive marine deposit of bones in the world, are presented in the June 2009 issue of the journal *Geology*.



*Teeth such as this from the extinct 40-foot-long shark **Carcharocles megalodon** are common in the Sharktooth Hill Bone Bed because, like modern sharks, these extinct sharks also shed teeth throughout their lives.*

The mix of shark bones and teeth, turtle shells three times the size of today's leatherbacks, and ancient whale, seal, dolphin and fish skeletons, comprise a unique six-to-20-inch-thick layer of fossil bones, 10 miles of it exposed, that covers nearly 50 square miles just outside and northeast of Bakersfield.

Since the bed's discovery in the 1850s, paleontologists have battled over an obvious question: How did the bones get there? Was this a killing ground for megalodon, a 40-foot version of today's great white shark? Was it a long-term breeding area for seals and other marine mammals, like Mexico's Scammon's lagoon is for the California gray whale? Did a widespread catastrophe, like a red tide or volcanic eruption, lead to a massive die-off?

The new and extensive study of the fossils and the geology of Sharktooth Hill tells a less dramatic story, but an important one, for understanding the origin of rich fossil accumulations, said Nicholas Pyenson, a former UC Berkeley graduate student who is now a post-doctoral fellow at the University of British Columbia.

"If you look at the geology of this fossil bed, it's not intuitive how it formed," Pyenson said. "We really put together all lines of evidence, with the fossil evidence being a big part of it, to obtain a snapshot of that period of time."

Pyenson and his colleagues, totaling five UC Berkeley Ph.D.s and UC Berkeley integrative biology professor Jere Lipps, hope that the study will draw renewed attention to the bone bed, which Lipps said needs protection even though a small portion of it was added to the National Natural Landmark registry in 1976. "This deposit, if properly developed, would look just like Dinosaur National Monument," said Lipps, referring to a popular park in Colorado and Utah. "(Sharktooth Hill) is actually much more extensive, and the top of the bone bed has complete, articulated skeletons of seals and other marine mammals."

One 12-foot-long fossil seal skeleton that Lipps helped excavate during the 50 years he has visited the bone bed was mounted and displayed for decades at the Natural History Museum of Los Angeles County (NHM), which houses thousands of fossils excavated from the Sharktooth Hill deposits during expeditions in the 1960s and 1980s. Other collections are in the California Academy of Sciences, San Diego Natural History Museum, Buena Vista Museum of Natural History in Bakersfield, and UC Berkeley's Museum of Paleontology (UCMP), where students over the years have made studies of the bone bed's extinct sea turtles, sharks, marine mammals and seabirds. Lipps is a faculty curator in the UCMP.

The paper's other coauthors - all of whom obtained their Ph.D.s from UC Berkeley - are Randall B. Irmis, now an assistant professor of geology and geophysics at the University of Utah, and Lawrence G. Barnes, Edward D. Mitchell Jr. and Samuel A. McLeod of NHM's Department of Vertebrate Paleontology.

When the bone bed formed between 15,900,000 and 15,200,000 years ago, the climate was warming, sea level was at a peak, California's Central Valley was an inland sea dubbed the Temblor Sea and the emerging Sierra Nevada was shoreline. By closely studying the geology of the Sharktooth Hill area, the paleontologists determined that it was part of an underwater shelf in a large embayment, directly opposite a wide opening to the sea.

Pyenson and Irmis examined some 3,000 fossilized bone and teeth specimens in the collections of many museums, including the NHM and UCMP, and they and Lipps also cut out a meter-square section of the bone bed, complete with the rock layers above and below, and transported it to UC Berkeley for study.

Below the bone bed, they found several feet of mudstone interlaced with shrimp burrows, typical of ocean floor sediment several hundred to several thousand feet below the surface. The bone bed itself averaged 200 bones per square meter, most of them larger bones, with almost no sediment. Most were disarticulated, as if the animal carcasses had decayed and their bones had been scattered by currents.

"The bones look a bit rotten," Lipps said, "as if they lay on the seafloor for a long time and were abraded by water with sand in it." Many bones had manganese nodules and growths, which form on bones that sit for long periods in sea water before being covered by sediment.

Toward the top of the bone bed, some articulated skeletons of seals and whales were found, while in the layer above the bone bed, most skeletons were articulated and encased in sediment.

The team's conclusion is that the climatic conditions were such that currents carried sediment around the bone beds for 100,000 to 700,000 years, during which time bones remained exposed on the ocean floor and accumulated in a big and shifting pile.

Given the rarity of bones marked by shark bites, plus the occurrence of terrestrial animals such as tapirs and horses that must have washed out to sea, predation by sharks like *Carcharocles megalodon* seems unlikely to have been the major source of the bone bed, the authors wrote. Because of few young or juvenile specimens, the team also discounted the hypothesis that this was a breeding ground for early seals such as *Allodesmus*. The absence of volcanic ash makes a volcanic catastrophe unlikely, while the presence of land mammal fossils makes red tide an unlikely cause.

A reconstructed skeleton of the extinct seal Allodesmus from the Sharktooth Hill Bone Bed, now on display at the San Diego Natural History Museum.



"These animals were dying over the whole area, but no sediment deposition was going on, possibly related to rising sea levels that snuffed out silt and sand deposition or restricted it to the very near-shore environment," Pyenson said. "Once sea level started going down, then more sediment began to erode from near shore."

Pyenson noted that, while bone beds around the world occur in diverse land and marine environments, the team's analysis of the Sharktooth Hill Bone Bed could have implications for other fossil-rich marine deposits.

The work was funded by UCMP and UC Berkeley's Department of Integrative Biology, as well as by grants from the Geological Society of America and the American Museum of Natural History, and graduate fellowships from the National Science Foundation.

Common chemotherapy drug triggers fatal allergic reactions

Patients with curable early stage breast cancer died from chemotherapy solvent

CHICAGO -- A chemotherapy drug that is supposed to help save cancer patients' lives, instead resulted in life-threatening and sometimes fatal allergic reactions.

A new study from the Research on Adverse Drug Events and Reports (RADAR) pharmacovigilance program at Northwestern University Feinberg School of Medicine identified 287 unique cases of hypersensitivity reactions submitted to the FDA's Adverse Event Report System between 1997 and 2007 with 109 (38 percent) deaths in patients who received Cremophor-based paclitaxel, a solvent-administered taxane chemotherapy. The study was led by Charles Bennett, M.D., RADAR program coordinator and a professor of hematology/oncology at Northwestern's Feinberg School, and Dennis Raisch, a professor of pharmacy at the University of New Mexico. The report was presented at the 45th Annual Meeting of the American Society of Clinical Oncology held recently in Orlando, Fla.

Adverse event reports generally only represent from 1 to 10 percent of actual incidence, so the number of hypersensitivity reactions and deaths is likely significantly higher. The severe allergic reactions are believed to be caused by Cremophor, the chemical solvent - a derivative of castor oil -- that is used to dissolve some insoluble drugs before they can be injected into the blood stream.

Two patients who died from an allergic reaction had early-stage breast cancer, which had been surgically removed, and were being treated with Cremophor-containing paclitaxel to prevent the cancer from coming back. Both of these patients had received medications before the chemotherapy to reduce the risk of hypersensitivity reactions.

"The deaths of women with early-stage breast cancer are particularly disturbing because without the adverse reaction, they could have likely had 40 years of life ahead of them," Bennett said.

RADAR investigators also found that 22 percent of all fatalities occurred in patients despite patients having received premedication to prevent hypersensitivity reactions, while another 15 percent of such patients experienced life-threatening respiratory arrest.

Cremophor-containing paclitaxel has been associated with hypersensitivity reactions, with responses ranging from mild skin conditions to more severe effects, including anaphylaxis and cardiac collapse. Current U.S. product labeling for Cremophor containing paclitaxel includes a black-box warning alerting physicians and patients of potential toxicity and recommending the use of corticosteroids and other medications before chemotherapy administration to reduce the risk of hypersensitivity reactions.

"The results of our review suggest that physicians should be vigilant in monitoring the safety of their patients undergoing chemotherapy treatment," said Bennett, who also is the A.C. Buehler Professor in Economics and Aging at the Feinberg School and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

"Patients receiving Cremophor-based paclitaxel should be given medications to prevent hypersensitivity reactions, but what is sobering, as the study has shown and as the black-box warning indicates, women suffer anaphylaxis despite receiving steroid premedication," Bennett said. "Physicians should be diligent in reporting adverse events to regulatory agencies to better monitor the impact of Cremophor on patient safety. Physicians may also want to consider exploring other alternative chemotherapy options that do not include Cremophor."

In addition to the two women with early-stage breast cancer who died after treatment with the Cremophor-based paclitaxel, four other women with early-stage breast cancer experienced life-threatening anaphylaxis reactions. Each of them had received prior medications to prevent the reactions.

"The fatal outcomes observed in patients with early-stage breast cancer were particularly striking as this is a patient population with a good prognosis that is generally treated with curative intent," said Raisch.

For the report, Bennett and Raisch reviewed adverse event reports submitted to regulatory agencies in the U.S., Europe and Japan. The most common cancer diagnosis for these patients with allergic reactions was lung cancer followed by breast cancer and ovarian cancer.

Self-regulation game predicts kindergarten achievement

CORVALLIS, Ore. -- Early childhood development researchers have discovered that a simple, five-minute self-regulation game not only can predict end-of-year achievement in math, literacy and vocabulary, but also was associated with the equivalent of several months of additional learning in kindergarten.

Claire Ponitz from the University of Virginia and Megan McClelland of Oregon State University assessed the effectiveness of a game called the Head-Toes-Knees-Shoulders (HTKS) task, which is a new version of the

Head-to-Toes task developed by researchers at the University of Michigan. Both tasks have proved effective at predicting academic skills among preschool age children. Their results were published in the newest issue of the journal, *Developmental Psychology*.

The researchers assessed a group of 343 kindergarteners from Oregon and Michigan. Their self-regulation, or ability to control behavior, was measured with the Head-Toes-Knees-Shoulders task, a structured observation requiring children to perform the opposite of a response to four different oral commands. For example, children were instructed to touch their toes if told to touch their head, and vice versa.

They found that students who performed well on his behavior task in the fall achieved strong scores in reading, vocabulary and math in the spring, compared to students who had low performance on the task. In addition, the research showed that the children who performed well on the task scored 3.4 months ahead of peers who performed at average levels on mathematics learning.

"It's amazing that this game works as well as it does," McClelland said. "It is simple to administer, fun for the kids, and predicts children's academic achievement."

One area where the task did not make a difference was assessing children's interpersonal skills. McClelland explained that the game is not "emotion-oriented," meaning it is not set up to trigger an emotional response. Instead, the Head-Toes-Knees-Shoulders task tests children on important classroom-related behavior such as listening, following directions and remembering instructions. "We know this task predicts end-of-year achievement," she said. "Now we want to take the game to the next level."

McClelland is planning to do an extensive evaluation of the task for her next research project, testing the task with an even larger group of children. She also has a number of research projects under way with OSU graduate students, including one that uses a variety of fun games to improve a child's ability to regulate their behavior.

She said she has made a simple DVD that demonstrates the task, and in response has received requests from around the world from researchers who want to use the task with young children.

"The evidence strongly suggests that improving self-regulation is directly related to academic achievement and behavior," McClelland said. "If we can make a difference early in a child's life, they have that much more of a chance at success."

J.S. Matthews and Frederick Morrison from the University of Michigan contributed to this research, which was funded by a grant from the Department of Education and National Institutes of Health's National Institute of Child Health and Human Development. For the past two years, Ponitz's work has been funded through an Institute for Education Sciences Postdoctoral training grant to the University of Virginia.

Stopping diabetes damage with vitamin C

First test in humans gets dramatic results from blood sugar control and antioxidant

Researchers at the Harold Hamm Oklahoma Diabetes Center have found a way to stop the damage caused by Type 1 diabetes with the combination of insulin and a common vitamin found in most medicine cabinets.

While neither therapy produced desired results when used alone, the combination of insulin to control blood sugar together with the use of Vitamin C, stopped blood vessel damage caused by the disease in patients with poor glucose control. The findings appear this week in the *Journal of Clinical Endocrinology and Metabolism*.

"We had tested this theory on research models, but this is the first time anyone has shown the therapy's effectiveness in people," said Michael Ihnat, Ph.D., principal investigator and a pharmacologist at the OU College of Medicine Department of Cell Biology.

Ihnat said they are now studying the therapy in patients with Type 2 diabetes.

The goal of the work being done by Ihnat and British scientists from the University of Warwick led by Dr. Antonio Ceriello is to find a way to stop the damage to blood vessels that is caused by diabetes. The damage, known as endothelial dysfunction, is associated with most forms of cardiovascular disease such as hypertension, coronary artery disease, chronic heart failure, peripheral artery disease, diabetes and chronic renal failure.

By reducing or stopping the damage, patients with diabetes could avoid some of the painful and fatal consequences of the disease that include heart disease, reduced circulation and amputation, kidney disease and diabetic retinopathy, which can lead to blindness.

Insulin and many other drugs have long been used to control blood sugar, but Ihnat – in an earlier project with scientists in Italy and Hungary – found that cells have a "memory" that causes damage to continue even when blood sugar is controlled. By adding antioxidants like Vitamin C, Ihnat found that cell "memory" disappeared and cell function and oxidation stress were normalized.

"We have speculated that this happens with endothelial dysfunction, but we did not know until now if it was effective in humans. We finally were able to test it and proved it to be true," Ihnat said. "For patients with diabetes, this means simply getting their glucose under control is not enough. An antioxidant-based therapy

combined with glucose control will give patients more of an advantage and lessen the chance of complications with diabetes."

While researchers do suggest diabetic patients eat foods and take multivitamins rich in antioxidants like Vitamin C, they warn that additional study is needed. The Vitamin C utilized in their study was given at very high doses and administered directly into the blood stream, so it is unlikely someone would get similar results with an over-the-counter vitamin supplement.

The team is now working to determine how antioxidants work at the molecular level to halt the destructive chain reaction set in motion by high blood sugar levels. In addition, they are evaluating several other antioxidants with an ultimate hope that their work will translate into simple, effective and inexpensive treatments for the control of diabetes.

The Journal of Clinical Endocrinology & Metabolism is the world's leading peer-reviewed journal for endocrine clinical research and cutting-edge clinical practice reviews.

Dr. Ihnat's latest work, which is funded by the VA Medical Center, can be found online at <http://jcem.endojournals.org/cgi/content/abstract/jc.2009-0762v1>.

Personal Health

Well-Chosen Words in the Doctor's Office

By JANE E. BRODY

What do you want from your doctor, especially if you have a serious or life-threatening illness?

Researchers who conducted interviews a few years ago with 192 patients at the Mayo Clinics in Scottsdale, Ariz., and Rochester, Minn., identified seven "ideal physician behaviors." Patients want their doctors to be "confident, empathetic, humane, personal, forthright, respectful and thorough," the researchers wrote in Mayo Clinic Proceedings in 2006.

At the same time, of course, patients want their health problems properly diagnosed and competently treated. How, in the course of the 15 minutes that the typical patient gets to spend with a doctor, can all this happen?

With doctors increasingly pressed for time, how can they offer both the clinical expertise and the compassionate care that all patients deserve? And what can patients do to get what they most want from their doctors?

Building Trust

In her new book, "Only 10 Seconds to Care: Help and Hope for Busy Clinicians" (ACP Press), Dr. Wendy Schlessel Harpham combines her experience as an internist and her nearly 18 years of experience as a cancer patient to show how simple actions and well-chosen words on the part of medical professionals can make an enormous difference in a patient's emotional and physical well-being.

Dr. Walter F. Baile, a psychiatrist at the M. D. Anderson Cancer Center in Houston, said in an interview that the book was replete with "clinical pearls - succinct ways that physicians can affect patients' well-being and make them feel supported." Building a patient's trust and confidence, he said, is healing.

Many studies have shown that when doctors provide compassionate care, that increases the likelihood that patients will follow medical advice and practice self-care, which in turn reduces complications and their need for repeated treatments and costly hospitalizations.

Larry B. Mauksch, a specialist in doctor-patient communication in the department of family medicine at the University of Washington in Seattle, urges doctors to build rapport with their patients by greeting them warmly by name, asking briefly about important events in their lives, maintaining eye contact, focusing on the patient without interruptions, and displaying empathy through words and body language.

To make the most of each visit, Mr. Mauksch suggested that doctors first ask about patients' concerns and then focus on just one or two of their most pressing medical problems, saving others for later visits.

Keeping Hope Alive

In her book, Dr. Harpham writes that dealing with patients' emotions "is a vital task for healthcare professionals." She applauds the response of an oncologist who said, after the first of many recurrences of her cancer, "I can only imagine what this feels like, but I'll do all I can to help you."

Dr. Baile cautions doctors against trying to "fix" the emotion when bad news upsets a patient. Rather, he said, "they should empathize and align with the patient and say something like: 'I can see you weren't expecting this news. I understand that you're upset by it. I'm disappointed too that we didn't get a better response to the treatment.' "

Dr. Harpham said there was a world of difference between "if" and "when" in discussing the chance that cancer will recur. The word "when" is a prediction of doom that can make it difficult or impossible for patients to find joy, she said.

“In contrast,” she writes, “a prognosis preceded by ‘if’ introduces uncertainty. This hint of possibility encourages patients to strive for a balance of hope and acceptance that helps them work and play, laugh and love in the face of a fragile future. For patients to be free to find the balance that helps them live, the door must be left open for them to find hope.”

Rather than focus solely on the expected outcome when a prognosis is dismal, Dr. Harpham urges doctors to “share both your expectations and your hopes with your patients.” She says that “people can expect one thing and hope for another” and reminds health professionals that they are “obligated never to extinguish hope.”

She concludes, “We foster hope by telling patients that we are prepared to care for them through the likely outcome and are hoping they make an unexpected and inexplicable recovery that proves our prognosis wrong.”

As Mr. Mauksch put it, “The physician’s commitment is not just to cure but also to care.”

For physicians who need help in developing effective communication skills, Dr. Baile’s medical center has created a video library at www.mdanderson.org/icare.

How Patients Can Help

Because time is short in any medical visit, it is often up to patients to prepare by writing down their most pressing concerns and questions.

Dr. Baile advises patients to gather some information about their disease and its treatment before seeing the doctor, but not to “oversearch.” Too many statistics and case histories can be overwhelming, and all that information is useful only to a point: each case is different, and each patient is different.

Patients should ask the doctor in advance whether they can record the conversation. It is also helpful to take along a relative or friend who can take notes and ask relevant questions. One study found that when patients had someone to help them talk with their doctor, they were more satisfied with the information they got and with the doctor’s interpersonal skills.

Mr. Mauksch said patients could help set an agenda for a medical visit by saying upfront, “I need you to know what I’m going through and what my questions are.” If not, he said, doctors will fill the time with information that is not necessarily what concerns the patient, who may be more worried about how she will look after treatment than about details of the pathology report.

Before leaving the doctor’s office, patients should make sure they understand the instructions and treatment plan, including what they should do to take care of themselves and when they should contact the doctor about side effects or new developments.

For questions that come up after a visit, Dr. Baile suggested that patients ask about the best way to contact the doctor. Many doctors today communicate through e-mail; others use nurses or midlevel practitioners, he said.

Most important of all, perhaps, is for patients to be honest and forthright. Too often, patients withhold critical information or lie because the truth is embarrassing or because they don’t want to disappoint the doctor by admitting that they did not follow the advice or the precise treatment plan.

Parasite may increase your odds of an auto accident

* 09 June 2009 by **Debora MacKenzie**

IF YOU lack a certain protein on your blood cells and are infected with a common parasite, you may be more likely to crash your car.

Toxoplasma, or toxo for short, starts its life cycle in rodents. To spread, it manipulates rodents' brains, making them reckless and more likely to be eaten by cats, which then pass on the parasite through their faeces. People can catch it from eating undercooked meat from animals that had contact with cat faeces. The infection lasts for life.

It can harm fetuses, but was otherwise thought to be harmless. Recently, however, evidence has emerged that the parasite can affect our brain. People with toxo seem to have slower reactions, while those who have had traffic accidents are more likely to have toxo.

Now it seems toxo's effect on the brain may be limited to people with a certain blood type. Jaroslav Flegr and colleagues at Charles University in Prague, Czech Republic, had previously discovered that toxo affected reaction times mostly in people whose blood type was rhesus negative. So they monitored 3890 military drivers for 18 months. Those who were Rh-negative and had toxo were 2.5 times as likely to have an accident as uninfected drivers who were Rh-negative, or any Rh-positive drivers (BMC Infectious Diseases, DOI: 10.1186/1471-2334-9-72).

People who are Rh-negative lack a protein on the surface of their blood cells. Flegr says he doesn't know why toxo's effect on the brain should be determined by this protein.

Flegr says these results suggest that between 400,000 and a million of the world's annual road deaths might be due to toxo infection. He suggests regularly testing Rh-negative pilots, air traffic controllers and truck drivers for the infection.

Joanne Webster of Imperial College London says the work indicates that *Toxoplasma* does indeed alter human behaviour, but that studies must now be done on a larger number of people.

Discovery raises new doubts about dinosaur-bird links

CORVALLIS, Ore. – Researchers at Oregon State University have made a fundamental new discovery about how birds breathe and have a lung capacity that allows for flight – and the finding means it's unlikely that birds descended from any known theropod dinosaurs.

The conclusions add to other evolving evidence that may finally force many paleontologists to reconsider their long-held belief that modern birds are the direct descendants of ancient, meat-eating dinosaurs, OSU researchers say.

"It's really kind of amazing that after centuries of studying birds and flight we still didn't understand a basic aspect of bird biology," said John Ruben, an OSU professor of zoology. "This discovery probably means that birds evolved on a parallel path alongside dinosaurs, starting that process before most dinosaur species even existed." These studies were just published in *The Journal of Morphology*, and were funded by the National Science Foundation.

It's been known for decades that the femur, or thigh bone in birds is largely fixed and makes birds into "knee runners," unlike virtually all other land animals, the OSU experts say. What was just discovered, however, is that it's this fixed position of bird bones and musculature that keeps their air-sac lung from collapsing when the bird inhales.

Warm-blooded birds need about 20 times more oxygen than cold-blooded reptiles, and have evolved a unique lung structure that allows for a high rate of gas exchange and high activity level. Their unusual thigh complex is what helps support the lung and prevent its collapse.

"This is fundamental to bird physiology," said Devon Quick, an OSU instructor of zoology who completed this work as part of her doctoral studies. "It's really strange that no one realized this before. The position of the thigh bone and muscles in birds is critical to their lung function, which in turn is what gives them enough lung capacity for flight."

However, every other animal that has walked on land, the scientists said, has a moveable thigh bone that is involved in their motion – including humans, elephants, dogs, lizards and – in the ancient past – dinosaurs.

The implication, the researchers said, is that birds almost certainly did not descend from theropod dinosaurs, such as tyrannosaurus or allosaurus. The findings add to a growing body of evidence in the past two decades that challenge some of the most widely-held beliefs about animal evolution.

"For one thing, birds are found earlier in the fossil record than the dinosaurs they are supposed to have descended from," Ruben said. "That's a pretty serious problem, and there are other inconsistencies with the bird-from-dinosaur theories. "But one of the primary reasons many scientists kept pointing to birds as having descended from dinosaurs was similarities in their lungs," Ruben said.

"However, theropod dinosaurs had a moving femur and therefore could not have had a lung that worked like that in birds. Their abdominal air sac, if they had one, would have collapsed. That undercuts a critical piece of supporting evidence for the dinosaur-bird link.

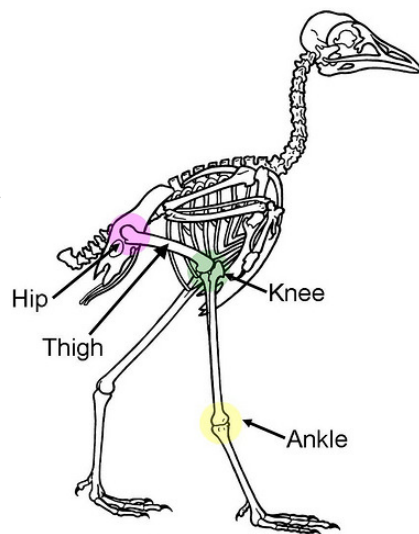
"A velociraptor did not just sprout feathers at some point and fly off into the sunset," Ruben said.

The newest findings, the researchers said, are more consistent with birds having evolved separately from dinosaurs and developing their own unique characteristics, including feathers, wings and a unique lung and locomotion system.

There are some similarities between birds and dinosaurs, and it is possible, they said, that birds and dinosaurs may have shared a common ancestor, such as the small, reptilian "thecondonts," which may then have evolved on separate evolutionary paths into birds, crocodiles and dinosaurs. The lung structure and physiology of crocodiles, in fact, is much more similar to dinosaurs than it is to birds.

"During walking and running in birds, hindlimb movement is generated primarily at the knee and ankle joints; in humans, movement occurs at the knee, ankle and hip joints. The bird's thigh does not move substantially from its nearly horizontal position where it provides rigid lateral support to the thin walled air-sacs of the respiratory system."

"We aren't suggesting that dinosaurs and birds may not have had a common ancestor somewhere in the distant past," Quick said. "That's quite possible and is routinely found in evolution. It just seems pretty clear



now that birds were evolving all along on their own and did not descend directly from the theropod dinosaurs, which lived many millions of years later."

OSU research on avian biology and physiology was among the first in the nation to begin calling into question the dinosaur-bird link since the 1990s. Other findings have been made since then, at OSU and other institutions, which also raise doubts. But old theories die hard, Ruben said, especially when it comes to some of the most distinctive and romanticized animal species in world history.

"Frankly, there's a lot of museum politics involved in this, a lot of careers committed to a particular point of view even if new scientific evidence raises questions," Ruben said. In some museum displays, he said, the birds-descended-from-dinosaurs evolutionary theory has been portrayed as a largely accepted fact, with an asterisk pointing out in small type that "some scientists disagree."

"Our work at OSU used to be pretty much the only asterisk they were talking about," Ruben said. "But now there are more asterisks all the time. That's part of the process of science."

Editor's Note: The publication this story is based on can be found on the web at <http://www3.interscience.wiley.com/cgi-bin/fulltext/122395783/PDFSTART> and an image of a bird skeleton to illustrate the story is available at: <http://www.flickr.com/photos/33247428@N08/3608028849/>

New antibiotics could come from a DNA binding compound that kills bacteria in 2 minutes

A synthetic DNA binding compound has proved surprisingly effective at binding to the DNA of bacteria and killing all the bacteria it touched within two minutes. The DNA binding properties of the compound were first discovered in the Department of Chemistry at the University of Warwick by Professor Mike Hannon and Professor Alison Rodger (Professor Mike Hannon is now at the University of Birmingham). However the strength of its antibiotic powers have now made it a compound of high interest for University of Warwick researchers working on the development of novel antibiotics.

Dr Adair Richards from the University of Warwick said:

"This research will assist the design of new compounds that can attack bacteria in a highly effective way which gets around the methods bacteria have developed to resist our current antibacterial drugs. As this antibiotic compound operates by targeting DNA, it should avoid all current resistance mechanisms of multi-resistant bacteria such as MRSA."

The compound $[\text{Fe}_2\text{L}_3]^{4+}$ is an iron triple helicate with three organic strands wrapped around two iron centres to give a helix which looks cylindrical in shape and neatly fits within the major groove of a DNA helix. It is about the same size as the parts of a protein that recognise and bind with particular sequences of DNA. The high positive charge of the compound enhances its ability to bind to DNA which is negatively charged.

When the iron-helicate binds to the major groove of DNA it coils the DNA so that it is no longer available to bind to anything else and is not able to drive biological or chemical processes. Initially the researchers focused on the application of this useful property for targeting the DNA of cancer cells as it could bind to, coil up and shut down the cancer cell's DNA either killing the cell or stopping it replicate. However the team quickly realised that it might also be a very clever way of targeting drug-resistant bacteria.

New research at the University of Warwick, led by Dr Adair Richards and Dr Albert Bolhuis, has now found that the $[\text{Fe}_2\text{L}_3]^{4+}$ does indeed have a powerful effect on bacteria. When introduced to two test bacteria *Bacillus subtilis* and *E. coli* they found that it quickly bound to the bacteria's DNA and killed virtually every cell within two minutes of being introduced - though the concentration required for this is high.

Professor Alison Rodger, Professor of Biophysical Chemistry at the University of Warwick, said:

"We were surprised at how quickly this compound killed bacteria and these results make this compound a key lead compound for researchers working on the development of novel antibiotics to target drug resistant bacteria."

The researchers will next try and understand how and why the compound can cross the bacteria cell wall and membranes. They plan to test a wide range of compounds to look for relatives of the iron helicate that have the same mechanism for action in collaboration with researchers around the world.

Professor Mike Hannon from the University of Birmingham said: "This research is a great example of how the Universities of Birmingham and Warwick are working together to deliver exciting new research that can impact on medicine and healthcare - key themes of the AWM "Birmingham Science City" initiative which seeks to make the West Midlands the leading player in science and technology in the UK."

*The research has just been published in the International Journal of Antimicrobial Agents in a paper entitled **Antimicrobial activity of an iron triple helicate** by Dr Adair D. Richards, and Professor Alison Rodger from the University of Warwick, Professor Michael J. Hannon from the University of Birmingham and Dr Albert Bolhuis from Bath University. Issue 33 pp469-472 [http://www.ijaaonline.com/article/S0924-8579\(08\)00577-3](http://www.ijaaonline.com/article/S0924-8579(08)00577-3)*

Botox injections can significantly improve quality of life for people with overactive bladders

Botox is well known for its cosmetic uses, but researchers have now found that it can also significantly improve people's quality of life if they suffer from another problem that increases with age, an overactive bladder (OAB). A study published in the June issue of *BJU International* shows that patients who had Botox injections to control bladder problems reported significant improvements in their lives as well as their symptoms for at least 24 weeks.

UK urologists from Guy's Hospital and King's College London carried out a randomised, double-blind placebo trial on 34 patients with an average age of 50. Seven men and nine women received the Botox injections while eight men and ten women received the placebo.

"The Botox or placebo injections were administered using a flexible injection needle inside a cystoscope, a long tube that enables urologists to see inside the bladder" explains consultant urological surgeon Prokar Dasgupta from Guy's Hospital and King's College London School of Medicine.

"This minimally invasive technique involved 20 injections – five in the midline posterior bladder wall, five in the left lateral wall, five in the right lateral wall and five across the dome of the bladder. In all, 200ml of Botox or placebo was administered."

Patients in both groups were assessed when they started the study and at four, 12 and 24 weeks after they received the injection. All the patients who took part in the study had failed to tolerate or respond to anticholinergic drugs, which, along with lifestyle modifications and bladder training, are traditionally used to manage OAB.

Patients who received the Botox injections reported significant improvements when it came to a number of quality of life factors. These were measured using the King's Health Questionnaire, a zero to 100 scale, which was developed in the late 1990s to assess women with urinary incontinence. High scores recorded on the scale indicate a lower quality of life. All the factors the researchers studied showed a reduction.

The median (mid point) improvements from baseline to 12 weeks were:

* Incontinence impact – from 100 to 65	* Emotions – from 100 to 65
* Role limitations – from 83 to 50	* Severity measures – from 67 to 34
* Physical limitations – from 75 to 42	* Sleep/energy – from 83 to 58
* Social limitations - from 72 to 39	* Personal relationships – from 67 to 50.

Symptom severity in the Botox group fell from 17 to 12 when it was measured on a zero to 30 scale.

The only improvement in the placebo group was role limitations, from a median level of 83 to 66. The rest of the categories showed no improvement.

At 12 weeks the study was unblinded so that both the clinicians and patients knew who was receiving the Botox injections. Further improvements were noted in all categories during this extended period, including sleep and energy and personal relationships, which had not performed as well as the other categories in the first 12 weeks.

Previous research has shown that as many as one in six people over the age of 40 suffer from an overactive bladder and that the condition can have a very adverse affect on people's quality of life.

"Our study showed a significant relationship between the overall improvement in OAB symptoms and improved quality of life scores" says Mr Dasgupta.

"For example, at four weeks urgency and urge urinary incontinence were statistically correlated with improvements in quality of life and the same was true at 12 weeks for frequency and urgency.

"The overall benefits lasted at least 24 weeks after the injections were administered, with patients reporting both a reduction in bothersome bladder symptoms and an improved quality of life."

Notes to editors Improvement in quality of life after botulinum toxin-A injections for idiopathic detrusor overactivity: results from a randomised double-blind placebo-controlled trial. Sahai et al. *BJU International*. 103, 1509-1515. (June 2009)

Archaeological dating by re-firing ancient pots

Researchers in the UK have created a new way of dating archaeological artefacts that involves heating ancient pots to unlock their internal clocks. The relatively simple technique could become as important for dating ceramics as carbon dating is for organic materials, say the researchers at the Universities of Manchester and Edinburgh. The team has already dated ceramics from the Roman, medieval and modern periods to a high degree of accuracy, and they are now looking to establish a global research facility for the technique.

The method relies on the fact that fired clay ceramics - like bricks, tile and pottery - start to chemically combine with water as soon as they are exposed to the atmosphere. A big breakthrough came in 2003 when the researchers realized that this process has occurred at a predictable rate throughout history, related to

temperatures. Now the researchers have turned their theory into a practical dating method and present their findings in Proceedings of the Royal Society A.

Moira Wilson of the University of Manchester and her team document how “rehydroxlation dating” has so far dated objects up to 2000 years old, and they believe it could extend back as far as 10,000 years. “Given the number and intensity of [dating] debates in archaeology, there is a huge gap in the field for this,” Wilson told physicsworld.com.

Slow chemical process

Wilson was quick to point out that the water uptake in rehydroxlation is not the same as absorption — it is a much slower chemical process. The researchers established that the rate at which ceramic materials gain extra water in this process obeys a (time)^{1/4} power law. They calculated that the rate of reaction is independent of atmospheric moisture levels but is governed by the ambient temperature averaged over a ceramic’s lifetime.

The dating procedure involves measuring the mass of a sample of ceramic and then heating it to around 500 degrees Celsius in a furnace, which removes the water. The re-fired ceramic is then weighed immediately, using a highly accurate microbalance, to determine precisely the rate of water recombination. Once the rate is known, the age of the artefact can be extrapolated. “There are no loose ends with this - everything ties in,” said Wilson.



Lancashire hotpots: 500°C until all the water has gone

The researchers dated a Roman brick, known to be 2001, as 2000 years old. They also tested a “mystery brick”, with the real age revealed to them only after their testing was completed — they got 340 years, and its known age was 339 to 344. An interesting thing occurred when they tested their technique on a medieval brick from Canterbury: after repeated testing dated it at 66 years, they realized that the intense heat generated during a Second World War blitz had re-fired the brick and effectively reset its clock.

Self-calibrating

At present, the most widely used alternative technique is thermoluminescence, which involves measuring the amount of light given off by a sample because this is related to the dose of radiation an artefact has received across its lifetime. One of the limitations is that it requires a lot of extra information about the archaeological site such as radiation levels, which may not be accessible if artefacts have already been sitting in a museum for many years. Perhaps the most significant feature of this new water-based technique is that - as with radiocarbon dating - it is self-calibrating, based on rehydroxylation alone.

“The time-dependent processes that they have studied looks very interesting,” said Ian Bailiff, an archaeologist at Durham University in the UK. However, Bailiff is a bit sceptical about the reliability of historic temperature records. “The devil is likely to be in the detail - the chronometric mechanism is temperature dependent, and much work may need to be done to obtain calibration data.”

The researchers are now planning to test whether their dating technique can be applied to earthenware, bone china and porcelain. Wilson told physicsworld.com that one of the main difficulties so far has been getting access to ceramics from museums and collectors who are yet to be convinced by the new technique. She believes this situation will improve if her team can establish an international research centre in the UK - she is currently looking into ways of achieving this. *About the author: James Dacey is a reporter for physicsworld.com*

Q & A

A Charley Horse in Bed

By C. CLAIBORNE RAY

Q. Why does one get muscle cramps while sleeping or resting?

A. In most cases, there is no apparent cause for hard knots in the muscles, usually in the calves, that are not associated with vigorous exercise, medical authorities say. Nighttime attacks of leg cramps are quite common, especially in older people, and can be very painful though usually not dangerous.

Most night cramps are not associated with serious underlying diseases, but diabetes and circulatory problems are among the conditions that should be ruled out by a doctor, especially if the cramps are frequent and severe. Cramping can also be a side effect of some prescription drugs.

One popular suggested explanation for the involuntary contractions involves overactive nerve networks in the large leg muscles, but there is no conclusive evidence as to whether this is true or what the cause may be.



Victoria Roberts

Other researchers suggest that cramps are an effect of dehydration, which is known to be involved in spasms after exercise. Common sense suggests drinking enough water through the day and before going to bed, as well as avoiding heavy bed covers that keep the toes from pointing up. Gentle stretching exercises may help.

If you develop a cramp, you can help relax the knotted muscle with gentle stretching and massage; walking or standing if you can manage it; and perhaps a warm bath or shower.

Work of Field Museum scientist addresses question of chance in evolution

As Darwin observed, natural selection leading to adaptation of individuals and populations is occurring gradually and all the time. But over very long spans of time, the major channels of genetic organization, organism form, and the different ways organisms develop arose as outcomes of history-dependent variation that is now channeled, or constrained, within different groups of organisms. For example, most cats look like cats, develop like cats, but have a fossil record that begins from less than cat-like ancestors. So do snails, and crabs, and so on. But what if the broad evolutionary diversification of one of these groups were repeated by a few species in a single genus tens of millions of years after that initial diversification? What would that say about the roles of contingency, constraint, and adaptation? In other words, how big is the role of chance in the history of life?

An international team of researchers including Field Museum curator Scott Lidgard, PhD, has discovered a group of closely related living species that independently repeated the different step-like changes that occurred in the major diversification of their kind during the Cretaceous Period, roughly 100 to 90 million years ago. But this group of species arose 80 million years later!

The findings of Dr. Lidgard and his collaborators will be published online this week by the British journal, *Proceedings of the Royal Society B*. Dr. Lidgard's research focuses on cheilostome bryozoans, marine animal colonies whose bodies are made up of many genetically identical box-like individuals (zooids). In the simplest, most primitive cheilostomes, the soft feeding organ is squeezed out of the box by muscles pulling on a flexible membrane. The next step in diversification was calcified spines around the membrane, then fusion of the spines, then reduction of the fused spinal shield and membrane and invention of a water sac inside the box to provide enough volume to squeeze out the feeding organ. Lineages showing each of these stages are alive today. Then as now, these steps are seen as evolved defenses against small predators and parasites on the colony surface.

What is remarkable is that the molecular genealogy of the living species shows their origin only 15 million years ago, with the same trajectory as in the distant past! Evidence suggests that trajectory has occurred again and again in other groups. The authors argue that the original trajectory was highly contingent on a set of initial conditions, but that given the possibilities afforded by time, a genetic background would arise (like flipping a coin long enough to achieve 10 heads or tails in a row) that was visible to natural selection, most likely driven by predation. Acting together, the eventual realization of a particular genetic and developmental channel, and natural selection opened the way for an adaptive solution.

Writing in air not pie in the sky

DURHAM, N.C. -- It's a familiar scene in airports and train stations. Hands full with luggage, briefcase, laptop or coat and there's something you need to remember, like the level and row numbers where you parked your car in the deck. What do you do?

Instead of relying on your memory, or finding a place to put all your stuff down to find a pen and paper, wouldn't it be so convenient to simply write "level 4, row H" in the air and be able to retrieve it later?

Engineering students at Duke University have taken advantage of the accelerometers in emerging cell phones to create an application that permits users to write short notes in the air with their phone, and have that message automatically sent to an e-mail address.

Accelerometers are the devices in phones that not only keep track of the phone's movements, but make it possible for the display screens to rotate from landscape to portrait modes depending on how the phone is rotated. These devices are always "on," so there is no additional burden on the phone to use this new application.

"We developed an application that uses the built-in accelerometers in cell phones to recognize human writing," said Sandip Agrawal, electrical and computer engineering senior at Duke's Pratt School of Engineering, who with Duke graduate student Ionut Constandache developed the PhonePoint Pen. "By holding the phone like a pen, you can write short messages or draw simple diagrams in the air.

"The accelerometer converts the gestures to images, which can be sent to any e-mail address for future reference," Constandache said. "Also, say you're in a class and there is an interesting slide on the screen. We foresee being able to take a photo of the slide and write a quick note on it for future reference. The potential uses are practically limitless. That this prototype works validates the feasibility of such a pen."

Agrawal, a Pratt Engineering Undergraduate Fellow, received the inaugural Hoffman + Krippner Award for Excellence in Student Engineering for the development of the PhonePoint Pen application. The award, created by the German technology firm Hoffman + Krippner, was presented Tuesday, June 9 during the 2009 Sensors Expo and Conference in Chicago.

While this first generation application permits the writing of short messages or simple drawings, it is only a matter of time before this prototype system will be able to handle larger and more complex air-writing capabilities, according to Agrawal's mentor, Romit Roy Choudhury, assistant professor of electrical and computer engineering.

"One of the efforts of our group (<http://synrg.ee.duke.edu/microblog.html>) is to take a fresh look at how people get their information into the Internet," Roy Choudhury said. "We're trying to get past the whole idea of typing on a keyboard or using a stylus to enter information into devices. Many people get discouraged with current phones and their small keys. As phones get smaller, this frustration will only grow.

"And today, especially now in the age of Twitter and micro-blogs, the speed in which you send information becomes more important," Roy Choudhury said. "To be able to write quickly using only one hand would be very attractive to many people."

Although challenges still remain to broaden the capabilities of the PhonePoint Pen, the engineers are confident they can be solved. Currently, air-writers must pause briefly between letters, which can slow the process down and rules out the use of cursive writing. Also, each letter must be written large. These improvements would come as a result of improved algorithms and more sophisticated accelerometers, the scientists said.

"It is only a matter of time before we improve the performance of this application," Agrawal said. "We plan to further augment the pen with real-time feedback, character recognition and better support for drawing diagrams."

Roy Choudhury expects that the PhonePoint Pen prototype will be available for download within the next few months.

Another member of the team was computer engineer Shравan Gaonkar at the University of Illinois Urbana-Champaign. Roy Choudhury's research is supported by the National Science Foundation, Nokia and Verizon.

Cancer: The cost of being smarter than chimps?

Are the cognitively superior brains of humans, in part, responsible for our higher rates of cancer? That's a question that has nagged at John McDonald, chair of Georgia Tech's School of Biology and chief research scientist at the Ovarian Cancer Institute, for a while. Now, after an initial study, it seems that McDonald is on to something. The new study is available online in the journal *Medical Hypothesis* and will appear in the forthcoming issue of the journal.

"I was always intrigued by the fact that chimpanzees appear to have lower rates of cancer than humans," said McDonald. "So we went back and reanalyzed some previously reported gene expression studies including data that were not used in the original analyses."

McDonald and his graduate students, Gaurav Arora and Nalini Polivarapu, compared chimp-human gene expression patterns in five tissues: brain, testes, liver, kidneys and heart. They found distinct differences in the way apoptosis - or programmed cell death - operates, suggesting that humans do not "self-destroy" cells as effectively as chimpanzees do. Apoptosis is one of the primary mechanisms by which our bodies destroy cancer cells.

"The results from our analysis suggest that humans aren't as efficient as chimpanzees in carrying out programmed cell death. We believe this difference may have evolved as a way to increase brain size and associated cognitive ability in humans, but the cost could be an increased propensity for cancer," said McDonald.

Like all evolutionary hypotheses, this can't be proven absolutely, according to McDonald. However, his lab has recently obtained additional direct experimental evidence consistent with the hypothesis that apoptotic function is more efficient in chimps than in humans.

Humans prefer cockiness to expertise

* 10 June 2009 by Peter Aldhous

EVER wondered why the pundits who failed to predict the current economic crisis are still being paid for their opinions? It's a consequence of the way human psychology works in a free market, according to a study of how people's self-confidence affects the way others respond to their advice.

The research, by Don Moore of Carnegie Mellon University in Pittsburgh, Pennsylvania, shows that we prefer advice from a confident source, even to the point that we are willing to forgive a poor track record. Moore argues that in competitive situations, this can drive those offering advice to increasingly exaggerate how sure they are. And it spells bad news for scientists who try to be honest about gaps in their knowledge.

In Moore's experiment, volunteers were given cash for correctly guessing the weight of people from their photographs. In each of the eight rounds of the study, the guessers bought advice from one of four other volunteers. The guessers could see in advance how confident each of these advisers was (see table), but not which weights they had opted for.

From the start, the more confident advisers found more buyers for their advice, and this caused the advisers to give answers that were more and more precise as the game progressed. This escalation in precision disappeared when guessers simply had to choose whether or not to buy the advice of a single adviser. In the later rounds, guessers tended to avoid advisers who had been wrong previously, but this effect was more than outweighed by the bias towards confidence.

The findings add weight to the idea that if offering expert opinion is your stock-in-trade, it pays to appear confident. Describing his work at an Association for Psychological Science meeting in San Francisco last month, Moore said that following the advice of the most confident person often makes sense, as there is evidence that precision and expertise do tend to go hand in hand. For example, people give a narrower range of answers when asked about subjects with which they are more familiar (Organizational Behavior and Human Decision Processes, vol 107, p 179).

There are times, however, when this link breaks down. With complex but politicised subjects such as global warming, for example, scientific experts who stress uncertainties lose out to activists or lobbyists with a more emphatic message. So if honest advice risks being ignored, what is a responsible scientific adviser to do? "It's an excellent question, and I'm not sure that I have a great answer," says Moore.

Periodic table gets a new element

By Victoria Gill Science reporter, BBC News

The ubiquitous periodic table will soon have a new addition - the "super-heavy" element 112.

More than a decade after experiments first produced a single atom of the element, a team of German scientists has been credited with its discovery.

The team, led by Sigurd Hofmann at the Centre for Heavy Ion Research, must propose a name for their find, before it can be formally added to the table.

Scientists continue the race to discover more super-heavy elements.

Professor Hofmann began his quest to add to the periodic table in 1976.

The fusion experiments he and his colleagues carried out at the centre have already revealed the existence of elements with atomic numbers 107-111.

These are known as "super-heavy elements" - their numbers represent the number of protons which, together with neutrons, give the atom the vast majority of its mass.

To create element 112, Professor Hofmann's team used a 120m-long particle accelerator to fire a beam of charged zinc atoms (or zinc ions) at lead atoms. Nuclei of the two elements merged, or fused, to form the nucleus of the new element.

These very large and heavy nuclei are also very unstable. They begin to fall apart or "decay" very soon after being formed - within a few milliseconds, in this case.

This releases energy, which scientists can measure to find out the size of the decaying nucleus.

But such experiments produce very few successful fusions, and scientists need increasingly powerful accelerators to run experiments for longer and find the elusive, unstable elements.

This is why it took such a long time for element 112 to be officially recognised by the International Union of Pure and Applied Chemistry (IUPAC).

Confidence pays

Volunteers acting as "advisers" profited by selling their advice to other volunteers - who in turn won cash by guessing a person's weight

ADVISERS CAN SPREAD THEIR ESTIMATES OF A PARTICULAR PERSON'S WEIGHT DEPENDING ON HOW CONFIDENT THEY ARE				
Estimated weight (lbs)	ADVISER A	ADVISER B	ADVISER C	ADVISER D
120-129		5%		
130-139		5%		
140-149		20%		
150-159		50%	20%	
160-169	15%	10%	20%	
170-179	70%	5%	40%	
180-189	15%	5%	10%	100%
190-199			10%	
200-209				
210-219				

INFORMATION GIVEN TO "GUESSERS" WHO THEN HAD TO BUY ADVICE FROM ONE OF THE ADVISERS			
ADVISER A	ADVISER B	ADVISER C	ADVISER D
15%	20%	20%	
70%	50%	20%	100%
15%	10%	40%	



Its discovery had to be independently verified, and so far only four atoms have ever been observed.

IUPAC temporarily named the element ununbium, as "ununbi" is derived from the figures "one one two" in Latin; but Professor Hofmann's team now has the task of proposing its official name.

He is currently keeping the shortlist under wraps.

Working together

Teams in Russia, the US and Japan are taking part in what Professor Hofmann described as the "friendly competition" to discover new, heavier elements.

In 2006, Professor Hofmann's competitors at the Joint Institute for Nuclear Research (JINR) in Dubna, Russia, claimed the discovery of element 118. It was made by bombarding a californium target with a beam of calcium ions.

"We have confirmed some of these results," Professor Hofmann told BBC News.

But he is now setting his sights higher. "We tried the same experiment to get to element 120. We've not seen it yet, but we believe the element exists and, with a long enough beam time, it could be produced," he said. "It's certainly a race, and it's nice to be first."

1 H																	2 He
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu	
87 Fr	88 Ra	89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr	
119 Uum																	

Periodic table with elements colored according to the half-life of their most stable isotope.

- Stable elements;
- Radioactive elements with very long-lived isotopes. Their half-lives of over four million years confers them very small, if not negligible radioactivities;
- Radioactive elements that may present low health hazards. Their most stable isotopes have half-lives between 800 and 34,000 years. Because of this, they usually have some commercial applications;
- Radioactive elements that are known to pose high safety risks. Their most stable isotopes have half-lives between one day and 103 years. Their radioactivities confers them little potential for commercial uses;
- Highly radioactive elements. Their most stable isotopes have half-lives between one day and several minutes. They pose severe health risks. Few of them receive uses outside basic research;
- Extremely radioactive elements. Very little is known about these elements due to their extreme instability and radioactivity.

Looking like daddy has material rewards

* 14:19 10 June 2009 by Ewen Callaway

Children who look and smell like their father receive more of their support, compared to kids who resemble dad less. The study of 30 Senegalese families has provided the first direct link between a father's investment in his children and his physical resemblance to them, though other work has hinted at this connection.

For instance, a study conducted at London's Heathrow Airport found that fathers invested extra time and money in children who looked and behaved like them, compared with dads who said their kid's looks and personalities differed from their own.

Such uncharitable behaviour may seem shocking, but evolutionary theory predicts it. Without a DNA test and an appearance on the Jerry Springer Show, a father can never be absolutely certain that a child is his own.

Therefore, it makes evolutionary sense to divvy out limited resources – be they time, food or money – to children more likely to be legitimate.

Who's the daddy?

The behaviour has an evolutionary advantage because there are always going to be illegitimate children, says Alexandra Alvergne, a biological anthropologist at the Institute of Evolutionary Sciences in Montpellier, France, who led the new study. A 2006 paper estimated illegitimacy rates at between 0.8 per cent and 30 per cent among different populations around the world, with an average of 3.3 per cent.

Alvergne did not know the paternity status of the 60 children involved in this study, but she guesses that a couple of them could have been illegitimate. Yet because she and her co-authors were interested in the perception of father-child resemblance, actually paternity did not matter.

Watch and sniff

To determine which children looked and smelled most like their fathers, Alvergne's team systematically involved more than 100 people from a distant village, who were not familiar with the kids. These "raters" were asked to match a child's digital image to an image of one of three potential fathers. For smell, villagers sniffed a T-shirt the child had worn for a night and compared it to T-shirts worn by two potential fathers.

They correctly matched the child to the right father based on photos half the time, which is well above chance. But only men picked out fathers based on T-shirt smell at rates above chance, the researchers found.

The team next compared these ratings to an objective measure of paternal investment, based on the time fathers spent with each child in a day, a standard psychological questionnaire of father involvement, and a survey of financial and emotional support. Children that looked and smelled more like their fathers tended to receive more paternal investments, Alvergne and her colleagues found. Factors such as a child's age, sex, or birth order did not predict fathers' investments, nor did the father's own age or wealth.

Moreover, after accounting for age, children who received additional support from their father tended to weigh more and have thicker arms – both indicators of good nutrition – compared to children who got less fatherly support.

'Wham, bam!'

It makes sense for fathers to apportion their efforts wisely, says Kermyt Anderson, an anthropologist at the University of Oklahoma in Norman "Human males do spend a lot of time investing in their kids and they invest quite heavily," he says. That is a sharp contrast with other mammals, including our closest primate kin. "In 90 per cent of mammals, a father's investment ends in ejaculation – wham, bam, thank you, ma'am!"

Frank Marlowe, an anthropologist at Florida State University in Tallahassee, thinks fathers in western cultures probably act the same way. "There's no reason to think that they're going to find something very different here."

In unpublished work, Alvergne says her team has found that western fathers invest more in children that resemble them, though improved nutrition probably doesn't explain the investment as it did in Senegal, she says.

However, a recent long-term study of English fathers and children found that the more time a father spent with his kids, the more successful they are as adults.

Journal reference: Animal Behaviour (DOI: 10.1016/j.anbehav.2009.03.019)

Off-label morning sickness drug deemed safe for fetuses -- Ben-Gurion U. researchers
Collaborative research findings published in New England Journal of Medicine support safe use of metoclopramide for morning sickness nausea

BEER-SHEVA, ISRAEL, – Metoclopramide, a drug approved in the U.S. for nausea, vomiting and heartburn poses no significant risks for the fetus according to a large cohort study published in the June 11 issue of the prestigious New England Journal of Medicine, "The Safety of Metoclopramide Use in the First Trimester of Pregnancy" (N Engl J Med 2009;360:24 June 11, 2009).

According to the pediatrician and clinical pharmacologist, principal investigator Dr. Rafael Gorodischer, prof. emeritus at Ben-Gurion University of the Negev, "Metoclopramide is the drug of choice in Europe and Israel for "morning sickness-like" symptoms of nausea and vomiting, which are common in pregnant women. In the U.S. however, it is only used in the most severe cases, as it is an "off-label" use for nausea and vomiting during pregnancy. The findings of this very large cohort study examining infants born to mothers who were exposed to metoclopramide during the first trimester provide significant reassurance for the safety of the fetus when the drug is given to women to relieve nausea and vomiting during pregnancy."

Between 50 percent to 80 percent of pregnant women experience nausea and vomiting during the first trimester and beyond, which can be severe.

This study is collaboration between Ben-Gurion University of the Negev, Soroka University Medical Center and Clalit Health Services -- all in Beer-Sheva, Israel -- along with the Division of Pharmacology, Hospital for Sick Children in Toronto, Canada. The study is part of the doctoral thesis of Ilan Matok and was conducted by the three Israeli entities as part of the BeMORE collaboration (Ben-Gurion MotheRisk Obstetric Registry of Exposure). The study of the safety of other medications commonly used off-label in pregnancy is an ongoing project of BeMORE investigators in large cohorts of women in Southern Israel.

According to principal investigator epidemiologist Dr. Amalia Levy of the BGU Faculty of Health Sciences, and chairwoman of the BeMORE collaboration, "of the vast majority of medications approved for use, there is insufficient data from human studies to determine whether the benefits of therapy exceed the risk to the fetus. Medicines are approved for use only after there is sufficient scientific evidence demonstrating the drug safety and effectiveness for its intended uses. There is extensive experience with the use of this medication in non-pregnant persons, with evidence of overall low rates of adverse effects when it is used as recommended."

The safety of metoclopramide use during the first trimester of pregnancy was investigated by linking a database of medications dispensed over 10 years to all women registered in Clalit Health Services in the Southern District of Israel, with databases containing maternal and infant hospital records of Soroka University Medical Center, during the same period. In the study, 3,458 (or 4.2 percent) were exposed to metoclopramide during the first trimester of pregnancy of the 81,703 infants born to mothers during the study period.

The rate of major congenital malformations identified in the group that was exposed to metoclopramide during the first trimester was 5.3 percent (182 of 3458 infants), as compared with a rate of 4.9 percent (3834 of 78,245 infants).

As a result, exposure to metoclopramide among this group was not associated with significantly increased risks of major congenital malformations. The results were unchanged when therapeutic abortions of exposed fetuses were included in the analysis. In addition, infants exposed in utero had no increased risk of perinatal mortality, low birth weight or premature birth.

Data of this study support the labeling of metoclopramide for nausea and vomiting during pregnancy.

Our exposure to controversial chemical may be greater than dose considered safe

People are likely being exposed to the commonly used chemical bisphenol A (BPA) at levels much higher than the recommended safe daily dose, according to a new study in monkeys. The results will be presented Thursday at The Endocrine Society's 91st Annual Meeting in Washington, D.C.

"BPA is now known to be a potent estrogen," said Frederick vom Saal, PhD, a co-author of the new study and a professor of biological sciences at the University of Missouri-Columbia. "Human and animal studies indicate it could be related to diabetes, heart disease, liver abnormalities, miscarriage and other reproductive abnormalities, as well as prostate and breast cancer."

The U.S. Food and Drug Administration (FDA) declared BPA is safe based on estimates that people consume only small amounts each day from food. However, recent research indicated that U.S. adults are exposed to more BPA from multiple sources than previously thought, vom Saal said.

BPA is found in polycarbonate plastic food and beverage containers, such as water and infant bottles, as well as in the epoxy resin lining of cans and other sources. The chemical can leach into food and beverages, according to the National Institutes of Health, which funded the study by vom Saal and colleagues.

"Between 8 and 9 billion pounds of BPA are used in products every year," vom Saal said.

In their study, he and his colleagues fed five female adult monkeys an oral dose of BPA (400 micrograms per kilogram of body weight). This amount is more than 400 times higher than the amount that the U.S. Food and Drug Administration (FDA) estimates that human adults are exposed to and 8 times higher than the estimated safe daily amount to consume, according to vom Saal.

Yet the blood levels of biologically active BPA over the next 24 hours were lower in the monkeys than the average levels found in people in the United States and other developed countries, vom Saal said. For levels to be higher in people when measured, their exposure dose must be greater than that given to the monkeys, he explained.

"These results suggest that the average person is likely exposed to a daily dose of BPA that far exceeds the current estimated safe daily intake dose," vom Saal said.

He said that BPA exposure must come from many unknown sources, in addition to food and beverage containers. Like drugs, BPA acts in pulses, with each exposure creating a high-level pulse before it is cleared in the urine, according to vom Saal.

The researchers are continuing the study in more monkeys, but vom Saal said they do not expect to get different findings because the data in the first five animals were "very consistent." The species of monkey that they used (rhesus) metabolizes BPA similar to humans, he added.

First-degree relatives of patients with bicuspid aortic valve should be screened

Bicuspid Aortic Valve (BAV), a condition in which patients' aortic valves have just two leaflets instead of the normal three, is the most common cardiac anomaly, affecting up to two percent of the general population. The defect can result in calcification deposits on the heart valve, leakage of the valve and may result in a feeling of tightness in the chest as well as shortness of breath. The condition is easily diagnosed; often physicians can hear a "click" or a murmur when they listen to a BAV patient's heart with a stethoscope.

Studies have shown that BAV is likely genetic, although the gene has not been identified, and in some families, incidence of this defect could run as high as 20 percent.

A new study, published in the Journal of the American College of Cardiology, suggests that nearly a third of first-degree relatives (siblings, children or parents) of BAV patients are likely to have enlarged aortas, a potentially serious condition that can only be detected by undergoing transthoracic echocardiograms. This was found even in the absence of any abnormalities of the heart valve itself.

According to the study, 32 percent of first-degree relatives with no heart valve abnormality had significantly larger aortas that expected for age, gender and body size as compared to no enlargement seen in control patients. Also, the study found that the aortas of the first-degree relatives had abnormal stiffness similar to the patients with congenital bicuspid valve. Generally, when aortas are 50 millimeters in diameter, surgery is recommended in order to prevent a rupture of the aorta.

"If you know that a relative does have bicuspid aortic valve, then you know that you should be screened," said study author Kirsten Tolstrup, MD, assistant director of the Cardiac Noninvasive Laboratory at the Cedars-Sinai Heart Institute. "BAV appears to be a genetic condition that has many different manifestations, so we will be studying the genes."

Kirsten Tolstrup, MD, assistant director of the Cardiac Noninvasive Laboratory at the Cedars-Sinai Heart Institute, is available to discuss the study's findings and provide additional details.

This study, conducted among 54 patients with bicuspid aortic valve and 48 first-degree relatives of those patients as well as 45 matched controls found:

- * 32 percent of apparently healthy first-degree relatives have enlarged aortas
- * 53 percent of BAV patients had enlarged aortas
- * 9.4 percent of first-degree relatives had BAV

The findings suggest that patients with bicuspid aortic valve and their first-degree relatives should have a screening echocardiogram to be evaluated for dilated aorta and bicuspid aortic valve.

The study abstract can be accessed at <http://content.onlinejacc.org>

Citation: Journal of the American College of Cardiology, June 8, 2009, "Aortopathy is Prevalent in Relatives of Bicuspid Aortic Valve Patients"

New definition could further limit habitable zones around distant suns

As astronomers gaze toward nearby planetary systems in search of life, they are focusing their attention on each system's habitable zone, where heat radiated from the star is just right to keep a planet's water in liquid form.

A number of planets have been discovered orbiting red dwarf stars, which make up about three-quarters of the stars close to our solar system. Potentially habitable planets must orbit close to those stars – perhaps one-fiftieth the distance of Earth to the sun – since those stars are smaller and generate less heat than our sun.

But new calculations indicate that, with planets so close, tidal forces exerted on planets by the parent star's gravity could limit what is regarded as a star's habitable zone and change the criteria for planets where life could potentially take root.

Scientists believe liquid water is essential for life. But a planet also must have plate tectonics to pull excess carbon from its atmosphere and confine it in rocks to prevent runaway greenhouse warming. Tectonics, or the movement of the plates that make up a planet's surface, typically is driven by radioactive decay in the planet's core, but a star's gravity can cause tides in the planet, which creates more energy to drive plate tectonics.

"If you have plate tectonics, then you can have long-term climate stability, which we think is a prerequisite for life," said Rory Barnes, a University of Washington postdoctoral researcher in astronomy.

However, tectonic forces cannot be so severe that geologic events quickly repave a planet's surface and destroy life that might have gotten a foothold, he said. The planet must be at a distance where tugging from the star's gravitational field generates tectonics without setting off extreme volcanic activity that resurfaces the planet in too short a time for life to prosper.

Barnes is lead author of a paper to be published by The Astrophysical Journal Letters that uses new calculations from computer modeling to define a "tidal habitable zone." Co-authors are Brian Jackson and Richard Greenberg from the University of Arizona and Sean Raymond from the University of Colorado. The research was funded by NASA. "Overall, the effect of this work is to reduce the number of habitable environments in the universe, or at least what we have thought of as habitable environments," Barnes said. "The best places to look for habitability are where this new definition and the old definition overlap."

The new calculations have implications for planets previously considered too small for habitability. An example is Mars, which used to experience tectonics but that activity ceased as heat from the planet's decaying inner core dissipated. But as planets get closer to their suns, the gravitational pull gets stronger, tidal forces increase and more energy is released. If Mars were to move closer to the sun, the sun's tidal tugs could possibly restart the tectonics, releasing gases from the core to provide more atmosphere. If Mars harbors liquid water, at that point it could be habitable for life as we know it.

Various moons of Jupiter have long been considered as potentially harboring life. But one of them, Io, has so much volcanic activity, the result of tidal forces from Jupiter, that it is not regarded as a good candidate. Tectonic activity remakes Io's surface in less than 1 million years.

"If that were to happen on Earth, it would be hard to imagine how life would develop," Barnes said.

A potential Earth-like planet, but eight times more massive, called Gliese 581d was discovered in 2007 about 20 light years away in the constellation Libra. At first it was thought the planet was too far from its sun, Gliese 581, to have liquid water, but recent observations have determined the orbit is within the habitable zone for liquid water. However, the planet is outside the habitable zone for its sun's tidal forces, which the authors believe drastically limits the possibility of life.

"Our model predicts that tides may contribute only one-quarter of the heating required to make the planet habitable, so a lot of heat from decay of radioactive isotopes may be required to make up the difference," Jackson said.

Barnes added, "The bottom line is that tidal forcing is an important factor that we are going to have to consider when looking for habitable planets."

For more information, contact Barnes at 206-543-8979 or rory@astro.washington.edu.

The paper is available at <http://www.astro.washington.edu/users/rory/publications/bjgr09.pdf>

Radio telescope images reveal planet-forming disk orbiting twin suns

Astronomers are announcing today that a sequence of images collected with the Smithsonian's Submillimeter Array (SMA) clearly reveals the presence of a rotating molecular disk orbiting the young binary star system V4046 Sagittarii. The SMA images provide an unusually vivid snapshot of the process of formation of giant planets, comets, and Pluto-like bodies. The results also confirm that such objects may just as easily form around double stars as around single stars like our Sun. These findings are being presented by UCLA graduate student David Rodriguez in a press conference at the American Astronomical Society meeting in Pasadena, Calif.

"It's a case of seeing is believing," says Joel Kastner of the Rochester (NY) Institute of Technology, the lead scientist on the study. "We had the first evidence for this rotating disk in radio telescope observations of V4046 Sagittarii that we made last summer. But at that point, all we had were molecular spectra, and there are different ways to interpret the spectra. Once we saw the image data from the SMA, there was no doubt that we have a rotating disk here."

Co-author David Wilner of the Harvard-Smithsonian Center for Astrophysics (CfA) adds, "This is strong evidence that planets can form around binary stars, which expands the number of places we can look for extrasolar planets. Somewhere in our galaxy, an alien world may enjoy double sunrises and double sunsets."

Wilner is one of the world's experts on radiointerferometry, the technique used in this study to form images with the SMA's multiple radio antennas. The other contributor to the SMA study of V4046 Sagittarii led by RIT's Kastner and UCLA's Rodriguez is Ben Zuckerman of UCLA.



This artist's conception of the V4046 Sagittarii system highlights the disk-shaped molecular gas cloud imaged by the Submillimeter Array. The gaseous disk, which orbits the twin suns, shows that planets could form around double stars as easily as around a single star like our Sun. David A. Aguilar (CfA)

According to Rodriguez, the images clearly demonstrate that the molecular disk orbiting the V4046 Sagittarii binary system extends from within the approximate radius of Neptune's orbit out to about 10 times that orbit. This region corresponds to the zone where the solar system's giant planets, as well as its Pluto-like Kuiper Belt objects, may have formed.

"We believe that V4046 Sagittarii provides one of the clearest examples yet discovered of a Keplerian, planet-forming disk orbiting a young star system," Wilner says. "This particular system is made that much more remarkable by the fact that it consists of a pair of solar-mass stars that are approximately 12 million years old and are separated by a mere 5 solar diameters."

"This could be the oldest known orbiting protoplanetary molecular disk. It shows that, at least for some stars, formation of Jovian-mass planets may continue well after a few million years, which astronomers have deduced is characteristic of the formation time for most such planets," Zuckerman says.

Findings of this study build on previous work published in the December 2008 issue of *Astronomy and Astrophysics* in which Kastner and his team first suggested that the case of V4046 Sagittarii illustrates well how planets may form easily around certain types of binary stars.

"We thought the molecular gas around these two stars almost literally represented 'smoking gun' evidence of recent or possibly ongoing 'giant' Jupiter-like planet formation around the binary star system," Kastner says. "The SMA images showing an orbiting disk certainly support that idea."

The evidence for a molecular disk orbiting these twin young suns in the constellation Sagittarius suggested to the scientists that many such binary systems should also host as-yet-undetected planets.

"The most successful technique used so far for the discovery of extrasolar planets - that of measurement of precision radial velocities - is exceedingly difficult for close binary stars such as V4046 Sagittarii. So these radio observations are probing a new region of discovery space for extrasolar planets," says Rodriguez.

"At a distance of only 240 light-years from the solar system, the V4046 Sagittarii binary is at least two times closer to Earth than almost all known planet-forming star systems, which gives us a good shot at imaging any planets that have already formed and are now orbiting the stars," he continues.

Kastner and collaborators had previously used the 30-meter radiotelescope operated by the Institut de Radio Astronomie Millimetrique (IRAM) to study radio molecular spectra emitted from the vicinity of the twin stars. The scientists used these data to identify the raw materials for planet formation around V4046 Sagittarii - carbon monoxide and hydrogen cyanide - in the noxious circumstellar gas cloud.

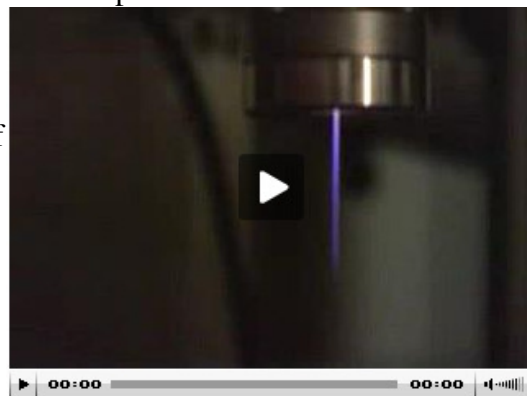
"In this case the stars are so close together, and the profile of the gas - in terms of the types of molecules that are there - is so much like the types of gaseous disks that we see around single stars, that we now have a direct link between planets forming around single stars and planets forming around double stars," Kastner says.

Cool plasma packs heat against biofilms

University of Southern California Dentistry-Engineering partnership results in promising new tool for fighting infections.

Though it looks like a tiny purple blowtorch, a pencil-sized plume of plasma on the tip of a small probe remains at room temperature as it swiftly dismantles tough bacterial colonies deep inside a human tooth. But it's not another futuristic product of George Lucas' imagination. It's the exciting work of USC School of Dentistry and Viterbi School of Engineering researchers looking for new ways to safely fight tenacious biofilm infections in patients – and it could revolutionize many facets of medicine.

Two of the study's authors are Chunqi Jiang, a research assistant professor in the Ming Hsieh Department of Electrical Engineering-Electrophysics, and Parish Sedghizadeh, assistant professor of clinical dentistry and Director of the USC Center for Biofilms. "Nanosecond Pulsed Plasma Dental Probe" appears in the June 2009 issue of *Plasma Processes and Polymers*.



[VIDEO: A small plasma probe can destroy biofilm infections, yet is cool and safe to the touch.](#) Sedghizadeh explained that biofilms are complex colonies of bacteria suspended in a slimy matrix that grants them added protection from conventional antibiotics. Biofilms are responsible for many hard-to-fight infections in the mouth and elsewhere. But in the study, biofilms cultivated in the root canal of extracted human teeth were easily destroyed with the plasma dental probe, as evidenced by scanning electron microscope images of near-pristine tooth surfaces after plasma treatment.

Plasma, the fourth state of matter, consists of electrons, ions, and neutral species and is the most common form found in space, stars, and lightning, Jiang said. But while many natural plasmas are hot, or thermal, the probe developed for the study is a non-thermal, room temperature plasma that's safe to touch. The researchers placed temperature sensors on the extracted teeth before treatment and found that the temperature of the tooth increased for just five degrees after 10 minutes of exposure to the plasma, Jiang said.

The cooler nature of the experimental plasma comes from its pulsed power supply. Instead of employing a steady stream of energy to the probe, the pulsed power supply sends 100-nanosecond pulses of several kilovolts to the probe once every millisecond, with an average power less than 2 Watts, Jiang said.

"Atomic oxygen [a single atom of oxygen, instead of the more common O₂ molecule] appears to be the antibacterial agent," according to plasma emission spectroscopy obtained during the experiments, she said.

Sedghizadeh said the oxygen free radicals might be disrupting the cellular membranes of the biofilms in order to cause their demise and that the plasma plume's adjustable, fluid reach allowed the disinfection to occur even in the hardest-to-reach areas of the root canal.

Given that preliminary research indicates that non-thermal plasma is safe for surrounding tissues, Sedghizadeh said he was optimistic about its future dental and medical uses. Much like the spread of laser technology from research and surgical applications to routine clinical and consumer uses, plasma could change everything; especially since nonthermal plasmas don't harbor the risks of tissue burns and eye damage that lasers do, he said.

"Plasma is the future," Sedghizadeh said. "It's been used before for other sterilization purposes but not for clinical medical applications, and we hope to be the first to apply it in a clinical setting."

"We believe we're the first team to apply plasma for biofilm disinfection in root canals," Jiang added. "This collaboration is very unique. We're attacking frontier problems, and we're happy to be broadening our fields."

Stress makes your hair go gray

Those pesky graying hairs that tend to crop up with age really are signs of stress, reveals a new report in the June 12 issue of *Cell*, a Cell Press publication.

Researchers have discovered that the kind of "genotoxic stress" that does damage to DNA depletes the melanocyte stem cells (MSCs) within hair follicles that are responsible for making those pigment-producing cells. Rather than dying off, when the going gets tough, those precious stem cells differentiate, forming fully mature melanocytes themselves. Anything that can limit the stress might stop the graying from happening, the researchers said.

"The DNA in cells is under constant attack by exogenously- and endogenously-arising DNA-damaging agents such as mutagenic chemicals, ultraviolet light and ionizing radiation," said Emi Nishimura of Tokyo Medical and Dental University. "It is estimated that a single cell in mammals can encounter approximately 100,000 DNA damaging events per day." Consequently, she explained, cells have elaborate ways to repair damaged DNA and prevent the lesions from being passed on to their daughter cells.

"Once stem cells are damaged irreversibly, the damaged stem cells need to be eliminated to maintain the quality of the stem cell pools," Nishimura continued. "We found that excessive genotoxic stress triggers differentiation of melanocyte stem cells." She says that differentiation might be a more sophisticated way to get rid of those cells than stimulating their death.

Nishimura's group earlier traced the loss of hair color to the gradual dying off of the stem cells that maintain a continuous supply of new melanocytes, giving hair its youthful color. Those specialized stem cells are not only lost, they also turn into fully committed pigment cells and in the wrong place.

Now, they show in mice that irreparable DNA damage, as caused by ionizing radiation, is responsible. They further found that the "caretaker gene" known as ATM (for ataxia telangiectasia mutated) serves as a so-called stemness checkpoint, protecting against MSCs differentiation. That's why people with Ataxia-telangiectasia, an aging syndrome caused by a mutation in the ATM gene, go gray prematurely.

The findings lend support to the notion that genome instability is a significant factor underlying aging in general, the researchers said. They also support the "stem cell aging hypothesis," which proposes that DNA damage to long-lived stem cells can be a major cause for the symptoms that come with age. In addition to the aging-associated stem cell depletion typically seen in melanocyte stem cells, qualitative and quantitative changes to other body stem cells have been reported in blood stem cells, cardiac muscle, and skeletal muscle, the researchers said. Stresses on stem cell pools and genome maintenance failures have also been implicated in the decline of tissue renewal capacity and the accelerated appearance of aging-related characteristics.

"In this study, we discovered that hair graying, the most obvious aging phenotype, can be caused by the genomic damage response through stem cell differentiation, which suggests that physiological hair graying can be triggered by the accumulation of unavoidable DNA damage and DNA-damage response associated with aging through MSC differentiation," they wrote.

The researchers include Ken Inomata, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan, KOSÉ Corporation, Tokyo, Japan, Hokkaido University Graduate School of Medicine; Takahiro Aoto, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan, Tokyo Medical and Dental University, Tokyo, Japan; Nguyen Thanh Binh, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan; Natsuko Okamoto, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan, Kyoto University Graduate School of Medicine, Kyoto, Japan; Shintaro Tanimura, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan, Hokkaido University Graduate School of Medicine; Tomohiko Wakayama, Kanazawa University, Ishikawa, Japan; Shoichi Iseki, Kanazawa University, Ishikawa, Japan; Eiji Hara, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan; Takuji Masunaga, KOSÉ Corporation, Tokyo, Japan; Hiroshi Shimizu, Hokkaido University Graduate School of Medicine; and Emi K. Nishimura, Kanazawa University, Takaramachi, Kanazawa, Ishikawa, Japan, Tokyo Medical and Dental University, Tokyo, Japan.

*Inomata et al.: "Genotoxic Stress Abrogates Renewal of Melanocyte Stem Cells by Triggering Their Differentiation." Publishing in *Cell* 137, 1088-1099, June 12, 2009. DOI 10.1016/j.cell.2009.03.037 www.cell.com.*

CRAP paper accepted by journal

Updated 10:47 12 June 2009 by Peter Aldhous

At New Scientist we love a good hoax, especially one that both amuses and makes a serious point about the communication of science. So kudos to Philip Davis, a graduate student in library and information science at Cornell University in Ithaca, New York, who revealed yesterday on The Scholarly Kitchen blog that he got a nonsensical computer-generated paper accepted for publication in a peer-reviewed journal.

Earlier this year, Davis started receiving unsolicited emails from Bentham Science Publishers, which publishes more than 200 "open-access" journals - which turn the conventional business model of academic publishing on its head by charging publication fees to the authors of research papers, and then making the content available for free.

As the emails stacked up, Davis was not only encouraged to submit papers, but was also invited to serve on the editorial board of some of Bentham's journals - for which he was told he would be allowed to publish one free article

each year. "I received solicitations for journals for which I had no subject expertise at all," says Davis. "It really painted a picture of vanity publishing."

Sheer nonsense

So Davis teamed up with Kent Anderson, a member of the publishing team at The New England Journal of Medicine, to put Bentham's editorial standards to the test. The pair turned to SCIgen, a program that generates nonsensical computer science papers, and submitted the resulting paper to The Open Information Science Journal, published by Bentham.

The paper, entitled "Deconstructing Access Points" (pdf) made no sense whatsoever, as this sample reveals:

In this section, we discuss existing research into red-black trees, vacuum tubes, and courseware [10]. On a similar note, recent work by Takahashi suggests a methodology for providing robust modalities, but does not offer an implementation [9].

Acronym clue

Davis and Anderson, writing under the noms de plume David Phillips and Andrew Kent, also dropped a hefty hint of the hoax by giving their institutional affiliation as the Center for Research in Applied Phrenology, or CRAP. Yet four months after the article was submitted, "David Phillips" received an email from Sana Mokarram, Bentham's assistant manager of publication:

This is to inform you that your submitted article has been accepted for publication after peer-reviewing process in TOISCIJ. I would be highly grateful to you if you please fill and sign the attached fee form and covering letter and send them back via email as soon as possible to avoid further delay in publication.

The publication fee was \$800, to be sent to a PO Box in the United Arab Emirates. Having made his point, Davis withdrew the paper.

Mahmood Alam, Bentham's director of publications, responded to queries from New Scientist by email: "In this particular case we were aware that the article submitted was a hoax, and we tried to find out the identity of the individual by pretending the article had been accepted for publication when in fact it was not."

"Why hasn't he attempted to contact me directly in order to determine my true identity?" Davis responds.

Pay to speak

This is just the latest use of SCIgen to probe the vetting of scientific papers. The program was devised by Jeremy Stribling, Daniel Aguayo and Maxwell Krohn, graduate students at the Massachusetts Institute of Technology, who first used it to generate a spoof paper that was accepted for presentation at the 2005 World Multi-Conference on Systemics, Cybernetics and Informatics (WMSCI), which charged speakers \$390 to attend.

The MIT students evidently weren't the only people annoyed by WMSCI's unsolicited emails and pay-to-play approach: for those not offended by profanity, here is another submission to the 2005 conference [pdf format, contains possibly offensive language] that approaches genius, especially in figures 1 and 2.

Like conferences that rely on recruiting speakers to make money, Davis argues that little-known open-access journals may be under pressure to drop their standards for accepting papers to boost their revenue. To be fair to Bentham, however, an earlier bogus paper submitted by Davis to another of its publications, The Open Software Engineering Journal, was rejected after peer review.

History of hoaxes

What's more, it seems that even some journals that charge readers for their content may be prone to accepting utter nonsense. The SCIgen website reports another incident from 2007, in which graduate students at Sharif University in Iran got a SCIgen-concocted paper accepted by Applied Mathematics and Computation, a journal published by Elsevier (part of Reed-Elsevier, the publishing giant that owns New Scientist).

After the spoof was revealed, the pre-publication version of the paper was removed from Elsevier's ScienceDirect website. Still, the succinct proof-correcting queries sent to the hoaxers by Elsevier, made available here by the SCIgen team (pdf), make for interesting reading.

Melvin Scott, a retired mathematician based in Ocean Isle Beach, North Carolina, who serves as editor-in-chief of Applied Mathematics and Computation, says that the paper was accepted by an editor who has since left the journal. "I've revamped the editorial board significantly," he adds.

Editor of journal targeted by hoaxers resigns

17:30 12 June 2009 by Peter Aldhous

The revelation that a journal had apparently accepted a nonsensical computer-generated paper submitted by hoaxers has led to the resignation of the publication's editor-in-chief.

Bambang Parmanto, a health information scientist at the University of Pittsburgh, resigned yesterday from The Open Information Science Journal after being contacted by a reporter from The Scientist asking for his comments on the hoax. "I never saw the paper," says Parmanto. "It's a breakdown in the process."

Mahmood Alam, director of publications with Bentham Science Publishers, which runs the journal, said in an email to New Scientist yesterday that staff pretended to accept the paper in order to find out the hoaxers' identities.

Parmanto says that he first learned of this explanation from Alam yesterday. In his resignation letter, Parmanto says that he suggested that all editorial decisions in future must be taken by scientific editors, rather than Bentham staff.

Blocking a muscle growth-limiting hormone protects against obesity and atherosclerosis

Knockout of myostatin, a growth factor that limits muscle growth, can decrease body fat and promote resistance against developing atherosclerosis, or "hardening" of the arteries, according to a new study conducted in mice. The results will be presented Thursday at The Endocrine Society's 91st Annual Meeting in Washington, D.C.

"Obesity increases the risk of atherosclerosis, which accounts for 75% of all cardiovascular events, such as heart attacks and strokes," said study co-author Shalender Bhasin, MD, professor of medicine at Boston University School of Medicine and chief of the Section of Endocrinology, Diabetes, and Nutrition at Boston Medical Center. "Current strategies aimed at preventing heart disease consist primarily of lowering cholesterol levels, but patients reaching the desired cholesterol levels are still at risk for atherosclerosis if they have other risk factors, such as obesity."

Humans and animals with a mutation in the myostatin gene are extremely muscular and have little fat, past research shows. Also, when the gene encoding myostatin is knocked out in mice, their muscle mass increases.

Bhasin and his co-workers wanted to find out if inhibiting myostatin in mice could resist the development of diet-induced obesity and of atherosclerosis, the buildup of lipid deposits called plaque that can narrow and clog coronary arteries.

The researchers took mice that were genetically altered to develop atherosclerosis and then cross-bred them with myostatin knockout mice. Ten generations later, they had mice who were genetically predisposed to both atherosclerosis and inactivation of myostatin. For controls, they studied mice with a genetic predisposition for atherosclerosis but with intact myostatin gene. All mice received a high-fat diet for 12 weeks, to spur the development of atherosclerosis.

Compared with controls, the mice with deleted myostatin gene had much less body fat and 30 percent lower fasting blood sugar and 80% lower fasting insulin levels, showing a reduction in obesity and a strong resistance to developing diabetes, the authors reported. They also had 50 percent lower low-density-lipoprotein ("bad") cholesterol and 30 to 60 percent lower levels of total cholesterol and triglycerides (fats in the blood), respectively. These results indicate protection against the development of atherosclerosis, according to Bhasin.

More research is needed to demonstrate the safety and effectiveness of myostatin inhibitors in humans, Bhasin said. However, he said that this therapeutic strategy already is possible. Experimental drugs called myostatin blockers or inhibitors are being studied as potential treatments of muscle wasting disorders and limb injuries.

Some currently available nutritional supplements are touted as myostatin inhibitors, but Bhasin said he doubts they are effective.

Powen Tu, a medical student at Boston University School of Medicine, will present the study, which was funded by the National Institutes of Health.

Successful weight loss with dieting is linked to vitamin D levels

Vitamin D levels in the body at the start of a low-calorie diet predict weight loss success, a new study found. The results, which suggest a possible role for vitamin D in weight loss, were presented at The Endocrine Society's 91st Annual Meeting in Washington, D.C.

"Vitamin D deficiency is associated with obesity, but it is not clear if inadequate vitamin D causes obesity or the other way around," said the study's lead author, Shalamar Sibley, MD, MPH, an assistant professor of medicine at the University of Minnesota.

In this study, the authors attempted to determine whether baseline vitamin D levels before calorie restriction affect subsequent weight loss. They measured circulating blood levels of vitamin D in 38 overweight men and women before and after the subjects followed a diet plan for 11 weeks consisting of 750 calories a day fewer than their estimated total needs. Subjects also had their fat distribution measured with DXA (bone densitometry) scans.

On average, subjects had vitamin D levels that many experts would consider to be in the insufficient range, according to Sibley. However, the authors found that baseline, or pre-diet, vitamin D levels predicted weight loss in a linear relationship. For every increase of 1 ng/mL in level of 25-hydroxycholecalciferol—the precursor form of vitamin D and a commonly used indicator of vitamin D status—subjects ended up losing almost a half pound (0.196 kg) more on their calorie-restricted diet. For each 1-ng/mL increase in the active or "hormonal" form of vitamin D (1,25-dihydroxycholecalciferol), subjects lost nearly one-quarter pound (0.107 kg) more.

Additionally, higher baseline vitamin D levels (both the precursor and active forms) predicted greater loss of abdominal fat. "Our results suggest the possibility that the addition of vitamin D to a reduced-calorie diet will lead to better weight loss," Sibley said.

She cautioned, however, that more research is needed. "Our findings," she said, "need to be followed up by the right kind of controlled clinical trial to determine if there is a role for vitamin D supplementation in helping people lose weight when they attempt to cut back on what they eat."

The National Institutes of Health, the University of Minnesota, and the Pennock Family Endowment at the University of Minnesota funded this study.

The dark side of animation ***Could animated slides be stifling learning***

We've all sat through one of those presentations where the animated slides are more interesting than the speaker. Bold and brassy titles slide into view, tasty slices of pie chart fill the screen one by one, and a hail of arrows spikes the points the lecturer hopes to highlight.

But, are these custom animations and slide fades and dissolves actually adding anything to the lecture, or do they have a dark side that detracts from the message and impacts negatively on the message being presented?

Microsoft PowerPoint has, over the last couple of decades, become the tool of choice for creating instructional slideshows. Long gone for most are the overhead projector with its fickle fan and its high-temperature and temperamental bulb, the smudgy marker pen, and the transparent plastic sheet.

Instead, lecturers, speakers and anyone else with a visual message to present with their talk uses PowerPoint and its ilk to present their digital slides. According to the authors of a study in the *International Journal of Innovation and Learning* published this month, many instructors use these options regularly with the impression that such effects enhance student learning by allowing concepts to be introduced incrementally.

Stephen Mahar of the University of North Carolina Wilmington and colleagues have explored the impact of custom animation in PowerPoint lectures and examined the idea that custom animation may, in fact, negatively impact student learning.

To test their hypothesis, the team recorded two versions of a PowerPoint lecture. The presentations differed only in the presence of animation to incrementally present information. They then showed students either the animated or non-animated lecture and then tested the students recall and comprehension of the lecture.

The team found a marked difference in average student performance, with those seeing the non-animated lecture performing much better in the tests than those who watched the animated lecture. Students were able to recall details of the static graphics much better. Animated slides meant to present information incrementally actually require greater concentration, which makes it harder to remember content as well as reducing overall exposure time to the "complete" slide, the researchers found.

Although students appear to like the use of animations in lectures delivered using PowerPoint, there is now strong evidence that animation is nothing more than an entertaining distraction.

The team points out that their study was applied only to the teaching of new concepts. It is possible that teaching a technique might work more effectively with animated, rather than static, slides. Follow-up work will investigate that possibility." *The dark side of custom animation" in Int. J. Innovation and Learning, 2009, 6, 581-592*

Unique roots let plant forage in the snow

* 12:41 12 June 2009 by Colin Barras

High-altitude plants spend a lot of the year covered in thick snow, but one species at least appears to relish its icy canopy.

Botanists have discovered that *Corydalis conorhiza* grows a never-before described network of roots that reach upwards into the overlying snowpack to grab nutrients. This makes the plant the first species known to forage for nutrients in the snow.

"It's remarkable that [the roots] haven't been noticed before," says Hans Cornelissen at VU University in Amsterdam, The Netherlands. "But they are easy to miss because they decay rapidly after snow melt and are soon unrecognisable." After the short growing season and the return of the snow, a new network of roots grows again.



The new "snow roots" growing around Corydalis conorhiza (Image: V. G. Onipchenko)

Cornelissen and his team made the discovery high in the Caucasus mountains in southern Russia. The ground remains snow-covered except during a short growing season in the height of summer.

Lucky find

Exploring the region after the snow melt, Cornelissen's team discovered that *C. conorhiza* specimens were surrounded by a thick layer of matted roots growing upwards and out of the soil (see photo, above right). The team realised that the roots, seemingly growing into thin air, would for most of the year be covered in snow – and so they dubbed them "snow roots".

"Snow roots are fundamentally different in structure from soil-dwelling roots, even in the same species," says Cornelissen. They are much thinner, and rot away soon after exposure to the air.

The next step was to work out what the snow roots are for. The team already knew that nitrogen and phosphorus are limiting growing factors in the high-altitude environment, but they found that the standard soil roots of the plant host fungi that give the plant a phosphorus boost.

The team reasoned that the unusual roots must be used to gather nitrogen that is trapped in snow flakes as they form. To test the hypothesis they added a traceable isotope of nitrogen in water to snow above C. conorrhiza plants. After a few days, the team found that parts of the plant were rich in the isotope.

Head start

As a control, the team also laced the snow above a dandelion with only soil roots that also grows in the area. They found it didn't take on any of the foreign nitrogen.

Feeding off nitrogen in the snow in this way could give the species an important boost, says Cornelissen. "The growing season is only a few months long, and it really helps to take up nitrogen and translocate it to other parts of the plant before the season actually begins," he says. "We have some indication from very old literature that an unrelated plant might have the same adaptation," says Cornelissen. "If that can be confirmed, then snow roots have evolved at least twice independently." *Journal reference: Ecology Letters (in press)*

Scripps research team creates simple chemical system that mimics DNA

Findings offer possible clues about primordial world, and could eventually lead to exotic new materials

La Jolla, CA, –A team of Scripps Research scientists has created a new analog to DNA that assembles and disassembles itself without the need for enzymes. Because the new system comprises components that might reasonably be expected in a primordial world, the new chemical system could answer questions about how life could emerge. The work, reported in the June 11, 2009 issue of Science Express, an advance, online publication of the journal Science, might also be a starting point on the way to exotic new materials that repair themselves or transform in response to their environment.

Scientists are both bemused and fascinated by the question of how life could have arisen on Earth. One of the most prominent theories is that, before the emergence of DNA, the earliest forms of life used RNA to transmit their genetic codes. The late Leslie Orgel, a co-author of the new paper, first suggested this idea, known as the "RNA World."

One of the theory's challenges is that RNA is still so complex that many researchers believe something still simpler must have preceded it. "I have been working for years to learn what replicators and genetic systems might have come before the advent of the RNA World," says team leader of the new research Professor Reza Ghadiri, a Scripps Research chemist.

One key focus for Ghadiri's team has been amino acids' potential primordial role. In 1996, the group showed for the first time that amino acid strands, or peptides, can self-replicate under enzyme-free conditions. In the current work, the Ghadiri lab extends this focus by creating another type of information system that might be capable of something akin to Darwinian evolution. "This work is a beginning step toward that goal," says Ghadiri.

Simpler Building Blocks

While much of the past work with DNA analogs such as PNA has focused on nucleobases already anchored to their backbone units, Ghadiri had the idea of working with simpler building blocks. If these blocks had easily reversed bonds, unlike DNA and PNA, it could avoid the need for enzymes while preserving key characteristics for encoding information. Looking back on the success of the experiments that have followed, Ghadiri says, "This is one of those things where you say to yourself, 'Why didn't I think of this before?'"

The resulting new system involves two main component types. The backbone units are peptides linked in a set pattern with the amino acid cysteine exposed and available to react. These peptides interact with the same nucleobases found in DNA, but each nucleobase is bound to an organic compound known as a thioester.

Thioester bonds reversibly with the cysteine on the peptides to form thioester peptide nucleic acid (tPNA). This allows the nucleobases to attach and disassemble on their own without enzymes, so that a given peptide strand will hold a shifting array of nucleobases. This process is something like soldiers walking around a field achieving a certain formation then moving into a new formation.

If an unzipped segment of DNA is added as a template to a solution with the tPNA components, the nucleobase soldiers will automatically assume a formation on peptide strands that complements the DNA according to standard Watson-Crick pairing of adenine with thymine and cytosine with guanine.

The complementary tPNA and DNA strands bond, but these pairings can then be unzipped by adding to the mix complementary DNA strands, which outcompete the tPNA for space on the initial templates. The DNA-

DNA pairings remain stable, causing the tPNA components to resume their unstable shuffling until a new DNA template is added and the process begins again.

The Ghadiri team was also able to show that a strand of tPNA can act as a template, causing complementary tPNA formation and strand pairing, though they have not yet achieved self-replication for tPNA, an ultimate goal.

Tantalizing Possibilities

All of the chemical constituents of the assembled tPNA could have been found in a world before life began. "So it is tantalizing to think about the possibility of peptides and nucleic acids involved in primordial genetic systems," says Ghadiri. However, because the tPNA can so easily disassemble, the strands do not technically transmit information, and that transmission is how DNA drives life.

To better understand the potential tPNA primordial role, the team is now exploring ways that the tPNA units might be chemically transformed so that at some point the soldiers begin locking hands after achieving a certain formation, allowing the passage of information. The group is also working to determine tPNA's structure, which could resemble the famous DNA double helix or look altogether different.

Beyond origins of life questions, Ghadiri says the work also offers some distant but intriguing possibilities, especially considering that there are almost endless possibilities for creating systems similar to tPNA using differing chemical constituents. Such systems could lead to the formation of new enzymes or other chemicals capable of catalyzing reactions with biomedical or other uses. "The capacity to have nucleic acid-like folded structures with protein features will surely in my mind give us new functionalities," he says, though it is impossible to say yet what those new functionalities might be.

Ghadiri also imagines some science fiction-worthy options for tPNA-related materials such as plastics that can repair themselves when fractured. Another possibility, tied to the way that tPNA rearranges when exposed to differing templates, would be to create materials that can remodel themselves by similarly responding to changes in their environment. "You can in principle do many things, and we're enthusiastic about the prospects," says Ghadiri. "This is just the beginning."

In addition to Orgel and Ghadiri, authors on the paper, entitled "Self-Assembling Sequence-Adaptive Peptide Nucleic Acids," are Yasuvuki Ura, John Beierle, and Luke Leman, all from The Scripps Research Institute.

This work was supported in part by the Skaggs Institute for Chemical Biology, NASA Earth and Space Science Fellowship Program, and the NASA Science Mission Directorate's Planetary Science Division. The paper is dedicated to the memory of Leslie E. Orgel.

Urban myth disproved: Fingerprints do not improve grip friction

Fingerprints do not increase friction

Fingerprints mark us out as individuals and leave telltale signs of our presence on every object that we touch, but what are fingerprints really for? According to Roland Ennos, from the University of Manchester, other primates and tree-climbing koalas have fingerprints and some South American monkeys have ridged pads on their tree-gripping tails, so everyone presumed that fingerprints are there to help us hang onto objects that we grasp. This theory that fingerprints increase friction between the skin and whatever we grab onto has been around for over 100 years, but no one had directly tested the idea. Having already figured out why we have fingernails, Ennos was keen to find out whether fingerprints improve our grip, so he recruited Manchester undergraduate Peter Warman to test out fingerprint friction and publishes his results on June 12 2009 in the *Journal of Experimental Biology* at <http://jeb.biologists.org>.

Because the friction between two solid materials is usually related to the force of one of the materials pressing against the other, Ennos and Warman had to find a way of pushing a piece of acrylic glass (Perspex®) against Warman's finger before pulling the Perspex® along the student's finger to measure the amount of friction between the two. Ennos designed a system that could produce forces ranging from a gentle touch to a tight grip, and then Warman strapped his index finger into the machine to begin measuring his fingerprint's friction.

But after days of dragging the Perspex® along Warman's fingers and thumbs, it was clear that something wasn't quite right. Instead of the friction between each finger and the Perspex® increasing in proportion to the amount that the Perspex® pushed against Warman's fingers, it increased by a smaller fraction than Ennos had expected. Ennos realised that instead of behaving like a normal solid, the skin was behaving like rubber, where the friction is proportional to the contact area between the two surfaces.

To check that skin behaves more like rubber than a normal solid, the duo varied the area of each fingerpad that came into contact with the surface by dragging narrow and wide strips of Perspex® along Warman's fingerpads. They found that the friction did increase as more of the fingerprint came in contact with the surface, so the skin was behaving just like rubber.

Finally, the friction issue was clinched when Warman measured his fingerprints' surface area. The area of skin in contact with the Perspex® was always 33% less than if the fingerpads were smooth resulting in the maximum contact area. Fingerprints definitely don't improve a grip's friction because they reduce our skin's contact with objects that we hold, and even seem to loosen our grip in some circumstances.

So if fingerprints don't tighten our grasp on smooth surfaces, what are they for? Ennos explains that our fingerprints may function in other ways. They might have evolved to grip onto rough surfaces, like tree bark; the ridges may allow our skin to stretch and deform more easily, protecting it from damage; or they may allow water trapped between our finger pads and the surface to drain away and improve surface contact in wet conditions. Other researchers have suggested that the ridges could increase our fingerpads' touch sensitivity. Whatever our fingerprints are for, it seems that the idea that they provide friction for grip is just another urban myth.

<http://jeb.biologists.org>

Reference: Warman, P. H. and Ennos, A. R. (2009). Fingerprints are unlikely to increase the friction of primate fingerpads. *J. Exp. Biol.* 212, 2016-2022

Engraved pigments point to ancient symbolic tradition

Incisions on ochre from a South African cave suggest modern human behavior emerged around 100,000 years ago

By Bruce Bower

Scientists excavating a Stone Age cave on South Africa's southern coast have followed a trail of engraved pigments to what they suspect are the ancient roots of modern human behavior.

Analyses of 13 chunks of decorated red ochre (an iron oxide pigment) from Blombos Cave indicate that a cultural tradition of creating meaningful geometric designs stretched from around 100,000 to 75,000 years ago in southern Africa, say anthropologist Christopher Henshilwood of the University of the Witwatersrand in Johannesburg and his colleagues. Their report appears online and in an upcoming *Journal of Human Evolution*.



Geometric patterns incised on pieces of ancient pigment, such as these 100,000-year-old finds, may reveal the surprisingly ancient origins of modern human behavior. Courtesy of C. Henshilwood and F. d'Errico

Much debate surrounds the issue of when and where language, religion, symbolic decorations and other facets of modern human behavior originated. Researchers such as Henshilwood hypothesize that modern human behavior developed gradually in Africa, beginning more than 100,000 years ago. Others posit that a brain-boosting genetic mutation around 50,000 years ago fostered modern behavior in Africa. Some researchers suspect that behavioral advances first appeared in Europe, Asia and Africa at that later time.

Possible examples of symbolic behavior from around 100,000 years ago — such as proposed human burials in the Middle East and pigment use in Africa — have been controversial.

“What makes the Blombos engravings different is that some of them appear to represent a deliberate will to produce a complex abstract design,” Henshilwood says. “We have not before seen well-dated and unambiguous traces of this kind of behavior at 100,000 years ago.”

Further studies need to confirm that the ancient incisions were not the result of, say, slicing into ochre with stone tools in order to remove powder quickly, cautions anthropologist Curtis Marean of Arizona State University in Tempe, who studies ancient human behavior at another South African cave (SN: 10/20/07, p. 243).

Even if the Blombos pigments contain intentional designs, fully modern human behavior — such as the use of figurative art (SN: 6/20/09, p. 11) — didn't emerge until tens of thousands of years later, contends archaeologist Nicholas Conard of the University of Tuebingen, Germany.

Henshilwood and study coauthor Francesco d'Errico of the University of Bordeaux I in Talence, France, disagree. In their view, the Blombos pigments bear intentionally fashioned designs that held some sort of meaning and were passed down the generations for 25,000 years. Thus, the two researchers say, it's likely that a 100,000-year-old society already steeped in symbolic behavior originally produced the ochre engravings.

In 2002, Henshilwood's team described evidence of symbolic engravings on two other ochre pieces from Blombos Cave. Those 77,000-year-old finds were excavated in 1999 and 2000.

Engraved chunks of pigment in the new analysis were unearthed during the same excavations. Specimens came from either of three sediment levels with estimated ages of 72,000 years, 77,000 years and 100,000 years.

A microscopic analysis indicates that ochre designs were made by holding a piece of pigment with one hand while impressing lines into the pigment with the tip of a stone tool. On several pieces, patterns covered areas that had first been ground down.

Geometric patterns on the ochre pieces include cross-hatched designs, branching lines, parallel lines and right angles.

Pigment powder had also been removed from many of the recovered ochre chunks. Incised patterns may have served as models for pigment designs applied to animal skins or other material, the scientists speculate.

Excavations of Blombos Cave sediment from before 100,000 years ago have begun. "The discovery of more, and perhaps even more striking, engravings is very possible," Henshilwood says.

Don't Stand So Close to Me: Proximity Defines How We Think of Contagion

We judge probability and make risk judgments all the time, such as when we try new products or consider which stocks to trade. It would seem that our decisions would be rational and based on concrete factors; however, we are not always so pragmatic. Some judgments are not based solely on relevant information but can be influenced by subjective beliefs. For example, most of us would probably cringe at the thought of drinking a sugar solution that was labeled "sodium cyanide," even if we knew it was perfectly safe to drink. According to new research by consumer psychologists Arul Mishra and Himanshu Mishra from the University of Utah and Dhananjay Nayakankuppam from the University of Iowa, something as mundane as how objects are grouped together can have a significant impact on the decisions we make.

Volunteers selected a mug from one of two groups. In one group, the wrapped-up mugs were spaced far apart, while in the other group they were closer together. Some of the volunteers were told that one of the mugs was defective while the other volunteers were told that one of the mugs contained a gift coupon.

The volunteers who were told that one of the mugs contained a gift coupon selected from the mugs which were close together. Conversely, the volunteers who were informed that one of the mugs was defective chose from the group of mugs that were spaced far apart.

The researchers then performed a follow-up experiment: volunteers had to choose among ketchup bottles (as before, the bottles were in two groups, close together or spaced farther apart). This time, some of the participants were told that either one or three of the bottles had defective lids, while the remaining participants were told that either one or three of the bottles contained gift coupons. It turns out that the volunteers who were told that three of the bottles had defective lids were the most likely to choose from the spaced apart group and the volunteers who thought that three of the bottles contained gift coupons were the most likely to choose from the closely spaced group.

These results, reported in *Psychological Science*, a journal of the Association for Psychological Science, reveal that we tend to view products that are grouped close together as being "contagious." It appears that if one of the products has a prominent good or bad quality, we will see that quality as spreading among other objects which are close by, a phenomenon known as the "group-contagion effect." As the authors noted, these findings suggest that people tend "to choose from groups of closely arranged products in the gain domain and from groups of widely spaced products in the loss domain."

