Heart attacks become more common but less often fatal in women

Heart attacks appear to have become more common in middle-aged women over the past two decades, but all women and especially those younger than 55 have recently experienced a greater increase than men in their chances of survival following such a heart event, according to two reports in the October 26 issue of Archives of Internal Medicine, one of the JAMA/Archives journals.

Middle-aged women have historically had a lower overall risk of heart events and stroke than men of a similar age, according to background information in one of the articles. However, a recent report showing higher stroke rates among women than men in a sample representative of the U.S. population appeared to reveal a new phenomenon and raised the question of whether heart disease or heart attack were also becoming more prevalent among women.

Amytis Towfighi, M.D., of the University of Southern California, Los Angeles, and colleagues analyzed data from U.S. adults age 35 to 54 who participated in the National Health and Nutrition Examination Surveys (nationally representative surveys conducted by the government) during 1988 to 1994 (4,326 participants) and 1999 to 2004 (4,075 participants). The researchers assessed how often men and women had heart attacks and also compared their Framingham coronary risk score, a measurement of heart disease risk over 10 years that includes factors such as age, cholesterol levels, blood pressure and smoking history.

In both study periods, men age 35 to 54 years had more heart attacks than women in the same age group. However, the gap narrowed in more recent years as heart attacks decreased in prevalence among men and increased in prevalence among women (2.5 percent of men and 0.7 percent of women reported a history of heart attack in 1988-1994, whereas 2.2 percent of men and 1 percent of women did so in 1999-2004).

Between the two time periods, the average Framingham coronary risk score showed an improving trend among men but decreased among women. In male participants, total cholesterol levels remained stable, high-density lipoprotein (HDL or "good" cholesterol) levels and systolic (top number) blood pressure levels improved and smoking levels declined. The only risk factor that improved among women was HDL levels. Diabetes prevalence increased among both men and women, likely due to insulin resistance and the obesity epidemic in both sexes.

"Although men in their midlife years continue to have a higher prevalence of myocardial infarction and a higher 10-year risk of hard coronary heart disease than women of similar age, our study suggests that the risk is increasing in women, while decreasing in men," the authors write. "Therefore, intensification of efforts at screening for and treating vascular risk factors in women in their midlife years may be warranted."

In another report, Viola Vaccarino, M.D., Ph.D., of Emory University School of Medicine, Atlanta, and colleagues investigated trends in the rate of in-hospital deaths following heart attack from June 1, 1994, through Dec. 31, 2006. Data were collected from 916,380 patients through the National Registry of Myocardial Infarction.

In-hospital death rates decreased among all patients between 1994 and 2006, but decreased more markedly in women than in men. The reduced risk of death was largest in women younger than 55 years (a 52.9 percent reduction) and lowest in men of the same age (33.3 percent). The absolute decrease in the risk of death among patients younger than 55 was three times larger in women (2.7 percent) than men (0.9 percent).

"A large part (93 percent) of this sharper decrease in mortality of younger women compared with men in recent years was because the risk status of women on admission improved compared with that of men," the authors write. "Such improvement may be due to better recognition and management of coronary heart disease and its risk factors in women before the acute myocardial infarction event, as suggested by the narrowing sex difference in previous revascularization [surgical treatment for heart disease]."

(Arch Intern Med. 2009;169[19]:1762-1766 and 1767-1774. Available pre-embargo to the media at www.jamamedia.org.)

Editorial: Prevention Is Key for Women and Heart Disease

"Cardiovascular illnesses have been long neglected in their role as the primary cause of mortality in women, both by patients and physicians," write Sabine Oertelt-Prigione, M.D., and Vera Regitz-Zagrosek, M.D., Ph.D., of Charité Universitaetsmedizin, Berlin, in an accompanying editorial. "Men are still believed to be at greater risk for myocardial infarction and stroke and are thus more aggressively informed, counseled and treated for these diseases."

"The improvements described by Towfighi et al and Vaccarino et al are encouraging and indicate that we are on the right track. However, much needs to be done, especially in consideration of the increase in prevalence of risk factors as obesity and type 2 diabetes mellitus in the general population."

"As these studies show, increased and continuous vigorous attention to the prevention of cardiovascular risk factors—by healthy diet, regular physical activity and avoidance of smoke and smoking—is necessary for both men and women," they conclude. (Arch Intern Med. 2009;169[19]:1740-1741.

Advances in screening have offset an increase in Down syndrome

Research: Trends in Down syndrome live births and antenatal diagnoses in England and Wales from 1989 to 2008: Analysis of data from the National Down Syndrome Cytogenetic Register

The number of diagnoses of Down's syndrome has increased by almost three quarters (71%) from 1989/90 to 2007/08, largely due to the considerable increase in the number of older mothers over this period. However, the number of babies born with this condition during the same period fell by 1% because of antenatal screening and subsequent terminations, finds research published on bmj.com today.

Researchers from Barts and The London Medical School analysed data held on the National Down Syndrome Cytogenetic Register (NDSCR) since it was set up in January 1989. The register currently holds anonymous data on over 26,000 cases of Down's syndrome diagnosed antenatal or postnatally in England and Wales, this is around 93% of all diagnosed Down's births and pregnancy terminations in both countries.

Their results show that while there has been a stark increase in the proportion of younger women (below the age of 37) opting for screening (3% to 43%), the proportion of older women deciding to be screened has stayed constant at around 70%, despite improved tests.

And for all women with an antenatal diagnosis of Down's syndrome, the proportion who decided to terminate the pregnancy has also remained constant at around 9 in 10 (92%).

Lead author, Professor Joan Morris, says that, given older women have a far greater chance of having a baby with Down's (the risk for a 40 year old mother is 16 times that for a 25 year old mother), more research is needed to find out why around 30% of older women decide not to be tested. "It is important to ascertain whether the decision is an informed one and, if not, to address the lack of information," she says.

The authors conclude that as more women are having children later in life and a significant proportion of these mothers are deciding against screening "a large number of births with Down's syndrome are still likely, and that monitoring of the numbers of babies born with Down's syndrome is essential to ensure adequate provision for their needs."

Scientists Discover Gene that 'Cancer-Proofs' Rodent's Cells

Naked Mole Rat, the Only Known Cancerless Animal, Has Two-Tier Defense Against Cancer

Despite a 30-year lifespan that gives ample time for cells to grow cancerous, a small rodent species called a naked mole rat has never been found with tumors of any kind—and now biologists at the University of Rochester think they know why.

The findings, presented in today's issue of The Proceedings of the National Academy of Sciences, show that the mole rat's cells express a gene called p16 that makes the cells "claustrophobic," stopping the cells' proliferation when too many of them crowd together, cutting off runaway growth before it can start. The effect of p16 is so pronounced that when researchers mutated the cells to induce a tumor, the cells' growth barely changed, whereas regular mouse cells became fully cancerous.

Naked Mole Rats **(credit University of Rochester)**

"We think we've found the reason these mole rats don't get cancer, and it's a bit of a surprise," says Vera Gorbunova, associate professor of biology at the University of Rochester and lead investigator on the discovery. "It's very early to speculate about the implications, but if the effect of p16 can be simulated in humans we might have a way to halt cancer before it starts."

Naked mole rats are strange, ugly, nearly hairless mouse-like creatures that live in underground communities. Unlike any other mammal, these communities consist of queens and workers more reminiscent of bees than rodents. Naked mole rats can live up to 30 years, which is exceptionally long for a small rodent. Despite large numbers of naked mole-rats under observation, there has never been a single recorded case of a mole rat contracting cancer, says Gorbunova. Adding to their mystery is the fact that mole rats appear to age very little until the very end of their lives.

Over the last three years, Gorbunova and Andrei Seluanov, research professor of biology at the University of Rochester, have worked an unusual angle on the quest to understand cancer: Investigating rodents from across the globe to get an idea of the similarities and differences of how varied but closely related species deal with cancer.

In 2006, Gorbunova discovered that telomerase - an enzyme that can lengthen the lives of cells, but can also increase the rate of cancer - is highly active in small rodents, but not in large ones.

Until Gorbunova and Seluanov's research, the prevailing wisdom had assumed that an animal that lived as long as we humans do needed to suppress telomerase activity to guard against cancer. Telomerase helps cells reproduce, and cancer is essentially runaway cellular reproduction, so an animal living for 70 years has a lot of

chances for its cells to mutate into cancer, says Gorbunova. A mouse's life expectancy is shortened by other factors in nature, such as predation, so it was thought the mouse could afford the slim cancer risk to benefit from telomerase's ability to speed healing.

While the findings were a surprise, they revealed another question: What about small animals like the common grey squirrel that live for 24 years or more? With telomerase fully active over such a long period, why isn't cancer rampant in these creatures?

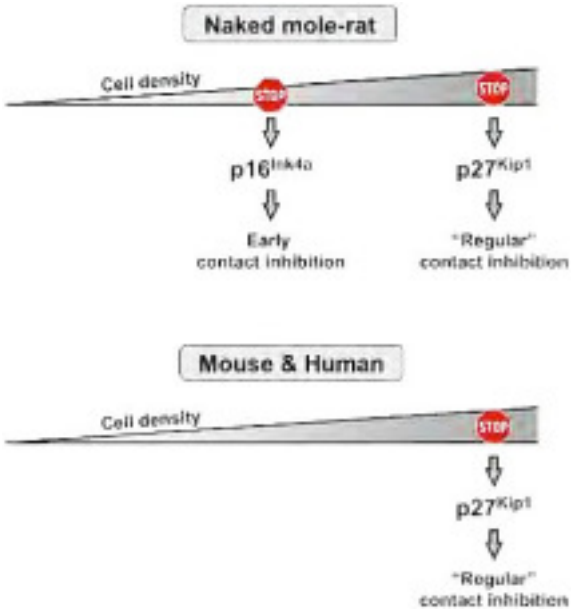
Gorbunova sought to answer that question, and in 2008 confirmed that small-bodied rodents with long lifespans had evolved a previously unknown anti-cancer mechanism that appears to be different from any anticancer mechanisms employed by humans or other large mammals.

At the time she was not able to identify just what the mechanism might be, saying: "We haven't come across this anticancer mechanism before because it doesn't exist in the two species most often used for cancer research: mice and humans. Mice are short-lived and humans are large-bodied. But this mechanism appears to exist only in small, long-lived animals."

Now, Gorbunova believes she has found the primary reason these small animals are staying cancer-free, and it appears to be a kind of overcrowding early-warning gene that the naked mole rat expresses in its cells.

When Gorbunova and her team began specifically investigating mole rat cells, they were surprised at how difficult it was to grow the cells in the lab for study. The cells simply refused to replicate once a certain number of them occupied a space. Other cells, such as human cells, also cease replication when their populations become too dense, but the mole rat cells were reaching their limit much earlier than other animals' cells.

"Since cancer is basically runaway cell replication, we realized that whatever was doing this was probably the same thing that prevented cancer from ever getting started in the mole rats," says Gorbunova.



'The naked mole rats' p16 gene kicks in early to stop cell overcrowding' **(credit University of Rochester)**

Like many animals, including humans, the mole rats have a gene called p27 that prevents cellular overcrowding, but the mole rats use another, earlier defense in gene p16. Cancer cells tend to find ways around p27, but mole rats have a double barrier that a cell must overcome before it can grow uncontrollably.

"We believe the additional layer of protection conferred by this two-tiered contact inhibition contributes to the remarkable tumor resistance of the naked mole rat," says Gorbunova in the PNAS paper.

Gorbunova and Seluanov are now planning to delve deeper into the mole rat's genetics to see if their cancer resistance might be applicable to humans.

This research was funded by the National Institutes of Health and the Ellison Medical Foundation.

Volcanoes Played Pivotal Role In Ancient Ice Age, Mass Extinction

Columbus, Ohio -- Researchers here have discovered the pivotal role that volcanoes played in a deadly ice age 450 million years ago.

Perhaps ironically, these volcanoes first caused global warming -- by releasing massive amounts of carbon dioxide into the atmosphere. When they stopped erupting, Earth's climate was thrown off balance, and the ice age began. The discovery underscores the importance of carbon in Earth's climate today, said Matthew Saltzman, associate professor of earth sciences at Ohio State University.

The results will appear in the journal Geology, in a paper now available online.

Previously, Saltzman and his team linked this same ice age to the rise of the Appalachian Mountains. As the exposed rock weathered, chemical reactions pulled carbon from Earth's atmosphere, causing a global cooling which ultimately killed two-thirds of all species on the planet.

Now the researchers have discovered the other half of the story: giant volcanoes that formed during the closing of the proto-Atlantic Ocean - known as the Iapetus Ocean - set the stage for the rise of the Appalachians and the ice age that followed.

"Our model shows that these Atlantic volcanoes were spewing carbon into the atmosphere at the same time the Appalachians were removing it," Saltzman explained. "For nearly 10 million years, the climate was at a stalemate. Then the eruptions abruptly stopped, and atmospheric carbon levels fell well below what they were in the time before volcanism. That kicked off the ice age," he said.

This is the first evidence that a decrease in carbon from volcanic degassing -- combined with continued weathering of the Appalachians - caused the long-enigmatic glaciation and extinction in the Ordovician period.

Here is the picture the researchers have assembled: 460 million years ago, during the Ordovician, volcanoes along the margin of what is now the Atlantic Ocean spewed massive amounts carbon dioxide into the atmosphere, turning the world into a hothouse. Lava from those volcanoes eventually collided with North America to form the Appalachian Mountains.

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Acid rain -- rich in carbon dioxide - pelted the newly exposed Appalachian rock and wore it away. Chemical reactions trapped the carbon in the resulting sediment, which formed reefs in the vast seas that covered North America.

For about 10 million years, the volcanoes continued to add carbon to the atmosphere as the Appalachians removed it, so the hothouse conditions remained stable. Life flourished in the warm oceans, including abundant species of trilobites and brachiopods.

Then, 450 million years ago, the eruptions stopped. But the Appalachians continued weathering, and atmospheric carbon levels plummeted. The Earth swung from a hothouse to an icehouse.

By 445 million years ago, glaciers had covered the south pole on top of the supercontinent of Gondwana (which would eventually break apart to form the continents of the southern hemisphere). Two-thirds of all species had perished.

When they started this research, Saltzman and his team knew that Earth's climate must have changed drastically at the end of the Ordovician. But they didn't know for certain that volcanoes were the driving force, explained Seth Young, who did this research for his doctoral degree at Ohio State. He is now a postdoctoral researcher at Indiana University.

"This was not necessarily what we expected when we started investigating, but as we combined our data sources, the story began to fall into place," Young said.

Using a computer model, they drew together measurements of isotopes of chemical elements -- including strontium from rocks in Nevada and neodymium from rocks in Virginia and Pennsylvania -- with measurements of volcanic ash beds in the same locations. Then they factored in temperature models developed by other researchers.

The ash deposits demonstrated when the volcanoes stopped erupting; the strontium levels indicated that large amounts of volcanic rock were being eroded and the sediment was flooding Earth's oceans during this time; and the neodymium levels pinpointed the Appalachians as the source of the sediment.

The new findings mesh well with what scientists know about these ancient proto-Atlantic volcanoes, which are thought to have produced the largest eruptions in Earth's history. They issued enough lava to form the Appalachians, enough ash to cover the far ends of the earth, and enough carbon to heat the globe. Atmospheric carbon levels grew 20 times higher than they are today.

This study shows that when those volcanoes stopped erupting, carbon levels dropped, and the climate swung dramatically back to cold. The timing coincides with today's best estimates of temperature fluctuations in the Ordovician.

"The ash beds start building up at the same time the Appalachian weathering begins, but then the record of volcanism ends, and the temperature drops," Saltzman said. "Knowing these details can help us understand how carbon in the atmosphere is changing Earth's climate today."

Next, the researchers will examine the role of the ancient volcanic ash more closely. While the ash was in the atmosphere - before it settled around the globe -- it might have blotted out the sun, and cooled the earth somewhat. Saltzman and his team want to make some estimate of this short-term cooling effect to refine their computer model.

Meanwhile, Young is just starting to re-analyze the same rock samples, this time looking for a different isotope - sulfur. This, he hopes, will offer clues to how much oxygen was in the oceans, and how that oxygen may have affected life in the Ordovician.

Other contributors to this work include Kenneth Foland, professor emeritus of earth sciences, and Jeff Linder, a research associate, both of Ohio State; and Lee Kump, professor of geosciences at Pennsylvania State University. *This research was partly supported by the National Science Foundation.*

Neanderthals 'had sex' with modern man

Jonathan Leake, Science Editor

Modern humans and Neanderthals had sex across the species barrier, according to a leading geneticist who is overseeing a project to compare their genomes.

Professor Svante Paabo, director of genetics at the renowned Max Planck Institute for Evolutionary Anthropology in Leipzig, will shortly publish his analysis of the entire Neanderthal genome, using DNA retrieved from fossils. He aims to compare it with the genomes of modern humans and chimpanzees to work out the ancestry of all three species.

Modern humans arrived in Europe from Africa about 40,000 years ago to find Neanderthals already living there. The two species then co-existed for 10,000-12,000 years before Neanderthals died out - a fact that has caused endless academic speculation about whether they interbred.

Paabo recently told a conference at the Cold Spring Harbor Laboratory near New York that he was now sure the two species had had sex - but a question remained about how "productive" it had been.

"What I'm really interested in is, did we have children back then and did those children contribute to our variation today?" he said. "I'm sure that they had sex, but did it give offspring that contributed to us? We will be able to answer quite rigorously with the new [Neanderthal genome] sequence."

Such an answer might ease the controversy over recent contradictory discoveries regarding Neanderthals. Some fossils seem to have both modern human and Neanderthal features, suggesting that the two species interbred. Yet DNA scans have shown that Neanderthal genes were very different from those of modern man.

Last week Professor Chris Stringer, head of human origins at the Natural History Museum, presented a conference at the Royal Society in London with an idea that could accommodate both sets of evidence.

"It's possible that Neanderthals and humans were genetically incompatible, so they could have interbred but their children would have been less fertile," said Stringer. This phenomenon is seen in many other species such as when lions breed with tigers and horses breed with zebras.

"I used to believe Neanderthals were primitive," said Stringer, "but in the last 10,000-15,000 years before they died out, around 30,000 years ago, Neanderthals were giving their dead complex burials and making tools and jewellery, such as pierced beads, like modern humans."

Due to the length of time that has elapsed since Neanderthals became extinct, any trace of their DNA in modern humans could have been diluted below detectable levels. Paabo hopes to overcome this by scanning the Neanderthal genome for the genes of modern humans.

Deadly stomach infection rising in community settings, Mayo Clinic study finds

Rochester, Minn. - Mayo Clinic researchers have found that a sometimes deadly stomach bug, Clostridium difficile, (http://www.mayoclinic.org/c-difficile/) is on the rise in outpatient settings. Clostridium difficile is a serious bacteria that can cause symptoms ranging from diarrhea to life-threatening inflammation of the colon. These findings were presented today at the 2009 American College of Gastroenterology (ACG) Annual Meeting in San Diego.

Clostridium difficile, often called C. difficile or "C. diff", is a bacterium that is resistant to some antibiotics and is most often contracted by the elderly in hospitals and nursing homes.

"Recent reports have shown increasing incidence and severity of C. difficile infection - especially in the older population," says Darrell Pardi, M.D., Mayo Clinic gastroenterologist and senior author on the study. "Our study examines why the cases are on the rise and who is getting the infection."

In this population-based study, researchers studied 385 cases of C. difficile bacterial infection from 1991-2005 to determine how many cases were hospital-acquired versus community-acquired infections. Of the cases, 192 were hospital-acquired and 35 were residents of nursing homes. Of these hospital-acquired cases, the median age of infection was 72 years; in contrast, 158 cases were community-acquired and the median age was 50 years. Thirty-five percent of the hospital infections had a severe illness compared to 22 percent of community infections who had a severe illness.

The patients with community-acquired infection were also less likely than the hospital-acquired group to have been exposed to antibiotics before their infection. Thus, many of the community-acquired infections lacked the traditional risk factors for infection, namely recent hospitalization and exposure to antibiotics.

There were no differences between community- and hospital-acquired infections in terms of what patients were treated with (primarily metronidazole), response rates, or recurrence rates after treatment.

"We are seeing more cases of C. difficile in the community, but they tend to be less severe and in a younger population," says Dr. Pardi. "The growing incidence of C. difficile infection in both inpatient and outpatient

settings could be linked to the increasing usage of antibiotics and to the possibility that C. difficile may be getting resistant to some of our newer antibiotics."

There are hundreds of kinds of bacteria found normally in the intestines. Many play beneficial roles in the body. When a patient takes an antibiotic to treat an infection, it often destroys beneficial bacteria as well as the bacteria that are causing the illness. Without enough healthy bacteria, dangerous pathogens such as C. difficile can quickly grow out of control. Once it takes hold, C. difficile can produce two virulent toxins that attack the lining of the intestine.

"Doctors have gotten better at spotting C. difficile in hospitals and nursing homes; however, now doctors and patients need to be more aware that you can get this infection as an outpatient and that a case of diarrhea or abdominal cramps at home could become serious," says Dr. Pardi.

According to the Centers for Disease Control and Prevention, each year in the United States, C. difficile is responsible for tens of thousands of diarrhea cases and at least 5,000 deaths.

The pain of torture can make the innocent seem guilty

Cambridge, Mass. - The rationale behind torture is that pain will make the guilty confess, but a new study by researchers at Harvard University finds that the pain of torture can make even the innocent seem guilty.

Participants in the study met a woman suspected of cheating to win money. The woman was then "tortured" by having her hand immersed in ice water while study participants listened to the session over an intercom. She never confessed to anything, but the more she suffered during the torture, the guiltier she was perceived to be.

The research, published in the "Journal of Experimental Social Psychology," was conducted by Kurt Gray, graduate student in psychology, and Daniel M. Wegner, professor of psychology, both in Harvard's Faculty of Arts and Sciences.

"Our research suggests that torture may not uncover guilt so much as lead to its perception," says Gray. "It is as though people who know of the victim's pain must somehow convince themselves that it was a good idea - and so come to believe that the person who was tortured deserved it."

Not all torture victims appear guilty, however. When participants in the study only listened to a recording of a previous torture session - rather than taking part as witnesses of ongoing torture - they saw the victim who expressed more pain as less guilty. Gray explains the different results as arising from different levels of complicity.

"Those who feel complicit with the torture have a need to justify the torture, and so link the victim's pain to blame," says Gray. "On the other hand, those distant from torture have no need to justify it and so can sympathize with the suffering of the victim, linking pain to innocence."

The study included 78 participants: half met the woman who was apparently tortured (actually a confederate of the experimenters who was, of course, not harmed at all), and half did not. Participants were told that the study was about moral behavior, and that the woman may have cheated by taking more money than she deserved. The experimenter suggested that a stressful situation might make a guilty person confess, so participants listened for a confession over a hidden intercom as she was subjected to the sham "torture."

The confederate did not admit to cheating but reacted to having her hand submerged in ice water with either indifference or with whimpering and pleading. Participants who had met her rated her as more guilty the more she suffered. Those who did not meet her rated her as more guilty when she felt less pain.

Gray suggests that these results offer an explanation for the debate swirling around torture. "Seeing others in pain can perpetuate ideological differences about the justifiability of torture," says Gray. "Those who initially advocate torture see those harmed as guilty, unlike those who initially reject torture and its methods."

The findings also shed light on the Abu Ghraib scandal, where prison guards tortured Iraqi detainees. Prison guards, who are close to the suffering of detainees, see detainees as more guilty the more they suffer, unlike the more distant general public.

The case is still open on whether torture actually makes victims more likely to tell the truth. This research suggests instead that the mere fact that someone was tortured leads observers to think that the truth was found.

Alcohol activates cellular changes that make tumor cells spread

Researchers at Rush University Medical Center explain link between alcohol and cancer

Alcohol consumption has long been linked to cancer and its spread, but the underlying mechanism has never been clear. Now, researchers at Rush University Medical Center have identified a cellular pathway that may explain the link.

In a study published in the current issue of Alcoholism: Clinical and Experimental Research, the researchers found that alcohol stimulates what is called the epithelial–to–mesenchymal transition, in which run-of-the-mill cancer cells morph into a more aggressive form and begin to spread throughout the body.

"Our data are the first to show that alcohol turns on certain signals inside a cell that are involved in this critical transition," said Christopher Forsyth, PhD, assistant professor of medicine and biochemistry at Rush University Medical Center and lead author of the study.

The epithelial-to-mesenchymal transition is a hot area of research right now, implicated in the process whereby cancer cells become metastatic. A large body of laboratory and clinical research suggests that it plays a key role in making cancer cells aggressive. "Cancer cells become dangerous when they metastasize," Forsyth said. "Surgery can remove a tumor, but aggressive tumor cells invade tissues throughout the body and take over. If we can thwart this transition, we can limit cancer's toll."

The researchers treated colon and breast cancer cell lines with alcohol and then looked for the biochemical hallmarks of the epithelial-to-mesenchymal transition, including evidence of a transcription factor called Snail and of the receptor for epidermal growth factor. Snail controls the epithelial-to-mesenchymal transition; when overexpressed in mice, it induces the formation of multiple tumors. Epidermal growth factor is required by many cancer cells. "They need lots of it," Forsyth said. "They are addicted to it."

Laboratory tests showed that alcohol activated both these and other biochemicals characteristic of the epithelial-to-mesenchymal transition. Tests also demonstrated that the alcohol-treated cells had lost their tight junctions with adjacent cells, a preparation for migrating, as metastatic cells do.

In addition, Forsyth and his colleagues found that the same roster of biomarkers was activated in normal intestinal cells treated with alcohol, suggesting that alcohol not only worsens the profile of existing cancer cells but also may initiate cancer by stimulating the epithelial-to-mesenchymal transition.

Other researchers at Rush involved in the study were Yueming Tang, PhD, Maliha Shaikh, MS, Dr. Lijuan Zhang and Dr. Ali Keshavarzian. Research support was provided in part by the National Institutes of Health.

UC Davis researchers identify dominant chemical that attracts mosquitoes to humans

Scientists at the University of California, Davis, have identified the dominant odor naturally produced in humans and birds that attracts the blood-feeding Culex mosquitoes, which transmit West Nile virus and other life-threatening diseases.

The groundbreaking research, published this week in the early online edition of the Proceedings of the National Academy of Sciences, explains why mosquitoes shifted hosts from birds to humans and paves the way for key developments in mosquito and disease control.

Entomology professor Walter Leal and postdoctoral researcher Zain Syed found that nonanal (sounds like NAWN-uh-nawl) is the powerful semiochemical that triggers the mosquitoes' keen sense of smell, directing them toward a blood meal. A semiochemical is a chemical substance or mixture that carries a message.

"Nonanal is how they find us," Leal said. "The antennae of the Culex quinquefasciatus are highly developed to detect even extremely low concentrations of nonanal." Mosquitoes detect smells with the olfactory receptor neurons of their antennae.

Birds, the main hosts of mosquitoes, serve as the reservoir for the West Nile virus, Leal said. When infected mosquitoes take a blood meal, they transmit the virus to their hosts, which include birds, humans, horses, dogs, cats, bats, chipmunks, skunks, squirrels and domestic rabbits. Since 1999, the U.S. Centers for Disease Control and Prevention have recorded 29,397 human cases and 1,147 fatalities in the United States alone.

The UC Davis researchers tested hundreds of naturally occurring compounds emitted by people and birds. They collected chemical odors from 16 adult human subjects, representing multiple races and ethnic groups.

"We then determined the specificity and sensitivity of the olfactory receptor neurons to the isolated compounds on the antennae of the mosquitoes," Syed said.

Leal and Syed found that nonanal acts synergistically with carbon dioxide, a known mosquito attractant. "We baited mosquito traps with a combination of nonanal and carbon dioxide and we were drawing in as many as 2,000 a night in Yolo County, near Davis," Syed said. "Nonanal, in combination with carbon dioxide, increased trap captures by more than 50 percent, compared to traps baited with carbon dioxide alone."

The UC Davis research was funded in part by the National Institutes of Health; a cooperative research agreement with Bedoukian Research, a supplier of specialty aroma and flavor ingredients headquartered in Connecticut; and the National Science Foundation.

Global Update

Tropical Disease: Neglected Tropical Ills Extract Steep Toll in Islamic World, a Journal Article Says

By DONALD G. McNEIL Jr.

Muslim nations shoulder a “devastating burden” of the world’s neglected tropical diseases, according to an article published Monday in the Public Library of Science Neglected Tropical Diseases journal. The article, a combination of analysis and editorial written by the journal’s editor, Peter J. Hotez, shows that the member

states of the Organization of the Islamic Conference account for 40 percent of the world's infestations with intestinal worms.

Worm infestations, which are most common in children, can stunt their growth and make them too tired to stay awake in school. They can cause dangerous anemia in pregnant women and disabling pain in farmers.

Member countries also have 20 percent of leprosy cases and 21 percent of blinding trachoma.

At the same time, the article said, there is no school of tropical medicine anywhere in the Islamic world, even though several Persian Gulf nations are building top-tier universities.

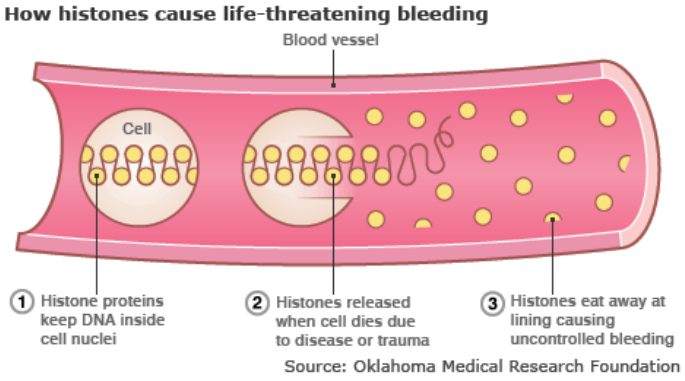
Dr. Hotez wrote that attacking neglected diseases - most of which have simple, inexpensive solutions - was a cost-efficient way to help poor people in Muslim countries. "Joint action between the G-8 countries and prominent families and governments in the Persian Gulf," he wrote, "would represent an impressive beginning."

In an interview, Dr. Hotez said he began work on his article after hearing President Obama in Cairo in June urge a new relationship between Islam and the West. Oil money, Western medical knowledge and better governance in some Muslim nations could quickly improve the lot of the poor, he said.

Antibody 'fixes internal bleeds'

Scientists say they have discovered an antibody that could minimise the major internal bleeding seen in traumas like bullet wounds and car crashes.

The team at Oklahoma Medical Research Foundation (OMRF) has discovered that a protein called histone is responsible for much of the damage. They say they have found a specific type of antibody that can block the ability of histone to cause damage. They say it could lead to new ways to treat diseases and serious injuries.



'Life threatening'

Writing in the journal, Nature Medicine, the OMRF researchers found that when mice had a bad blood stream infection (sepsis), their blood contained high levels of histones. They checked this in primates and humans and found the same result.

The histone protein normally sits in the nucleus of a cell, packed around the strands of DNA. It regulates the DNA, causing it to fold and form the characteristic double helix. When the cell is damaged by injury or disease, the histone is released into the blood system where it begins to kill the lining of blood vessels, causing damage, the OMRF researchers said. This, they believe, results in uncontrolled internal bleeding and fluid build-up in the tissues, which are life threatening.

Dr Charles Esmon, of OMRF who led the research, said: "When we realised that histones were so toxic, we immediately went to work looking for a way to stop their destructive tendencies."

Mouse antibody

Marc Monestier, a colleague at Temple University in Philadelphia, had already discovered a specific type of antibody known as a monoclonal antibody that could block the histones.

It had been observed that patients with auto-immune diseases make antibodies to the proteins in their cell nuclei but it was not known why. This antibody came from a mouse with an auto-immune disease.

The OMRF team have tested the antibody in mice with sepsis and it does stop the toxic effects of the histones and they recover, the researchers say. They now want to test it in primates and eventually humans.

Dr Esmon said histones were similar in all mammals because they were such basic building blocks. So a mouse antibody should work equally well in a human.

He said: "We think it was an adaptation during evolution. "Millions of years ago, when people and animals got ill, they did not die of heart attacks or car accidents they died of infectious diseases.

"Their immune systems went into overdrive throwing everything at it and we believe the histones in the cell nucleus, part of the basic building blocks of life, were the last resort."

Dr Stephen Prescott, president of OMRF, said: "These findings offer some clues as to why people suffering from one traumatic injury often experience a catastrophic 'cascade' of secondary traumatic events. "If we can figure out how to control the initial injury, perhaps that will stop the domino effect that so often follows."

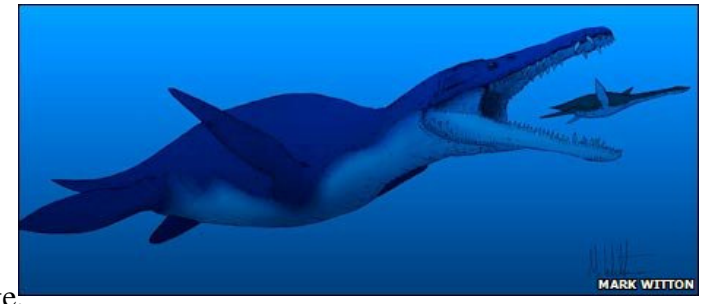
Colossal 'sea monster' unearthed

By Rebecca Morelle Science reporter, BBC News

The fossilised skull of a colossal "sea monster" has been unearthed along the UK's Jurassic Coast. The ferocious predator, which is called a pliosaur, terrorised the oceans 150 million years ago. The skull is 2.4m long, and experts say it could belong to one of the largest pliosaurs ever found: measuring up to 16m in length.

The fossil, which was found by a local collector, has been purchased by Dorset County Council. It was bought with money from the Heritage Lottery Fund, and it will now be scientifically analysed, prepared and then put on public display at Dorset County Museum.

Palaeontologist Richard Forrest told the BBC: "I had heard rumours that something big was turning up. But seeing this thing in the flesh, so to speak, is just jaw dropping. It is simply enormous."



Pliosaurs were a form of plesiosaur, a group of giant aquatic reptiles that dominated the seas around the same time that dinosaurs roamed the Earth.

They had short necks and huge, crocodilian-like heads that contained immensely powerful jaws and a set of huge, razor-sharp teeth. Using four paddle-like limbs to propel their bulky bodies through the water, they made easy work of passing prey such as dolphin-like ichthyosaurs and even other plesiosaurs.

David Martill, a palaeontologist from the University of Portsmouth, said: "These creatures were monsters.

"They had massive big muscles on their necks, and you would have imagined that they would bite into the animal and get a good grip, and then with these massive neck muscles they probably would have thrashed the animals around and torn chunks off. "It would have been a bit of a blood bath."

Big contender

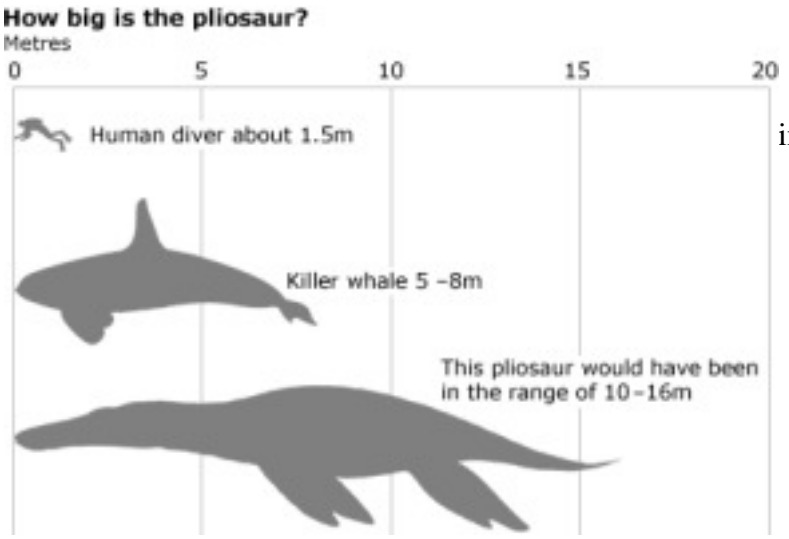
Experts think this latest discovery could represent one of the largest pliosaurs ever found. Dr Martill said: "This thing is absolutely enormous. When I saw it, it really just hit me how big it was." The fossil comprises a lower jaw and upper skull. And based on their length of 2.4m (7.9ft), it is estimated that the creature would have measured between 10 and 16m (33-52ft) from tip to tail, and would have weighed in at a hefty 7-12 tonnes.

This means it could rival recent finds made in Svalbard, where beasts dubbed "The Monster" and "Predator X" were thought to have measured 15m-long (49ft), and in Mexico, where the "Monster of Aramberri" was discovered in 2002, and is believed to have been of similar dimensions.

Dr Martill added: "We only have the head, so you cannot be absolutely precise.

"But it may be vying with the ones found in Svalbard and Mexico for the title of the world's largest."

The specimen is still in its rocky, unprepared form, but it is clear that it has been remarkably well preserved.



Richard Forrest, a plesiosaur expert, said: "Pliosaur skulls are very big, but not that robust, in general, and you tend to find them crushed flat - completely 'pancaked'. "What is fantastic about this new skull, not only is it absolutely enormous, but it is pretty much in 3D and not much distorted."

He added: "You have this wonderful lower jaw - and you can just see from the depth and the thickness that this was immensely strong. "It could have taken a human in one gulp; in fact, something like a T. Rex would have been breakfast for a beast like this."

Geological treasure trove

The fossil was discovered by a local collector along the Jurassic Coast, a 150km (95 mile) stretch of coastline covering Dorset and East Devon that spans 185 million years of geological history.

The exact location of the find is not being revealed, as Dorset County Council does not want to encourage people to head to the spot. The area is unstable and prone to rock falls and landslides.

Richard Edmonds, Dorset County Council's earth science manager for the Jurassic Coast, said: "This part of the coastline is eroding really rapidly and that means the fossils that are trapped and buried are constantly tumbling out on to the beach.

"The collector was lucky enough to come along on the day a large piece fell out of the cliff, and that gave him the clue to keep on looking. He spent the next four years coming back day after day, and as a result he has uncovered this absolutely incredible fossil. "It was an amazing effort."

Dr Edmonds believes that the rest of the giant may still be entombed in the rock, but it could take decades for it to emerge.

He said: "The ground is dipping very steeply, and as it is such a huge specimen it will be buried beneath layer-upon-layer of rock, so we will have to patiently wait for the next big landslide."

Using Heritage Lottery Funds, Dorset County Council has now purchased the fossil for £20,000.

David Tucker, the County's museums advisor, said: "Our aim is to purchase fossils found along the Jurassic Coast World Heritage Site and to get them into local museums - we want to put really exceptional fossils in museums."

The council is now meeting with experts to discuss how best to study and prepare the fossil.

Scientists say it will provide a fantastic opportunity, which could reveal a wealth of information about these giants of the seas, and the ancient world they once inhabited.

Well

The Human Body Is Built for Distance

By TARA PARKER-POPE

Does running a marathon push the body further than it is meant to go?

The conventional wisdom is that distance running leads to debilitating wear and tear, especially on the joints. But that hasn't stopped runners from flocking to starting lines in record numbers.

Last year in the United States, 425,000 marathoners crossed the finish line, an increase of 20 percent from the beginning of the decade, Running USA says. Next week about 40,000 people will take part in the New York City Marathon. Injury rates have also climbed, with some studies reporting that 90 percent of those who train for the 26.2-mile race sustain injuries in the process.

But now a best-selling book has reframed the debate about the wisdom of distance running. In "Born to Run" (Knopf), Christopher McDougall, an avid runner who had been vexed by injuries, explores the world of the Tarahumara Indians of Mexico, a tribe known for running extraordinary distances in nothing but thin-soled sandals. Mr. McDougall makes the case that running isn't inherently risky. Instead, he argues that the commercialization of urban marathons encourages overzealous training, while the promotion of high-tech shoes has led to poor running form and a rash of injuries.

"The sense of distance running being crazy is something new to late-20th-century America," Mr. McDougall told me. "It's only recently that running has become associated with pain and injury."

The scientific evidence supports the notion that humans evolved to be runners. In a 2007 paper in the journal Sports Medicine, Daniel E. Lieberman, a Harvard evolutionary biologist, and Dennis M. Bramble, a biologist at the University of Utah, wrote that several characteristics unique to humans suggested endurance running played an important role in our evolution.

Most mammals can sprint faster than humans - having four legs gives them the advantage. But when it comes to long distances, humans can outrun almost any animal. Because we cool by sweating rather than panting, we can stay cool at speeds and distances that would overheat other animals. On a hot day, the two scientists wrote, a human could even outrun a horse in a 26.2-mile marathon.

Why would evolution favor the distance runner? The prevailing theory is that endurance running allowed primitive humans to incorporate meat into their diet. They may have watched the sky for scavenging birds and then run long distances to reach a fresh kill and steal the meat from whatever animal was there first.

Other research suggests that before the development of slingshots or bows, early hunters engaged in persistence hunting, chasing an animal for hours until it overheated, making it easy to kill at close range. A 2006 report in the journal Current Anthropology documents persistence hunting among modern hunter-gatherers, including the Bushmen in Africa. "Ancient humans exploited the fact that humans are good runners in the heat," Dr. Bramble said. "We have such a great cooling system" - many sweat glands, little body hair.

There is other evidence that evolution favored endurance running. A study in The Journal of Experimental Biology last February showed that the short toes of the human foot allowed for more efficient running, compared with longer-toed animals. Increasing toe length as little as 20 percent doubles the mechanical work of the foot. Even the fact that the big toe is straight, rather than to the side, suggests that our feet evolved for running.

"The big toe is lined up with the rest, not divergent, the way you see with apes and our closest nonrunning relatives," Dr. Bramble said. "It's the main push-off in running: the last thing to leave the ground is that big toe."

Springlike ligaments and tendons in the feet and legs are crucial for running. (Our close relatives the chimpanzee and the ape don't have them.) A narrow waist and a midsection that can turn allow us to swing our arms and prevent us from zigzagging on the trail. Humans also have a far more developed sense of balance, an advantage that keeps the head stable as we run. And most humans can store about 20 miles' worth of glycogen in their muscles.

And the gluteus maximus, the largest muscle in the human body, is primarily engaged only during running. "Your butt is a running muscle; you barely use it when you walk," Dr. Lieberman said. "There are so many features in our bodies from our heads to our toes that make us good at running."

So if we're born to run, why are runners so often injured? A combination of factors is likely to play a role, experts say. Exercise early in life can affect the development of tendons and muscles, but many people don't start running until adulthood, so their bodies may not be as well developed for distance. Running on only artificial surfaces and in high-tech shoes can change the biomechanics of running, increasing the risks of injury.

What's the solution? Slower, easier training over a long period would most likely help; so would brief walk breaks, which mimic the behavior of the persistence hunter. And running on a variety of surfaces and in simpler shoes with less cushioning can restore natural running form.

Mr. McDougall says that while researching his book, he corrected his form and stopped using thickly cushioned shoes. He has run without injury for three years.

Cancers Can Vanish Without Treatment, but How?

By GINA KOLATA

Call it the arrow of cancer. Like the arrow of time, it was supposed to point in one direction. Cancers grew and worsened.

But as a paper in The Journal of the American Medical Association noted last week, data from more than two decades of screening for breast and prostate cancer call that view into question. Besides finding tumors that would be lethal if left untreated, screening appears to be finding many small tumors that would not be a problem if they were left alone, undiscovered by screening. They were destined to stop growing on their own or shrink, or even, at least in the case of some breast cancers, disappear.

"The old view is that cancer is a linear process," said Dr. Barnett Kramer, associate director for disease prevention at the National Institutes of Health. "A cell acquired a mutation, and little by little it acquired more and more mutations. Mutations are not supposed to revert spontaneously."

So, Dr. Kramer said, the image was "an arrow that moved in one direction." But now, he added, it is becoming increasingly clear that cancers require more than mutations to progress. They need the cooperation of surrounding cells and even, he said, "the whole organism, the person," whose immune system or hormone levels, for example, can squelch or fuel a tumor.

Cancer, Dr. Kramer said, is a dynamic process.

It was a view that was hard for some cancer doctors and researchers to accept. But some of the skeptics have changed their minds and decided that, contrary as it seems to everything they had thought, cancers can disappear on their own.

"At the end of the day, I'm not sure how certain I am about this, but I do believe it," said Dr. Robert M. Kaplan, the chairman of the department of health services at the School of Public Health at the University of California, Los Angeles, adding, "The weight of the evidence suggests that there is reason to believe."

Disappearing tumors are well known in testicular cancer. Dr. Jonathan Epstein at Johns Hopkins says it does not happen often, but it happens.

A young man may have a lump in his testicle, but when doctors remove the organ all they find is a big scar. The tumor that was there is gone. Or, they see a large scar and a tiny tumor because more than 95 percent of the tumor had disappeared on its own by the time the testicle was removed.

Or a young man will show up with a big tumor near his kidney. Doctors realize that it started somewhere else, so they look for its origin. Then they discover a scar in the man's testicle, the only remnant of the original cancer because no tumor is left.

Testicular cancer is unusual; most others do not disappear. But there is growing evidence that cancers can go backward or stop, and researchers are being forced to reassess their notions of what cancer is and how it develops.

Of course, cancers do not routinely go away, and no one is suggesting that patients avoid treatment because of such occasional occurrences.

"Biologically, it is a rare phenomenon to have an advanced cancer go into remission," said Dr. Martin Gleave, a professor of urology at the University of British Columbia.

But knowing more about how tumors develop and sometimes reverse course might help doctors decide which tumors can be left alone and which need to be treated, something that is now not known in most cases.

Cancer cells and precancerous cells are so common that nearly everyone by middle age or old age is riddled with them, said Thea Tlsty, a professor of pathology at the University of California, San Francisco. That was discovered in autopsy studies of people who died of other causes, with no idea that they had cancer cells or precancerous cells. They did not have large tumors or symptoms of cancer. "The really interesting question," Dr. Tlsty said, "is not so much why do we get cancer as why don't we get cancer?"

The earlier a cell is in its path toward an aggressive cancer, researchers say, the more likely it is to reverse course. So, for example, cells that are early precursors of cervical cancer are likely to revert. One study found that 60 percent of precancerous cervical cells, found with Pap tests, revert to normal within a year; 90 percent revert within three years.

And the dynamic process of cancer development appears to be the reason that screening for breast cancer or prostate cancer finds huge numbers of early cancers without a corresponding decline in late stage cancers.

If every one of those early cancers were destined to turn into an advanced cancer, then the total number of cancers should be the same after screening is introduced, but the increase in early cancers should be balanced by a decrease in advanced cancers.

That has not happened with screening for breast and prostate cancer. So the hypothesis is that many early cancers go nowhere. And, with breast cancer, there is indirect evidence that some actually disappear.

It is harder to document disappearing prostate cancers; researchers say they doubt it happens. Instead, they say, it seems as if many cancers start to grow then stop or grow very slowly, as has been shown in studies like one now being done at Johns Hopkins. When men have small tumors with cells that do not look terribly deranged, doctors at Johns Hopkins offer them an option of "active surveillance." They can forgo having their prostates removed or destroyed and be followed with biopsies. If their cancer progresses, they can then have their prostates removed.

Almost no one agrees to such a plan. "Most men want it out," Dr. Epstein said. But, still, the researchers have found about 450 men in the past four or five years who chose active surveillance. By contrast, 1,000 a year have their prostates removed at Johns Hopkins. From following those men who chose not to be treated, the investigators discovered that only about 20 percent to 30 percent of those small tumors progressed. And many that did progress still did not look particularly dangerous, although once the cancers started to grow the men had their prostates removed.

In Canada, researchers are doing a similar study with small kidney cancers, among the few cancers that are reported to regress occasionally, even when far advanced.

That was documented in a study, led by Dr. Gleave that compared an experimental treatment with a placebo in people with kidney cancer that had spread throughout their bodies.

As many as 6 percent who received a placebo had tumors that shrank or remained stable. The same thing happened in those who received the therapy, leading the researchers to conclude that the treatment did not improve outcomes.

The big unknown is the natural history of many small kidney tumors, many of which are early kidney cancers. How often do small tumors progress? Do they ever disappear? Do they all need surgical excision? At what stage do most kidney cancers reach a point of no return?

These days, Dr. Gleave said, more patients are having ultrasound or CT scans for other reasons and learning that there is a small lump on one of their kidneys. In the United States, the accepted practice is to take those tumors out. But, he asks, "Is that always necessary?"

His university is participating in a countrywide study of people with small kidney tumors, asking what happens when those tumors are routinely examined, with scans, to see if they grow. About 80 percent do not change or actually regress over the next three years.

With early detection, he said, "our net has become so fine that we are pulling in small fish as well as big fish." Now, he said, "we have to identify which small fish we can let go."

US FDA says omega-3 oils from GM soya are safe to eat

* 16:37 27 October 2009 **by Andy Coghlan**

Good news for fish stocks at last. A genetically modified soybean that produces oil containing omega-3 fatty acids – recommended for heart and brain health – could supplement fish as a source of these nutrients.

Last week, the US Food and Drug Administration made public its ruling that the oil produced by GM soybeans is safe to eat, meaning food companies can begin testing it in products such as margarine.

Developed by biotech giant Monsanto, the soybean is the first GM plant that has claimed health benefits for consumers, not just economic benefits to farmers. Two other companies, BASF (PDF) and Du Pont, say they are not far behind. BASF has developed GM canola plants that produce similar oils, while Du Pont makes them by fermenting micro-organisms, and says it plans to launch its first "omega-3" pill early next year.

Death watch

Omega-3 fatty acids have been estimated to reduce the risk of heart attack and stroke by up to 26 per cent, and of sudden cardiac death by 45 per cent. Earlier this year, a study by the Harvard School of Public Health concluded that a lack of omega-3 in the diet is the sixth leading cause of preventable deaths in the US (PLoS Medicine, DOI: 10.1371/journal.pmed.1000058).

A review of 97 studies in 2005 concluded that omega-3s are as effective at reducing the risk of heart attacks and strokes as statins, the leading class of cholesterol-lowering drugs. Some plants, such as linseed, naturally produce an omega-3 called alpha-linolenic acid (ALA), and one way to increase the amount of omega-3 in our diet is to eat these plants or margarines and other foodstuffs that contain added ALA.

However, only a tiny amount of ALA is converted by the body into a fatty acid it can use, prompting some nutritionists to say the labelling on omega-3-enhanced margarines is misleading.

Fish oils are rich in two related omega-3s, docosahexaenoic acid (DHA), which is important for nerves and the brain, and eicosapentaenoic acid (EPA), which is vital for cardiovascular health.

Gene tricks

BASF has inserted five genes from algae that naturally make EPA and DHA into the canola genome. Its product is still in development.

Monsanto has taken a different approach. It inserted two genes into the soybean genome, one from a plant related to primrose and one from a fungus. The modified soybean produces stearidonic acid, or SDA. Like ALA, SDA is converted into EPA in the body, but in much higher proportions – about a third, Monsanto says.

"To get 1 gram of EPA, you'd have to eat about 3 to 4 grams of SDA, and about 14 to 20 grams of ALA," says David Stark of Monsanto. However, Stark acknowledges that hardly any of the SDA is converted into the DHA needed for brain health.

Good for fish

The modified plant oils could ease the pressure on fish stocks, currently the principal source of omega-3 fatty acids.

At present, there is no official recommended daily intake of omega-3s. According to GOED Omega-3, an umbrella group for manufacturers of omega-3-containing products, the optimal intake is only reached in fish-eating nations such as Japan and Iceland, with typical per-capita consumption in western nations a fifth of this level.

Monsanto claims that meeting GOED's recommended intake in western nations could require as little as 400,000 hectares of its soybean crops. Less than half a hectare, it says, would provide the same amount of EPA as 10,000 servings of salmon.

One worry is that farmers may clear tropical rainforests to grow the oil-producing plants. But Solae of St Louis, Missouri, which will be commercialising the GM soybean, says that the crops are more suited to the temperate climate of North America.

Jack Winkler, head of the Nutrition Policy Unit at London Metropolitan University, is enthusiastic about the prospect of plant-derived omega-3s. "There are not enough fish in the sea to provide people with the EPA and DHA that we need. [This] is a very positive way forward."

Daniel Pauly, a fisheries specialist at the University of British Columbia in Vancouver, Canada, also welcomes the move. "Our stressed marine ecosystem would benefit from an alternative to fish oil as a source of omega-3s," he says.

However, in Europe at least, the new sources of omega-3s may encounter public resistance. Helen Wallace of GeneWatch UK, a lobby group in Buxton, Derbyshire, says: "It will be interesting to see if people in the US believe the benefits exist." Europeans have traditionally been wary of genetically modified crops and Wallace says they are also suspicious of medical claims about food. All this makes the future uncertain for the products in Europe.

Stanford study recommends change in treating pulmonary embolisms

STANFORD, Calif. — William Kuo, MD, was the on-call interventional radiologist one Friday night three years ago when he received a call from the intensive care unit at Stanford Hospital & Clinics. He was asked to attend to a 62-year-old woman who had collapsed at home and was rushed to the emergency room with massive blood clots in her lungs.

"I get very emotional when I think about what happened," said Kuo, assistant professor of radiology at the Stanford University School of Medicine. "I could immediately see the patient was not doing well. She was dying, and the ICU team had notified the family that she was going to die very soon."

What happened that night would set Kuo on a three-year mission to design and implement studies to reveal the safety and effectiveness of a new treatment called catheter-directed therapy or catheter-directed thrombolysis for massive blood clots in the lungs.

The results of the Stanford study, a meta-analysis of scientific data from around the world, showed that when this therapy was used to treat dangerous blood clots, it saves lives. In fact, the data indicated that the catheter procedure was life-saving in 86.5 percent of the cases studied, prompting Kuo and his co-authors to call for making the procedure the first-line treatment for pulmonary embolism. The study will be published Oct. 30 in the Journal of Vascular and Interventional Radiology.

"I remember that night so vividly," Kuo said of the events that led to his research. "The patient was by far the sickest I had ever seen on my angiography table. She couldn't breathe on her own. She was barely alive. There was no time to waste."

As in most cases of pulmonary embolism, blood clots had first formed in the patient's legs, then traveled to her lungs, interfering with oxygenation and the heart's ability to pump blood into the lungs. Because of the massive blood clots, she was quickly suffocating to death. The ICU staff had already done everything they could to save her.

She had been given an intravenous infusion of potent clot-busting medicine, a treatment called systemic thrombolysis, but that had already failed.

Kuo was initially consulted to perform a minor procedure - placement of a special filter in the major abdominal blood vessel to prevent more clots from traveling from the legs to the lungs, but he knew it would do little to save her. And then an idea came to him.

"I had been reading about experimental catheter-based treatments to remove these clots from the lungs," Kuo said. "I told the staff, 'We can do more than just insert a filter. We can go after these clots using specially-designed catheters.' The ICU staff was at first skeptical, but I just kept insisting because I knew it might save her life. We quickly obtained consent from the family and went ahead with it."

As a vascular and interventional radiologist, Kuo is experienced in guiding and maneuvering catheters and wires through blood vessels using real-time radiologic imaging. He uses these techniques to reach diseased areas and to treat a variety of conditions without open surgery. Kuo knew how to perform this type of targeted, less-invasive treatment.

He quickly made a small incision in the patient's neck, inserted a catheter - a thin plastic tube - into the blood vessel. He then used real-time X-ray images (fluoroscopy) to guide the catheter, navigating through the heart and finally reaching the blood clots within the lungs. First, he injected clot-busting medicine through the catheter directly into the clots. Then, he used the catheter to mechanically break up the clots. Finally, he suctioned them out. "It was quite a rush of adrenaline," he said.

The results were immediate. The patient's oxygenation improved, her blood pressure started to rise and she no longer required the potent blood-pressure drugs to keep her alive. The angiogram showed that blood was now able to flow into her lungs and the massive blood clots were much smaller.

"We just stood there," Kuo said, "and we were amazed that the treatment had saved her life. She walked out of the hospital nine days later." But that was just the beginning for Kuo.

"That one case changed my views on the existing treatment algorithm for this deadly disease, and I suddenly realized the limited options available for life-threatening pulmonary embolism. At that moment three years ago, I recognized that this was a potentially life-saving procedure; but I also realized that few physicians were aware of it. The experience from that case really inspired me to begin my clinical research."

The labor-intensive study involved collaboration with other expert interventional colleagues, a pulmonologist adept at meta-analysis, statisticians, medical librarians and interpreters to initiate a global search of scientific literature. The researchers sifted through 18 years of data collecting information on cases involving the use of catheter-directed therapy for treating massive pulmonary embolism.

"I wanted to know if other interventional physicians had recorded this experience," Kuo said. "Were they getting the same results we were seeing at Stanford?"

Kuo's research team discovered 594 patients in 18 countries who had undergone this therapy between 1990 and 2008. After statistically analyzing the data, they found that not only was the treatment effective, but it also appeared much safer than injecting the high-dose thrombolytic drug systemically or directly into the blood-stream where it can circulate throughout the body and cause dangerous bleeding in up to 20 percent of patients. By targeting blood clots directly, the catheter-based procedure was associated with only a 2.4 percent chance of major complications, and the procedure was life-saving in 86.5 percent of the 594 patients dying from PE.

The catheter-based technique involves targeted drug delivery, which typically uses a much lower dose of the potent thrombolytic drug because it is injected directly into diseased areas. Thus, it can be useful in patients who cannot tolerate the high-dose systemic drug treatment, which carries a significant risk of bleeding.

The researchers concluded that "modern catheter-directed therapy is a relatively safe and effective treatment for acute massive pulmonary embolism and should be considered as a first-line treatment."

Among the 530,000 to 600,000 cases of massive pulmonary embolism diagnosed each year in the United States, an estimated 300,000 patients die. If initiated early, catheter-directed therapy could save many of those lives. According to Kuo, "It's a matter of life and death. Catheter-directed therapy for acute pulmonary embolism saves lives, and we need to raise awareness not only among the general public but also within the medical community. This treatment saves lives."

There were no conflicts of interest reported by the authors of this study, which was self-funded by Kuo and the Cardiovascular-Interventional Radiology Section at Stanford.

Other contributing authors include: Michael Gould, MD, associate professor of pulmonary and critical care medicine; John Louie, MD, assistant professor of radiology; Jarrett Rosenberg, PhD, statistician; Daniel Sze, MD, associate professor of radiology; and Lawrence Hofmann, MD, associate professor and chief of cardiovascular-interventional radiology.

Cervical cancer vaccine reminds girls of sexual risks

* 21:00 27 October 2009 **by Linda Geddes**

Fears that vaccination against the virus that causes cervical cancer might encourage girls to become more sexually active are unfounded, suggests a survey of UK teenagers who have received or been offered the vaccine.

Nearly 80 per cent of girls questioned said that being vaccinated against human papillomavirus (HPV) reminded them of the risks of sexual contact. Only 14 per cent agreed that they might take more sexual risks because they had been vaccinated.

Loretta Brabin at the University of Manchester, UK, and her colleagues gave questionnaires to 553 girls offered the Cervarix vaccine in the UK between October 2007 and September 2008. "The vaccine actually made them more aware of the risks of sex," she says.

Six per cent of girls were forbidden from being vaccinated by their parents. Of these, just under half said they wanted to receive the vaccine. "This is the first insight into how a girl decides whether the vaccine is important to her and who influences her decision," says Brabin.

Journal reference: British Journal of Cancer, DOI: 10.1038/sj.bjc.6605362

Basics

A Molecule of Motivation, Dopamine Excels at Its Task

By NATALIE ANGIER

If you've ever had a problem with rodents and woken up to find that mice had chewed their way through the Cheerios, the Famous Amos, three packages of Ramen noodles, and even that carton of baker's yeast you had bought in a fit of "Ladies of the Canyon" wistfulness, you will appreciate just how freakish is the strain of laboratory mouse that lacks all motivation to eat.

The mouse is physically capable of eating. It still likes the taste of food. Put a kibble in its mouth, and it will chew and swallow, all the while wriggling its nose in apparent rodent satisfaction.

Yet left on its own, the mouse will not rouse itself for dinner. The mere thought of walking across the cage and lifting food pellets from the bowl fills it with overwhelming apathy. What is the point, really, of all this ingesting and excreting? Why bother? Days pass, the mouse doesn't eat, it hardly moves, and within a couple of weeks, it has starved itself to death.

Behind the rodent's fatal case of ennui is a severe deficit of dopamine, one of the essential signaling molecules in the brain. Dopamine has lately become quite fashionable, today's "it" neurotransmitter, just as serotonin was "it" in the Prozac-laced '90s.

People talk of getting their "dopamine rush" from chocolate, music, the stock market, the BlackBerry buzz on the thigh - anything that imparts a small, pleasurable thrill. Familiar agents of vice like cocaine, methamphetamine, alcohol and nicotine are known to stimulate the brain's dopamine circuits, as do increasingly popular stimulants like Adderall and Ritalin.

In the communal imagination, dopamine is about rewards, and feeling good, and wanting to feel good again, and if you don't watch out, you'll be hooked, a slave to the pleasure lines cruising through your brain. Hey,

why do you think they call it dopamine?

Yet as new research on dopamine-deficient mice and other studies reveal, the image of dopamine as our little Bacchus in the brain is misleading, just as was the previous caricature of serotonin as a neural happy face.

In the emerging view, discussed in part at the Society for Neuroscience meeting last week in Chicago, dopamine is less about pleasure and reward than about drive and motivation, about figuring out what you have to do to survive and then doing it. “When you can’t breathe, and you’re gasping for air, would you call that pleasurable?” said Nora D. Volkow, a dopamine researcher and director of the National Institute on Drug Abuse. “Or when you’re so hungry that you eat something disgusting, is that pleasurable?”

In both responses, Dr. Volkow said, the gasping for oxygen and the wolfing down of something you would ordinarily spurn, the dopamine pathways of the brain are at full throttle. “The whole brain is of one mindset,” she said. “The intense drive to get you out of a state of deprivation and keep you alive.”

Dopamine is also part of the brain’s salience filter, its get-a-load-of-this device. “You can’t pay attention to everything, but you want to be adept as an organism at recognizing things that are novel,” Dr. Volkow said. “You might not notice a fly in the room, but if that fly was fluorescent, your dopamine cells would fire.”

In addition, our dopamine-driven salience detector will focus on familiar objects that we have imbued with high value, both positive and negative: objects we want and objects we fear. If we love chocolate, our dopamine neurons will most likely start to fire at the sight of a pert little chocolate bean lying on the counter. But if we fear cockroaches, those same neurons may fire even harder when we notice that the “bean” has six legs. The pleasurable taste of chocolate per se, however, or the anxiety of cockroach phobia, may well be the handiwork of other signaling molecules, like opiates or stress hormones. Dopamine simply makes a relevant object almost impossible to ignore.

Should the brain want to ignore what it might otherwise notice, dopamine must be muzzled. Reporting recently in Nature Neuroscience, Regina M. Sullivan of New York University Medical Center, Gordon A. Barr of Children’s Hospital of Philadelphia and their colleagues found that, whereas rats older than 12 days would quickly develop an aversion to any odors that were paired with a mild electric shock, young rats would perversely show a preference for such odors if their mothers were nearby when the tutorial jolt was delivered. The researchers traced that infantile Candide spirit to a suppression of dopamine activity in the amygdala, where fear memories are born. Infant rats know their mother by smell, Dr. Sullivan explained, and they must not learn to avoid her, for even an abusive caretaker is better than none.

Large as its impact may be, dopamine is a compact molecule, built of 22 atoms, with the characteristic nitrogenous amine knob at one end. (Dopamine, by the way, takes its name from its chemical composition, and has nothing to do with the word dope - as in heroin or other recreational drugs - which is thought to derive from the Dutch term for stew.)

The dopamine production corps is tiny as well. Fewer than 1 percent of all neurons generate the neurotransmitter, most of them in midbrain structures like the substantia nigra, which helps control movement; it is the degradation of this population of dopamine cells that results in the tremors and other symptoms of Parkinson’s disease.

There is also dopamine activity higher up, in the prefrontal cortex parked right behind the forehead, that great executive brain where storylines are written, impulses controlled and excuses contrived. An impoverishment of prefrontal dopamine is thought to contribute to schizophrenia.

Wherever their station, brain cells respond to the release of dopamine through one or more of five distinct dopamine receptors poking up from their surface, proteins designed to lock onto dopamine and respond accordingly. Another key player is the dopamine transporter, a kind of janitor that picks up used dopamine molecules and sweeps them back into the cells where they were born. Recreational drugs like cocaine tend to block that transporter, allowing dopamine to linger in the neuronal vestibule and keep punching its signal along.

People differ from one another at every juncture of the dopamine matrix, in the tonal background pace at which their dopamine neurons rhythmically fire, the avidity with which the cells spike in response to need or news, and the ease with which hyperstimulated cells revert to baseline.

Some researchers have looked at genetic variations in receptor types for clues to personality differences. According to Dan T. A. Eisenberg of Northwestern University, scientists have detected a modest connection between a relatively elongated version of dopamine receptor No. 4 and a tendency toward impulsivity and risk-taking behavior, particularly financial risk-taking.

One can’t make too much of these preliminary correlations in behavioral genetics, but maybe before the next bailout, we should demand that bankers be tested for the presence of risky, long-form receptors. It’s the economy, dopamine.

Member of NFL Hall of Fame diagnosed with degenerative brain disease

All NFL and college football players studied post-mortem show signs of CTE

BOSTON – The Center for the Study of Traumatic Encephalopathy (CSTE) at Boston University School of Medicine (BUSM) announced today that a recently deceased member of the NFL Hall of Fame suffered from the degenerative brain disease Chronic Traumatic Encephalopathy (CTE) when he died, becoming the 10th former NFL player diagnosed with the disease.

Last week, CSTE researchers announced CTE had been diagnosed post-mortem in a former college football player who died at 42, the first advanced case in a non-NFL football player. Most concerning, all 11 of the former NFL and college football players studied post-mortem at the CSTE have shown signs of CTE.

Lou Creekmur, former offensive lineman for the Detroit Lions and eight-time Pro Bowl player, was diagnosed with CTE by neuropathologist and CSTE co-director Ann McKee, MD. Creekmur played 10 seasons for the Detroit Lions, and was famous for breaking his nose 13 times while playing without a facemask. He died July 5, 2009 from complications of dementia following a 30-year decline that included cognitive and behavioral issues such as memory loss, lack of attention and organization skills, increasingly intensive angry and aggressive outbursts.

CTE can only be diagnosed by examining brain tissue post-mortem. Creekmur's brain was studied by McKee who determined that he was suffering from CTE and not another cause of dementia such as Alzheimer's disease. McKee said, "This is an important case because we are confident many CTE cases are misdiagnosed as Alzheimer's disease. By examining his brain, I was able to confirm that there was absolutely no sign of Alzheimer's disease or any other type of neurodegenerative disease except for severe CTE. This is the most advanced case of CTE I've seen in a football player; his brain changes were similar to those of profoundly affected professional boxers."

President and CEO of the Alzheimer's Association Mass./N.H. Chapter James Wessler stated, "This is a very important finding that could explain the underlying cause of dementia in countless individuals who have had histories of repetitive head trauma."

The Creekmur case is also important in advancing discussion of what risk factors may play a role in causing CTE other than trauma. One hypothesis that has been put forward is that anabolic steroids could play a role in CTE. However, Creekmur played in the 1950s, a time that predates documented steroid use in the NFL, so the case proves CTE does occur in the absence of steroids.

Robert Stern, PhD, CSTE co-director, added, "The U.S. House Judiciary Committee is holding a hearing on the football head injury crisis on Oct. 28, and we feel that this evidence should be part of the discussion. The long-term consequences of brain trauma in sports are a tremendous public health problem. CTE is the only fully preventable cause of dementia. We need to make changes to the game of football, at all levels of play, which will decrease the risk of CTE to both pro and amateur athletes."

Creekmur was a member the NFL's Plan 88. The Plan was named for former NFL star John Mackey's jersey number. Mackey, a Hall-of-Fame tight end for the Colts in the 1960s and 70s, suffers from severe dementia. The Plan was created by the NFL to provide financial support to families of former players who suffer from some form of dementia. Members of the Plan have been diagnosed with "dementia," which refers to progressive memory and cognitive deficits significant enough to impair daily living. During life, it is not possible to determine the underlying disease that causes dementia. However, now that a Plan 88 member has been examined pathologically, CSTE scientists have proven it is possible to determine the cause of dementia, which in this case was repetitive trauma from football.

Creekmur's wife of 33 years, Caroline Creekmur, had extensive discussions with her husband prior to death about his brain trauma history, and is confident he remembered "16 or 17" concussions, none that caused loss of consciousness or necessitated a hospital visit. He did not have any significant head trauma since retiring from the NFL.

There are approximately 100 former NFL players whose families are receiving support through Plan 88, including Ralph Wenzel, age 66, former lineman for the Pittsburgh Steelers and San Diego Chargers, who now resides in an assisted living facility with advanced dementia. Upon learning of Creekmur's CTE diagnosis, Wenzel's wife, Dr. Eleanor Perfetto, stated, "Sadly, these findings do not come as a surprise. For those of us who have watched our husbands deteriorate and lose their independence from progressive dementia, our hope is that this research will one day lead to changes in the game of football such that other players and their families will not have to experience the pain that we have experienced."

CTE is characterized by the build-up of a toxic protein called tau in the form of neurofibrillary tangles (NFTs) and neuropil threads (NTs) throughout the brain. The abnormal protein initially impairs the normal functioning of the brain and eventually kills brain cells. Early on, CTE sufferers may display clinical symptoms

such as memory impairment, emotional instability, erratic behavior, depression and problems with impulse control. However, CTE eventually progresses to full-blown dementia. Although similar to Alzheimer's disease, CTE is an entirely distinct disease.

Bad driving may have genetic basis, UCI study finds

People with gene variant perform more than 20 percent worse on driving test

Bad drivers may in part have their genes to blame, suggests a new study by UC Irvine neuroscientists.

People with a particular gene variant performed more than 20 percent worse on a driving test than people without it - and a follow-up test a few days later yielded similar results. About 30 percent of Americans have the variant.

"These people make more errors from the get-go, and they forget more of what they learned after time away," said Dr. Steven Cramer, neurology associate professor and senior author of the study published recently in the journal Cerebral Cortex.

This gene variant limits the availability of a protein called brain-derived neurotrophic factor during activity. BDNF keeps memory strong by supporting communication among brain cells and keeping them functioning optimally. When a person is engaged in a particular task, BDNF is secreted in the brain area connected with that activity to help the body respond.

Previous studies have shown that in people with the variant, a smaller portion of the brain is stimulated when doing a task than in those with a normal BDNF gene. People with the variant also don't recover as well after a stroke. Given these differences, the UCI scientists wondered: Could the variant affect an activity such as driving?

"We wanted to study motor behavior, something more complex than finger-tapping," said Stephanie McHughen, graduate student and lead author of the study. "Driving seemed like a good choice because it has a learning curve and it's something most people know how to do."

The driving test was taken by 29 people - 22 without the gene variant and seven with it. They were asked to drive 15 laps on a simulator that required them to learn the nuances of a track programmed to have difficult curves and turns. Researchers recorded how well they stayed on the course over time. Four days later, the test was repeated.

Results showed that people with the variant did worse on both tests than the other participants, and they remembered less the second time. "Behavior derives from dozens and dozens of neurophysiologic events, so it's somewhat surprising this exercise bore fruit," Cramer said.

The gene variant isn't always bad, though. Studies have found that people with it maintain their usual mental sharpness longer than those without it when neurodegenerative diseases such as Parkinson's, Huntington's and multiple sclerosis are present.

"It's as if nature is trying to determine the best approach," Cramer said. "If you want to learn a new skill or have had a stroke and need to regenerate brain cells, there's evidence that having the variant is not good. But if you've got a disease that affects cognitive function, there's evidence it can act in your favor. The variant brings a different balance between flexibility and stability."

A test to determine whether someone has the gene variant is not commercially available.

"I'd be curious to know the genetics of people who get into car crashes," Cramer said. "I wonder if the accident rate is higher for drivers with the variant."

In addition to Cramer and McHughen, Paul Rodriguez, Laura Marchal-Crespo and Vincent Procaccio of UCI worked on the study, along with researchers from the University of Florida. The National Institutes of Health funded the study.

Fermi telescope caps its first year with a glimpse of space-time

During its first year of operations, NASA's Fermi Gamma Ray Space Telescope mapped the extreme sky with unprecedented resolution and sensitivity. It captured more than one thousand discrete sources of gamma rays -- the highest-energy form of light. Capping these achievements was a measurement that provided rare experimental evidence about the very structure of space and time, unified as space-time in Einstein's theories.

"Physicists would like to replace Einstein's vision of gravity - as expressed in his relativity theories - with something that handles all fundamental forces," said Peter Michelson, principal investigator of Fermi's Large Area Telescope, or LAT, at Stanford University in Palo Alto, Calif. "There are many ideas, but few ways to test them."

Many approaches to new theories of gravity picture space-time as having a shifting, frothy structure at physical scales trillions of times smaller than an electron. Some models predict that the foamy aspect of space-time will cause higher-energy gamma rays to move slightly more slowly than photons at lower energy.

Such a model would violate Einstein's edict that all electromagnetic radiation -- radio waves, infrared, visible light, X-rays and gamma rays -- travels through a vacuum at the same speed.

On May 10, 2009, Fermi and other satellites detected a so-called short gamma ray burst, designated GRB 090510. Astronomers think this type of explosion happens when neutron stars collide. Ground-based studies show the event took place in a galaxy 7.3 billion light-years away. Of the many gamma ray photons Fermi's LAT detected from the 2.1-second burst, two possessed energies differing by a million times. Yet after traveling some seven billion years, the pair arrived just nine-tenths of a second apart.

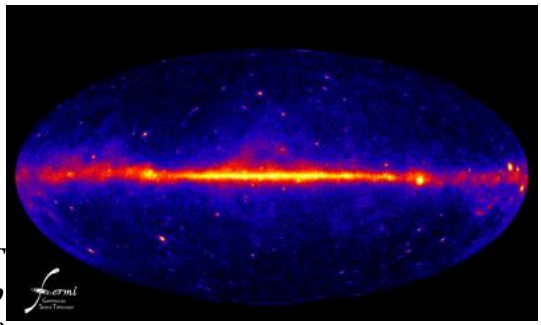
"This measurement eliminates any approach to a new theory of gravity that predicts a strong energy dependent change in the speed of light," Michelson said. "To one part in 100 million billion, these two photons traveled at the same speed. Einstein still rules."

Fermi's secondary instrument, the Gamma ray Burst Monitor, has observed low-energy gamma rays from more than 250 bursts. The LAT observed 12 of these bursts at higher energy, revealing three record setting blasts.

GRB 090510 displayed the fastest observed motions, with ejected matter moving at 99.99995 percent of light speed. The highest energy gamma ray yet seen from a burst -- 33.4 billion electron volts or about 13 billion times the energy of visible light -- came from September's GRB 090902B. Last year's GRB 080916C produced the greatest total energy, equivalent to 9,000 typical supernovae.

Scanning the entire sky every three hours, the LAT is giving Fermi scientists an increasingly detailed look at the extreme universe. "We've discovered more than a thousand persistent gamma ray sources -- five times the number previously known," said project scientist Julie McEnery at NASA's Goddard Space Flight Center in Greenbelt, Md. "And we've associated nearly half of them with objects known at other wavelengths."

Blazars -- distant galaxies whose massive black holes emit fast-moving jets of matter toward us -- are by far the most prevalent source, now numbering more than 500. In our own galaxy, gamma ray sources include 46 pulsars and two binary systems where a neutron star rapidly orbits a hot, young star.



This view of the gamma-ray sky constructed from one year of Fermi LAT observations is the best view of the extreme universe to date. The map shows the rate at which the LAT detects gamma rays with energies above 300 million electron volts -- about 120 million times the energy of visible light -- from different sky directions. Brighter colors equal higher rates. **NASA/DOE/Fermi LAT Collaboration**

"The Fermi team did a great job commissioning the spacecraft and starting its science observations," said Jon Morse, Astrophysics Division director at NASA Headquarters in Washington. "And now Fermi is more than fulfilling its unique scientific promise for making novel, high-impact discoveries about the extreme universe and the fabric of space-time."

NASA's Fermi Gamma Ray Space Telescope is an astrophysics and particle physics partnership, developed in collaboration with the U.S. Department of Energy, along with important contributions from academic institutions and partners in France, Germany, Italy, Japan, Sweden and the United States.

A new wrinkle in ancient ocean chemistry

A UC Riverside-led study reports on the effects of biological oxygen production nearly 100 million years before oxygen accumulated in the atmosphere

RIVERSIDE, Calif. – Scientists widely accept that around 2.4 billion years ago, the Earth's atmosphere underwent a dramatic change when oxygen levels rose sharply. Called the "Great Oxidation Event" (GOE), the oxygen spike marks an important milestone in Earth's history, the transformation from an oxygen-poor atmosphere to an oxygen-rich one paving the way for complex life to develop on the planet.

Two questions that remain unresolved in studies of the early Earth are when oxygen production via photosynthesis got started and when it began to alter the chemistry of Earth's ocean and atmosphere.

Now a research team led by geoscientists at the University of California, Riverside corroborates recent evidence that oxygen production began in Earth's oceans at least 100 million years before the GOE, and goes a step further in demonstrating that even very low concentrations of oxygen can have profound effects on ocean chemistry.

To arrive at their results, the researchers analyzed 2.5 billion-year-old black shales from Western Australia. Essentially representing fossilized pieces of the ancient seafloor, the fine layers within the rocks allowed the researchers to page through ocean chemistry's evolving history.

Specifically, the shales revealed that episodes of hydrogen sulfide accumulation in the oxygen-free deep ocean occurred nearly 100 million years before the GOE and up to 700 million years earlier than such conditions were predicted by past models for the early ocean. Scientists have long believed that the early ocean,

for more than half of Earth's 4.6 billion-year history, was characterized instead by high amounts of dissolved iron under conditions of essentially no oxygen.

"The conventional wisdom has been that appreciable atmospheric oxygen is needed for sulfidic conditions to develop in the ocean," said Chris Reinhard, a Ph.D. graduate student in the Department of Earth Sciences and one of the research team members. "We found, however, that sulfidic conditions in the ocean are possible even when there is very little oxygen around, below about 1/100,000th of the oxygen in the modern atmosphere."

Reinhard explained that at even very low oxygen levels in the atmosphere, the mineral pyrite can weather on the continents, resulting in the delivery of sulfate to the ocean by rivers. Sulfate is the key ingredient in hydrogen sulfide formation in the ocean.

Timothy Lyons, a professor of biogeochemistry, whose laboratory led the research, explained that the hydrogen sulfide in the ocean is a fingerprint of photosynthetic production of oxygen 2.5 billion years ago.

"A pre-GOE emergence for oxygenic photosynthesis is a matter of intense debate, and its resolution lies at the heart of understanding the evolution of diverse forms of life," he said. "We have found an important piece of that puzzle." Study results appear in the Oct. 30 issue of Science.

"Our data point to oxygen-producing photosynthesis long before concentrations of oxygen in the atmosphere were even a tiny fraction of what they are today, suggesting that oxygen-consuming chemical reactions were offsetting much of the production," said Reinhard, the lead author of the research paper.

The researchers argue that the presence of small amounts of oxygen may have stimulated the early evolution of eukaryotes – organisms whose cells bear nuclei – millions of years prior to the GOE.

"This initial oxygen production set the stage for the development of animals almost two billion years later," Lyons said. "The evolution of eukaryotes had to take place first."

The findings also have implications for the search for life on extrasolar planets.

"Our findings add to growing evidence suggesting that biological production of oxygen is a necessary but not sufficient condition for the evolution of complex life," Reinhard said. "A planetary atmosphere with abundant oxygen would provide a very promising biosignature. But one of the lessons here is that just because spectroscopic measurements don't detect oxygen in the atmosphere of another planet doesn't necessarily mean that no biological oxygen production is taking place."

To analyze the shales, Reinhard first pulverized them into a fine powder in Lyons's laboratory. Next, the powder was treated with a series of chemicals to extract different minerals. The extracts were then run on a mass-spectrometer at UC Riverside.

"One exciting thing about our discovery of sulfidic conditions occurring before the GOE is that it might shed light on ocean chemistry during other periods in the geologic record, such as a poorly understood 400 million-year interval between the GOE and around 1.8 billion years ago, a point in time when the deep oceans stopped showing signs of high iron concentrations," Reinhard said. "Now perhaps we have an explanation. If sulfidic conditions could occur with very small amounts of oxygen around, then they might have been even more common and widespread after the GOE."

Said Lyons, "This is important because oxygen-poor and sulfidic conditions almost certainly impacted the availability of nutrients essential to life, such as nitrogen and trace metals. The evolution of the ocean and atmosphere were in a cause-and-effect balance with the evolution of life."

Reinhard and Lyons were joined in the research by Clint Scott of UCR; Ariel Anbar of the Arizona State University, Tempe; and Rob Raiswell of the University of Leeds, United Kingdom.

The two-year study was supported by the National Science Foundation and NASA.

Left side grafting is procedure of choice for adult-to-adult living donor liver transplantation

Researchers find graft size not the only cause of 'small-for-size graft syndrome'

A recent study by doctors at Shinshu University, School of Medicine, in Japan determined that left side grafting has lower risk to donors compared to grafts taken from the right lobe, and it appears to be the procedure of choice for adult-to-adult living donor liver transplantation (LDLT). Researchers also found that graft size was not the only cause behind "small-for-size graft syndrome," a severe complication resulting in organ malfunction and transplant failure. These findings appear in the November issue of Liver Transplantation, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases.

In the current study, Toshihiko Ikegami, M.D. and colleagues report on the outcomes of the 120 adult LDLTs they performed through October 2007. Patients were divided into two groups: group S consisted of 33 patients who received liver grafts < 35% of their standard liver volume (SLV), and group L consisted of 87 patients who received liver grafts ≥ 35% of their SLV.

Results show the 1- and 5-year survival rates in group S were 80.7% and 64.2% respectively; and in group L 90.8% and 84.9%, with no significant difference between groups. Between 1 and 5 years after LDLT, 7 patients died with causes of death including cerebral infarction, recurrence of liver cancer, uterine cancer, and sepsis. "These deaths occurred in patients with good liver function who had resumed their normal lives," commented Dr. Ikegami. "The causes of death were not related to insufficient graft size."

Past studies have recommended a graft volume to recipient standard liver volume (GV/SLV) ratio of >40% and a graft-to-recipient weight ratio (GRWR) of ≥ 0.8% to achieve good graft and recipient survival rates. In the current study patients in group S had a good survival rate, despite a GV/SLV ratio below 35% and a GRWR not exceeding 0.8%. Dr. Ikegami points out, "Our research shows small graft size does not appear to be the only cause of small-for-size graft syndrome. The prognosis of recipients with liver grafts < 35% of their SLV is comparable to that of recipients with larger grafts."

According to the U.S. Department of Health and Human Services, 3,549 deceased donor and 249 LDLTs (5%) were performed in 2008. In Japan, 99% of all liver transplantations use living donors. The authors speculate that the lower percentage of LDLTs in the U.S. could be attributed to a highly publicized donor death in 2002 and that it is conceivable that the next donor death in Japan could lead to a similar resistance in that country. "We feel that left side grafts should be used more frequently in adult-to-adult LDLT, considering the lower risk to donors compared to right lobe grafts," recommended Dr. Ikegami.

Currently, the United Network for Organ Sharing (UNOS), an organization that facilitates all organ transplants in the U.S., indicates there are close to 16,000 patients on the waiting list to receive a liver. "As the world faces an incredible growth of patients requiring life-saving liver transplantation to treat their end stage liver disease, the need for LDLT will continue due to a lack of adequate alternative sources," said David Mulligan, M.D., from the Mayo Clinic Hospital in his editorial also published in the November issue of Liver Transplantation. "I believe we (liver transplant surgeons) should share techniques and learn new strategies as Dr. Ikegami's team reported, employing them in a balanced practice to achieve optimal results for recipients and donors so that both right and left liver grafts may be effectively transplanted in the appropriate clinical situations," added Dr. Mulligan.

Article: "Prognosis of Adult Patients Transplanted with Liver Grafts <35% of Their Standard Liver Volume," Toshihiko Ikegami, Yuichi Masuda, Yasunari Ohno, Atsuyoshi Mita, Akira Kobayashi, Koichi Urata, Yuichi Nakazawa, Shirou Miwa, Yasuhiko Hashikura, Shinichi Miyagawa. Liver Transplantation; Published Online: October 29, 2009 (DOI: 10.1002/lt.21716); Print Issue Date: November 2009.

Editorial: "Living Donor Liver Transplantation and Donor Graft Size: How small can we go to reduce risk to the donor and at what cost to the recipient?" David Mulligan. Liver Transplantation; Published Online: October 29, 2009 (DOI: 10.1002/lt.21922); Print Issue Date: November 2009

Scientists discover influenza's Achilles heel: Antioxidants

New research in the FASEB Journal opens the door for new drugs that could prevent severe flu-related lung damage

As the nation copes with a shortage of vaccines for H1N1 influenza, a team of Alabama researchers have raised hopes that they have found an Achilles' heel for all strains of the flu - antioxidants. In an article appearing in the November 2009 print issue of the FASEB Journal (http://www.fasebj.org) they show that antioxidants - the same substances found in plant-based foods - might hold the key in preventing the flu virus from wreaking havoc on our lungs.

"The recent outbreak of H1N1 influenza and the rapid spread of this strain across the world highlights the need to better understand how this virus damages the lungs and to find new treatments," said Sadis Matalon, co-author of the study. "Additionally, our research shows that antioxidants may prove beneficial in the treatment of flu."

Matalon and colleagues showed that the flu virus damages our lungs through its "M2 protein," which attacks the cells that line the inner surfaces of our lungs (epithelial cells). Specifically, the M2 protein disrupts lung epithelial cells' ability to remove liquid from inside of our lungs, setting the stage for pneumonia and other lung problems. The researchers made this discovery by conducting three sets of experiments using the M2 protein and the lung protein they damage. First, frog eggs were injected with the lung protein alone to measure its function. Second, researchers injected frog eggs with both the M2 protein and the lung protein and found that the function of the lung protein was significantly decreased. Using molecular biology techniques, scientists isolated the segment of the M2 protein responsible for the damage to the lung protein. Then they demonstrated that without this segment, the protein was unable to cause damage. Third, the full M2 protein (with the "offending" segment intact) and the lung protein were then re-injected into the frog eggs along with drugs known to remove oxidants. This too prevented the M2 protein from causing damage to the lung protein. These experiments were repeated using cells from human lungs with exactly the same results.

"Although vaccines will remain the first line of intervention against the flu for a long time to come, this study opens the door for entirely new treatments geared toward stopping the virus after you're sick," said Gerald Weissmann, M.D., Editor-in-Chief of the FASEB Journal, "and as Thanksgiving approaches, this discovery is another reason to drink red wine to your health."

2-pronged protein attack could be source of SARS virulence

GALVESTON, Texas - Ever since the previously unknown SARS virus emerged from southern China in 2003, University of Texas Medical Branch at Galveston virologists have focused on finding the source of the pathogen's virulence - its ability to cause disease. In the 2003 epidemic, for example, between 5 and 10 percent of those who fell sick from the SARS virus died, adding up to more than 900 fatalities worldwide.

Now, UTMB researchers have uncovered what they believe could be the major factor contributing to the SARS virus' virulence: the pathogen's use of a single viral protein to weaken host cell defenses by launching a "two-pronged" attack on cellular protein-synthesis machinery.

Their results show that copies of this viral protein, known as nsp1, directly interferes with the tiny cellular machines called ribosomes, which make the proteins, such as interferon beta, that are crucial for immune defense. (If the word "ribosome" sounds familiar, it's probably because the three scientists who first determined what the miniature protein factories look like and how they function won the 2009 Nobel Prize for Chemistry.) Nsp1 is also involved in degrading the biochemical messages that are decoded by these ribosomes to produce such proteins.

"This SARS virus protein, nsp1, binds to ribosomes to inactivate them and also modifies messenger RNA molecules to make them unreadable," said UTMB professor Shinji Makino, senior author of a paper on the discovery appearing in the online edition of Nature Structure and Molecular Biology. "We think that this property of nsp1 could be a major player in the virulence of SARS."

Makino and the article's other authors - postdoctoral fellows Wataru Kamitani, Cheng Huang and Kumari Lokugamage, and senior research scientist Krishna Narayanan - identified nsp1's dual effect with a series of experiments mainly done using purified nsp1 protein in a special "cell-free" system. This widely used test-tube platform, known as a "rabbit reticulocyte lysate" (RRL) system, contained only the subcellular structures and materials (ribosomes, amino acids and various control factors) that cells use to produce or "translate" proteins from messenger-RNA templates.

The researchers also developed a mutant form of the nsp1 protein that was incapable of interfering with RNA translation, employing it as an experimental control.

By measuring the outcomes produced by mixing a variety of different messenger-RNA templates with either nsp1 or mutant nsp1 in RRL, the investigators generated a strikingly detailed picture of how nsp1 interferes with ribosomes and degrades messenger RNA. Nsp1 grabs on to ribosomes, attaching to a specific part known as the 40s subunit to shut down protein production Meanwhile, the messenger RNA molecules being translated into proteins on these ribosomes are degraded by processes tied to nsp1.

"This is interesting in part because it's a new mechanism - no other known protein uses this strategy," Makino said. "But there are more practical reasons why it's important to understand viral virulence factors, particularly when you consider the potential need for treatments. There are viruses similar to SARS circulating in China, and we have no way of knowing whether this virus may come back."

The U.S. Public Health Service and the James W. McLaughlin Foundation supported this work.

Short heels make elite sprinters super speedy

When 100 m sprinters launches themselves from the starting blocks, the race can be won or lost in the first few strides. Acceleration through the first few strides is the key to winning gold. So when Stephen Piazza was approached by an American football star, who sprints in his position of wide receiver, to find out how he could improve his technique and training regime, Piazza decided to focus on the athlete's ankles to try to discover what gives elite sprinters the edge over ordinary mortals and publishes his findings on 30 October 2009 in The Journal of Experimental Biology at http://jeb.biologists.org.

The effectiveness of an accelerating sprinter's push off depends on the amount of leverage that the calf muscles have when pulling on the back of the heel to pull it up as it pushes the toes down, and off, the ground. Piazza figured that the athlete's foot would have a large distance from the ankle to the back of the heel to produce a long 'heel lever' for the calf muscle to pull on when pushing the toes down. In this case, the calf muscle would have to contract and pull the heel up over a long distance, so Piazza measured how far the athlete's tendon moved (translated) while pulling the athlete's heel up to see how it compared with that of non-sprinters. Piazza says 'I thought it would be one of the largest (tendon translations]) we had ever measured'. But when he and his student, Sabrina Lee, measured the distance, they were surprised to find that it was much shorter than average. Was the football star the exception or the rule?

Piazza decided to compare the Achilles' tendon translation of elite athletes with that of non-sprinters. Working with sprinters and long jumpers from Lock Haven University, and local non-sprinters, Piazza and Lee used ultrasound imaging to measure the tendon's translation as the subjects pointed their toes. Amazingly, the distance was 25% shorter in the elite athletes than in the non-sprinters. Instead of benefiting from the mechanical advantage of having a long heel lever, the sprinters seemed to be at a mechanical disadvantage because their heel levers were much shorter.

Puzzled by this unexpected discovery, Piazza turned to the literature to find out how animal sprinters' ankles are constructed, and quickly realised that the human elite athletes were built inline with their animal counterparts, which also have short heel levers. So how does this mechanically disadvantageous arrangement give elite sprinters the edge over weekend joggers?

Piazza and Lee realised that a fundamental property of all muscles could be responsible for the sprinters' unexpectedly short Achilles' tendon translations. He explains that muscles that contract quickly cannot generate much force, giving runners with a long moment arm a weak push off despite their increased mechanical advantage. However, muscles that contract slowly produce much greater forces that overcome the mechanical disadvantage of a short heel lever, giving sprinters with a short heel lever a powerful push off.

Testing his theory with a mathematical model of a sprinter's body, it was clear that the extra force generated by the calf muscle as it pulled the short heel lever would provide sprinters with the additional acceleration required to get ahead in the first few strides. And when the duo compared other physical characteristics between the sprinters and non-athletes, they noticed that the sprinters' toes were almost 1 cm longer than those of the non-sprinters. Not only could the sprinter generate more force while accelerating, but their longer toes allowed them to remain in contact with the ground longer during each stride, giving them longer to push against the surface and out perform slower sprinters.

REFERENCE: *Lee, S. S. M. and Piazza, S. J. (2009). Built for speed: musculoskeletal structure and sprinting ability. J. Exp. Biol. 212, 3700-3707.*

New analyses of dinosaur growth may wipe out one-third of species

Named dinosaurs may actually be juvenile or subadults of already known taxa

Paleontologists from the University of California, Berkeley, and the Museum of the Rockies have wiped out two species of dome-headed dinosaur, one of them named three years ago – with great fanfare – after Hogwarts, the school attended by Harry Potter.

Their demise comes after a three-horned dinosaur, Torosaurus, was assigned to the dustbin of history last month at the Society of Vertebrate Paleontology meeting in the United Kingdom, the loss in recent years of quite a few duck-billed hadrosaurs and the probable disappearance of Nanotyrannus, a supposedly miniature Tyrannosaurus rex.

These dinosaurs were not separate species, as some paleontologists claim, but different growth stages of previously named dinosaurs, according to a new study. The confusion is traced to their bizarre head ornaments, ranging from shields and domes to horns and spikes, which changed dramatically with age and sexual maturity, making the heads of youngsters look very different from those of adults.

"Juveniles and adults of these dinosaurs look very, very different from adults, and literally may resemble a different species," said dinosaur expert Mark B. Goodwin, assistant director of UC Berkeley's Museum of Paleontology. "But some scientists are confusing morphological differences at different growth stages with characteristics that are taxonomically important. The result is an inflated number of dinosaurs in the late Cretaceous."

Goodwin and John "Jack" Horner of the Museum of the Rockies at Montana State University in Bozeman, are the authors of a new paper analyzing North American dome-headed dinosaurs that appeared this week in the public access online journal PLoS One.

Unlike the original dinosaur die-off at the end of the Cretaceous period 65 million years ago, this loss of species is the result of a sustained effort by paleontologists to collect a full range of dinosaur fossils – not just the big ones. Their work has provided dinosaur specimens of various ages, allowing computed tomography (CT) scans and tissue study of the growth stages of dinosaurs.

In fact, Horner suggests that one-third of all named dinosaur species may never have existed, but are merely different stages in the growth of other known dinosaurs.

"What we are seeing in the Hell Creek Formation in Montana suggests that we may be overextended by a third," Horner said, a "wild guess" that may hold true for the various horned dinosaurs recently discovered in Asia from the Cretaceous. "A lot of the dinosaurs that have been named recently fall into that category."

The new paper, published online Oct. 27, contains a thorough analysis of three of the four named dome-headed dinosaurs from North America, including Pachycephalosaurus wyomingensis, the first "thick-headed" dinosaur discovered. After that dinosaur's description in 1943, many speculated that male pachycephalosaurs used their bowling ball-like domes to head-butt one another like big-horn sheep, though Goodwin and Horner disproved that notion in 2004 after a thorough study of the tissue structure of the dome.

Many paleontologists now realize that the elaborate head ornaments of dinosaurs, from the huge bony shield and three horns of Triceratops to the coxcomb-like head gear of some hadrosaurs, were not for combat, but served the same purpose as feathers in birds: to distinguish between species and indicate sexual maturity.

"Dinosaurs, like birds and many mammals, retain neoteny, that is, they retain their juvenile characteristics for a long period of growth," Horner said, "which is a strong indicator that they were very social animals, grouping in flocks or herds with long periods of parental care."

These head ornaments, which probably had horny coverings of keratin that may have been brightly-colored as they are in many birds, started growing when these dinosaurs reached about half their adult size, and were remodeled as these dinosaurs matured, continuing to change shape even into adulthood and old age, according to the researchers.

In the new paper, Horner and Goodwin compared the bone structures of Pachycephalosaurus with that of a domeheaded dinosaur, Stygimoloch spinifer, discovered in Montana by UC Berkeley paleontologists in 1973, and a dragon-like skull discovered in South Dakota and named in 2006 as a new species, Dracorex hogwartsia.

With the help of CT scans and microscopic analysis of slices through the bones of Pachycephalosaurus and Stygimoloch, the team concluded that Stygimoloch, with its high, narrow dome, growing tissue and unfused skull bones, was probably a pachycephalosaur subadult, in a stage just before sexual maturity.

Dracorex is one of a kind, and thus unavailable for dissection, but morphological analysis indicates it is a juvenile that hasn't yet formed a dome, although the top of its skull shows thickening suggestive of an emerging dome.

"Dracorex's flat skull, nodules on the front end and small spikes on back, and thickened but undomed frontoparietal bone all confirm that, ontogenetically, it is a juvenile Pachycephalosaurus," Goodwin said.

Comparison of these skulls to other fossils in the hands of private collectors confirm the conclusions, they said. In all, they looked at 21 dome-headed dinosaur skulls and cranial elements from North America.

The key to this analysis, Horner said, was years of field work in Montana by his team and Goodwin's in search of fossils of all sizes.

"We have gone out in the Hell Creek Formation for 11 years doing nothing but collecting absolutely everything we could find, which is the kind of collecting that is required," he said. "If you think about Triceratops, people had collected for 100 years and still hadn't found any juveniles. And we went out and spent 11 years collecting everything, and we found all kinds of them."

"Early paleontologists recognized the distinction between adults and juveniles, but people have lost track of looking at ontogeny – how the individual develops – when they discover a new fossil," Goodwin said. "Dinosaurs are not mammals, and they don't grow like mammals."

In fact, the so-called metaplastic bone on the heads of horned dinosaurs grows and dissolves, or resorbs, throughout life like no other bone, Horner said, and is reminiscent of the growth and loss of horns today in elk and deer. In earlier studies, Horner and Goodwin found dramatic remodeling of metaplastic bone in Triceratops, which led to their subsequent focus on dome-headed dinosaurs.

"Metaplastic bones get long and shorten, as in Triceratops, where the horn orientation is backwards in juveniles and forward in adults," Horner said. Even in older specimens, such as the fossil previously named Torosaurus, bone in the face shield resorbs to create holes along the margin. John Scannella, Horner's student at Montana State, presented a paper reclassifying Torosaurus as an old Triceratops at the Society for Vertebrate Paleontology meeting in Bristol, U.K., on Sept. 25.

"In order for that huge amount of bone to move, there has to be a lot of deposition and resorption," Horner said.

Horner and Goodwin continue to search for dinosaur fossils in the Hell Creek Formation, which is rich in Triceratops, dome-headed dinosaurs, hadrosaurs and tyrannosaurs. Analysis of growth stages in these taxa will have implications for other horned dinosaurs that are being uncovered in Asia and elsewhere.

"There are other horned dinosaurs I think may be over split," that is, split into too many new species rather than being lumped together as one species, Goodwin said.

This is your brain on fatty acids

Scientists discover lipid may be vital to learning

Saturated fats have a deservedly bad reputation, but Johns Hopkins scientists have discovered that a sticky lipid occurring naturally at high levels in the brain may help us memorize grandma's recipe for cinnamon buns, as well as recall how, decades ago, she served them up steaming from the oven.

The Hopkins team, reporting Oct. 29 in Neuron, reveals how palmitate, a fatty acid, marks certain brain proteins - NMDA receptors - that need to be activated for long-term memory and learning to take place. The fatty substance directs the receptors to specific locations in the outer membrane of brain cells, which continually strengthen and weaken their connections with each other, sculpting and resculpting new memory circuits.

Moreover, the researchers report, this fatty modification is a reversible process, with some sort of on-off switch, offering possibilities for manipulating it to enhance or even, perhaps, erase memory.

"Before now, no one knew that NMDA receptors change in response to the addition of palmitate," says Richard Huganir, Ph.D., professor and director of the Solomon H. Snyder Department of Neuroscience at Johns Hopkins.

Scientists have known that a brain signaling chemical called glutamate normally activates NMDA receptors, allowing two neurons to communicate with one another. However, they were less certain what allowed this receptor to assemble properly, or what caused it to make its way to the synapse, the specialized part of nerve cells where communication takes place.

The discovery emerged from work with live neurons in a dish, to which the scientists first fed radioactive palmitate, then separated out the NMDA receptors. By tracking radioactivity on X-ray film, they were able to determine that the fat had attached to the NMDA receptors.

Next, the scientists put both normal and altered NMDA receptors into non-brain cells that don't normally manufacture their own NMDA receptors. By tracking the radioactive fat, they were able to determine where on the NMDA receptor the fat had attached.

Results showed that the NMDA receptor undergoes "dual palmitoylation," in two different regions, each of which plays a distinct role in controlling the fate of the receptor in neurons. When the fat attaches to the first region, it stabilizes the receptor on the surface of neurons. When the fat attaches to the second region, the receptors accumulate inside neurons, perhaps awaiting a signal to send them to synapses. The researchers suspect that this could be part of a quality control measure, assuring that all the Lego-like protein subunits of the receptor are put together properly.

"It is rapidly becoming clear that palmitate regulates not only NMDA receptors, but also other brain proteins at work during signaling across synapses," says Gareth Thomas, Ph.D., a Howard Hughes Medical Institute postdoctoral fellow at Hopkins.

The researchers suspect that if palmitoylation fails, the result would be learning and memory impairment because if NMDA receptors don't make their way to the synapses – the specialized contact points between cells across which chemical messages flow – then communication between neurons is compromised.

"This new modification of the NMDA receptor deepens our molecular understanding of how synapses are regulated and how memories might be formed. It also reveals new potential drug targets, such as the enzymes that add or remove the palmitate," Huganir says. "If we could shift the balance of the palmitoylation, then perhaps we could affect and enhance learning and memory."

This study was supported by research grants from the National Institute of Mental Health and the Howard Hughes Medical Institute. Authors on the paper are Takashi Hayashi, Gareth Thomas and Richard Huganir of Johns Hopkins.

Henry Ford Hospital study: A MRSA strain linked to high death rates

A strain of MRSA that causes bloodstream infections is five times more lethal than other strains and has shown to have some resistance to the potent antibiotic drug vancomycin used to treat MRSA, according to a Henry Ford Hospital study.

The study found that 50 percent of the patients infected with the strain died within 30 days compared to 11 percent of patients infected with other MRSA strains.

The average 30-day mortality rate for MRSA bloodstream infections ranges from 10 percent to 30 percent.

Researchers say the strain USA600 contains unique characteristics that may be linked to the high mortality rate. But they say it is unclear whether other factors like the patients' older age, diseases or the spread of infection contributed to the poor outcomes collectively or with other factors. The average age of patients with the USA600 strain was 64; the average age of patients with other MRSA strains was 52.

The study is being presented at the 47th annual meeting of the Infectious Diseases Society of America Oct. 29-Nov.1 in Philadelphia.

"While many MRSA strains are associated with poor outcomes, the USA600 strain has shown to be more lethal and cause high mortality rates," says Carol Moore, PharmD., a research investigator in Henry Ford's Division of Infectious Diseases and lead author of the study.

"In light of the potential for the spread of this virulent and resistant strain and its associated mortality, it is essential that more effort be directed to better understanding this strain to develop measures for managing it."

MRSA, or Methicillin-resistant Staphylococcus aureus, is a bacterium that is resistant to common antibiotics like penicillin. It can cause skin, bloodstream and surgical wound infections and pneumonia. The majority of infections occur among patients in hospitals or other health care settings, though a growing number of infections are being acquired by otherwise healthy people outside those settings.

MRSA strains can be resistant to many drugs, though they are typically susceptible to the antibiotic vancomycin. MRSA infections are often treated with vancomycin administered intravenously. The USA600 strain in this study was shown to be more resistant to vancomycin. *The study was funded by Henry Ford Hospital.*

Commentary warns of unexpected consequences of proton pump inhibitor use in reflux disease

Alexandria, VA – Despite being highly effective and beneficial for many patients, unexpected consequences are emerging in patients who are prescribed proton pump inhibitors (PPIs) for reflux diseases. Physicians are warned to monitor these effects and prescribe these medications carefully, according to a new commentary published in the November 2009 issue of Otolaryngology – Head and Neck Surgery.

According to the authors, gastroesophageal reflux(GERD) and laryngopharyngeal reflux (LPR) are diseases that have undergone a remarkable growth in public health relevance over the last 20 years. While it has been known historically that more than 50 percent of adults in Western countries have occasional symptoms of reflux, there has been a more than four-fold increase in how many patients seek medical care for their symptoms.

PPIs are a class of important and generally safe medicines that prevent the release of stomach acid, which is one cause of the burning sensation many reflux patients experience. PPIs are among the most widely prescribed classes of medications for GERD and LPR diseases. But according to the authors, there is a growing body of literature demonstrating that acid is not the only causal agent of tissue damage in reflux disease, and that PPIs are not effective at treating all cases of GERD and LPR.

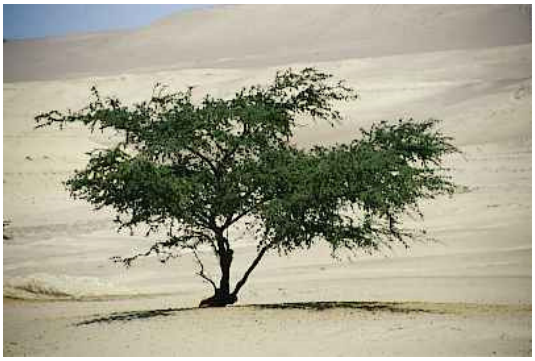
In addition to the evidence that acid isn't the only contributing agent in reflux disease, the authors' search of recent research on PPIs pointed out that there are many unexpected consequences and side effects from this class of drugs. They can include: increased rates of hip fractures, possibly related to altered calcium absorption; possible but yet unproven altered vitamin B12 and iron absorption, related to alteration of the gastric pH; increased odds of acquiring nosocomial Clostridium difficile-associated diarrhea; and increased odds of contracting community-acquired pneumonia.

The authors say while it may be premature to make global recommendations about PPI prescribing patterns, they applaud the idea of raising clinical awareness of this medication class and its potential unexpected consequences. In addition, appropriate evaluation and monitoring of patients taking PPIs will be important in determining the need and duration of the use of the medications. The authors further advise physicians treating reflux disease patients to weigh the risks of treatment versus the risks of not treating the disease, and to consider a goal of a more holistic approach that includes diet and lifestyle modification. These additional steps could prove beneficial in lowering healthcare costs associated with reflux diseases, and encourage patients to continue practicing behaviors that would improve their overall health.

Otolaryngology – Head and Neck Surgery is the official scientific journal of the American Academy of Otolaryngology – Head and Neck Surgery Foundation (AAO-HNSF). The study's authors are Kenneth W. Altman, MD, PhD, and James A Radosevich, PhD.

Nazcas' destruction of forests caused downfall

An ancient civilisation brought about its own demise by destroying forests which kept its delicate ecosystem in balance, according to researchers who claim the discovery has important implications for the modern world.



Archaeologists examining the remains of the Nazca, who once flourished in the valleys of south coastal Peru, discovered a sequence of human-induced events which led to their "catastrophic" collapse around 500 AD.

The Nazca civilisation, noted for creating vast patterns in the desert that can only be seen from the air, disappeared partly because it damaged the fragile ecosystem that held it in place, a study found.

Oliver Whaley, of the Royal Botanic Gardens, Kew, said: "The mistakes of prehistory offer us important lessons for our management of fragile, arid areas in the present."

In the study published in the journal Latin American Antiquity, the researchers found that the Nazca cleared areas of forest to make way for their own agriculture over the course of many generations. In doing so, the huarango tree, which once covered what is now a desert area, was gradually replaced by crops such as cotton and maize.

But the tree was crucial to the desert's fragile ecosystem as it enhanced soil fertility and moisture and helped to hold the Nasca's narrow, vulnerable irrigation channels in place, the researchers said. The Nazca eventually cut down so many trees that they reached a tipping point at which the arid ecosystem was irreversibly damaged.

An El Nino-style flood then occurred, but its impact would have been far less devastating had the forests which protected the delicate desert ecology still been there, they said.

Dr David Beresford-Jones, of the McDonald Institute for Archaeological Research at Cambridge University, said: "These were very particular forests. The huarango is a remarkable nitrogen-fixing tree and it was an important source of food, forage, timber and fuel for the local people.

"It is the ecological 'keystone' species in this desert zone, enhancing soil fertility and moisture, ameliorating desert extremes in the microclimate beneath its canopy and underpinning the floodplain with one of the deepest root systems of any tree known. "In time, gradual woodland clearance crossed an ecological threshold - sharply defined in such desert environments - exposing the landscape to the region's extraordinary desert winds and the effects of El Nino floods."

He said the study contradicted a popular view that Native American peoples always lived in harmony with their environment until the Spanish Conquest.

ARCHAEOLOGY

Revisiting discoveries a good idea

By Bradley T. Lepper

You might not be shocked to learn that science coverage by many media outlets tends to lean toward the extraordinary and sensational.

So it was only natural that many took notice when a group of scientists recently reported that a comet smashed into northeastern North America 12,900 years ago, igniting catastrophic firestorms that wiped out dozens of species of giant mammals as well as the Ice Age Clovis culture that hunted them.

Unfortunately, many did not follow up when further investigation shows claims like this are exaggerated or even entirely unfounded. Exploding comets and the deaths of millions of exotic animals are exciting; checking data and repeating analyses that might spoil the excitement are not.

This focus on scientific "candy" at the expense of the "meat and vegetables" means that many people miss out on the scientific method.

The so-called "Clovis comet" hypothesis was announced in 2007 and generated so much excitement that it was featured on the PBS science program NOVA in March.

The proponents of the theory said that they had found evidence of a comet impact, including magnetic microspherules, in the earth overlying 10 Clovis-age archaeological sites across North America.

University of Wyoming archaeologist Ted Surovell and several colleagues attempted to repeat the study and came up with startlingly different results. Their results appeared in the online edition of the Proceedings of the National Academy of Sciences in early October.

They tested the Clovis comet hypothesis by examining seven additional sites to see whether the pattern was repeated on the continental scale cited by the previous investigators.

Importantly, they also rechecked two of the same sites studied by the Clovis comet team.

Using the same methods, Surovell and his co-researchers were "unable to find high concentrations of magnetic particles and spherules" - even at the two sites previously studied by the original researchers.

In their conclusions, they rightly note that repeatability "is fundamental to the scientific method." If results can't be reproduced, then they "cannot be considered reliable or supportive of a hypothesis."

One of the sites was Shawnee-Minisink, a Clovis period site located in northeastern Pennsylvania, relatively close to the proposed point of impact of the hypothetical comet.

If the comet hypothesis is correct, then there should be abundant evidence there. In fact, Surovell and his team found no magnetic spherules at this site, or at the other two sites located in eastern North America.

This story illustrates why the scientific method works so well.

Scientists explore the universe, make discoveries and frame tentative explanations for the patterns they discern. Then they publish their conclusions in the scientific literature allowing other scientists working in the same discipline to challenge those ideas to see if they hold up to independent scrutiny.

If they don't, then the ideas are revealed to be dead-ends or wrong turns. Perhaps original investigators unconsciously fudged data to see what they wanted to see. Perhaps there was conscious fraud.

Regardless, the self-correcting nature of the scientific enterprise means that wrong turns are discovered and researchers are able to get back on the right track. I think this is a story that should be covered more often.

Bradley T. Lepper is curator of archaeology at the Ohio Historical Society.

U-M research shows chronically ill may be happier if they give up hope

Study shows that colostomy patients who felt their condition was irreversible reported better quality of life than those with faith that they would be cured

Ann Arbor, Mich. - Holding on to hope may not make patients happier as they deal with chronic illness or diseases, according to a new study by University of Michigan Health System researchers.

"Hope is an important part of happiness," said Peter A. Ubel, M.D., director of the U-M Center for Behavioral and Decision Sciences in Medicine and one of the authors of the happily hopeless study, "but there's a dark side of hope. Sometimes, if hope makes people put off getting on with their life, it can get in the way of happiness."

The results showed that people do not adapt well to situations if they are believed to be short-term. Ubel and his co-authors – both from U-M and Carnegie Mellon University -- studied patients who had new colostomies: their colons were removed and they had to have bowel movements in a pouch that lies outside their body.

At the time they received their colostomy, some patients were told that the colostomy was reversible — that they would undergo a second operation to reconnect their bowels after several months. Others were told that the colostomy was permanent and that they would never have normal bowel function again. The second group – the one without hope -- reported being happier over the next six months than those with reversible colostomies.

"We think they were happier because they got on with their lives. They realized the cards they were dealt, and recognized that they had no choice but to play with those cards," says Ubel, who is also a professor in the Department of Internal Medicine.

"The other group was waiting for their colostomy to be reversed," he added. "They contrasted their current life with the life they hoped to lead, and didn't make the best of their current situation."

The research was published in this month's edition of Health Psychology.

Ubel was joined in the research by Dylan M. Smith, Ph.D., a research specialist at the Ann Arbor VA Health Services Research and Development Center and a U-M psychologist; Aleksandra Jankovic, of U-M's Center for Behavioral and Decision Sciences in Medicine and George Loewenstein, professor in the Department of Social and Decision Sciences at Carnegie Mellon University.

Loewenstein said these results also may explain why people who lose a spouse to death often recover better emotionally over time than those who get divorced.

"If your husband or wife dies, you have closure. There aren't any lingering possibilities for reconciliation," Loewenstein said.

Ubel said health professionals find it easier to deliver optimistic news to patients even when they believe the prognosis is unfavorable, justifying it by assuming that holding on to hope was better for the patient.

Said Loewenstein: "It may be easier for a doctor to deliver a hopeful message to a patient, even when there isn't much objective reason for hope, but it may not be best for the patient."

"Hopeful messages may not be in the best interests of the patient and may interfere with the patient's emotional adaptation," Ubel says. "I don't think we should take hope away. But I think we have to be careful about building up people's hope so much that they put off living their lives."

The research was funded by the National Institute on Child Health and Human Development. Smith was supported by a career development award from the Department of Veterans Affairs.