Hormone thought to slow aging associated with increased risk of cancer death

Chevy Chase, MD - According to a new study accepted for publication in The Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM), older men with high levels of the hormone IGF-I (insulin-like growth factor 1) are at increased risk of cancer death, independent of age, lifestyle and cancer history.

IGF-I is a protein hormone similar in structure to insulin and is regulated in the body by growth hormone (GH). Levels of GH and IGF-I decline progressively with age in both men and women and this drop is thought to be related to deteriorating health conditions found with advanced age. In an attempt to combat aging some people use GH as its actions elevate IGF-1.This study however showed that older men who had higher levels of IGF-I were more likely to die from a cancer-related cause in the following 18 years than men with lower levels.

"This is the first population-based study to show an association of higher IGF-I levels with increased risk of a cancer-related death in older men," said Gail Laughlin, PhD, of the University of California San Diego, and corresponding author of the study. "Although the design of this study does not explicitly show that the higher IGF-I levels caused the cancer death, it does encourage more study as well as a reexamination of the use of IGF-I enhancing therapies as an anti-aging strategy."

In this study researchers used data on 633 men aged 50 and older from the Rancho Bernardo Study, a population-based study of healthy aging. Study participants took part in a research clinic examination between the years of 1988 and 1991 where their blood was obtained and IGF-1 was measured. All participants had their vital status followed through July 2006. Researchers found that men in this study who had IGF-I levels above 100 ng/ml had almost twice the risk of cancer death in the following 18 years than men with lower levels.

"In this study, the increased risk of cancer death for older men with high levels of IGF-I was not explained by differences in age, body size, lifestyle or cancer history," said Jacqueline Major, PhD, lead author on the study, now at the National Cancer Institute. "If these results are confirmed in other populations, these findings suggest that serum IGF-I may have potential importance as a biomarker for prognostic testing."

Other researchers working on the study include: the Principal Investigator and founder of the Rancho Bernardo Study, Elizabeth Barrett-Connor; and Donna Kritz-Silverstein and Deborah Wingard of the University of California, San Diego. The article, "Insulin-like Growth Factor-I (IGF-I) and Cancer Mortality in Older Men," will appear in the March 2010 issue of JCEM.

Regular analgesic use increases hearing loss in men

According to new study published in the American Journal of Medicine

New York, NY – In a study published in the March 2010 issue of The American Journal of Medicine, researchers determined that regular use of aspirin, acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) increases the risk of hearing loss in men, particularly in younger men, below age 60.

Hearing loss is the most common sensory disorder in the US, afflicting over 36 million people. Not only is hearing loss highly prevalent among the elderly, but approximately one third of those aged 40-49 years already suffer from hearing loss. Even mild hearing loss can compromise the ability to understand speech in the presence of background noise or multiple speakers, leading to social isolation, depression, and poorer quality of life.

Investigators from Harvard University, Brigham and Women's Hospital, Vanderbilt University and the Massachusetts Eye and Ear Infirmary, Boston looked at factors other than age and noise that might influence the risk of hearing lose. Aspirin, acetaminophen, and ibuprofen are the 3 most commonly used drugs in the US. The ototoxic effects of aspirin are well known and the ototoxicity of NSAIDs has been suggested, but the relation between acetaminophen and hearing loss has not been examined previously. The relationship between these drugs and hearing loss is an important public health issue.

Study participants were drawn from the Health Professionals Follow-up Study, which tracked over 26,000 men every 2 years for 18 years. A questionnaire determined analgesic use, hearing loss and a variety of physiological, medical and demographic factors.

For aspirin, regular users under 50 and those aged 50-59 years were 33% more likely to have hearing loss than were nonregular users, but there was no association among men aged 60 years and older. For NSAIDs, regular users aged under 50 were 61% more likely, those aged 50-59 were 32% more likely, and those aged 60 and older were 16% more likely to develop hearing loss than nonregular users of NSAIDs. For acetaminophen, regular users aged under 50 were 99% more likely, regular users aged 50-59 were 38% more likely, and those aged 60 and older were 16% more likely to have hearing loss than nonregular users of acetaminophen.

Writing in the article, Sharon G. Curhan, MD, ScM, Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Boston, and colleagues state, "Regular use of analgesics, specifically aspirin, NSAIDs, and acetaminophen, might increase the risk of adult hearing loss, particularly in younger individuals.

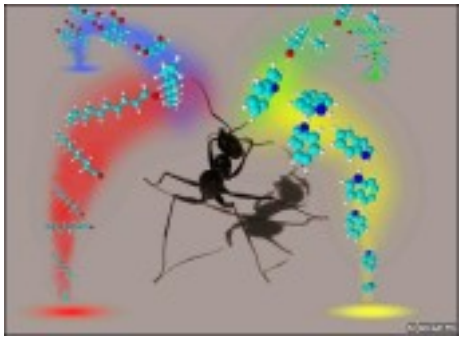
Given the high prevalence of regular analgesic use and health and social implications of hearing impairment, this represents an important public health issue."

The article is "Analgesic Use and the Risk of Hearing Loss in Men" by Sharon G. Curhan, MD, ScM, Roland Eavey, MD, Josef Shargorodsky, MD, Gary C. Curhan, MD, ScD. It appears in The American Journal of Medicine, Volume 123, Issue 3 (March 2010) published by Elsevier.

Ants navigate with 'stereo smell'

By Matt Walker Editor, Earth News

Desert ants in Tunisia smell in stereo, sensing odours from two different directions at the same time.



By sniffing the air with each antenna, the ants form a mental 'odour map' of their surroundings. They then use this map to find their way home, say scientists who report the discovery in the journal Animal Behaviour.

Pigeons, rats and even people may also smell in stereo, but ants are the first animal known to use it for navigation.

Dr Markus Knaden and colleagues Dr Kathrin Steck and Professor Bill Hansson of the Max-Planck Institute for Chemical Ecology in Jena, Germany investigated how the desert ant Cataglyphis fortis navigates around its surroundings.

An artist's impression of how an ant may sense smell, creating an odour map

Each day, individual ants will leave the nest entrance and travel up to 100m in search of food.

When they find some, they return straight home, somehow finding their tiny nest entrance again within a bleak, relatively featureless desert landscape.

Scientists knew the ant uses a sophisticated array of visual cues to find much of its way home. But Knaden's team has now found that the insect does much more than that. First, they placed four odours marked A, B, C and D around a barely visible nest entrance. They then tested the ants by removing and placing them in a remote location, without a nest entrance but with the same four odours.

The ants immediately headed to exactly where their nest should have been, confirming that they use the odours as olfactory landmarks. When the odours were mixed up, the ants became confused and unable to navigate their way home. "They had learned the olfactory scenery," Dr Knaden told the BBC.

Ants with one antenna were also unable to navigate using more than one smell, confirming that the insects required two antennae, and an ability to smell in stereo, to find their way around.

Other animals both navigate using smell, homing in on a single odour, and may smell in stereo.

In 2006 for example, rats were found to smell in stereo, being able to locate the direction of a food source with a single sniff. Many scientists suspect that pigeons also use smells to find their way home.

But until now, none have been found to do both, using a stereo sense of smell to create an odour map of the surrounding world.

"I more and more get the feeling that whatever task these ants have to solve, they succeed," says Dr Knaden.

"The hostile desert seems to demand a navigation strategy combining every possible navigational cue."

The pheromone myth: Sniffing out the truth

* 01 March 2010 by **Richard L. Doty**

FOR more than 50 years, researchers - many of them prominent scientists - have assumed that single or small sets of innate biochemicals trigger behavioural and endocrine responses in mammals of the same species. These agents, never chemically identified, were labelled "pheromones". The term was borrowed from insect studies of the early 1930s, where it replaced "ectohormone" (external hormone) to describe the single biochemicals which trigger predictable responses in relatively simple organisms.

It was not until the 1960s that the quest to find pheromones in mammals became a really big deal. In Science in 1962, endocrinologists Alan Parkes and Hilda Bruce wrote that "endocrinology has flowered magnificently in the last 40 years; exocrinology is now about to blossom". The father of sociobiology, E. O. Wilson, suggested the possibility that "pheromones are in a special sense the lineal ancestors of hormones" in a 1972 Scientific American article. Even Alex Comfort, author of the 1970s best-seller The Joy of Sex, argued in a Nature paper that pheromones were likely to exist in humans.

Since then, a plethora of studies has implicated pheromones in many mammalian activities, including sex, maternal behaviour, fighting, nesting, and the recognition of members of one's own species. Pheromones have been said to accelerate the onset of puberty, block pregnancies and influence oestrous cycles and hormonal surges in a range of mammals, although no one has ever identified the agents involved.

In humans, pheromones have been claimed to influence sexual behaviour, mood, length of menstrual cycles, even which seat people choose in waiting rooms. By 2000, dozens of brands of perfumes and aftershaves contained supposed pheromones, contributing to a multibillion-dollar industry. Even so, in 2005, the question of whether humans have pheromones was listed by Science among the top 100 unanswered scientific questions.

In my book, The Great Pheromone Myth, I argue on both empirical and theoretical grounds that mammalian pheromones do not exist. Parodying Lewis Carroll's 1876 children's poem, The Hunting of the Snark, I suggest the half-century-long search for mammalian pheromones has been a snark hunt.

Not only have mammalian pheromones not been found, but the idea oversimplifies the nature of chemical communication among mammals. "Pheromone" has no more scientific value in describing chemically mediated behaviours or endocrine processes than "visuomones", "audiomones", or "touchamones" would in describing phenomena created by non-chemical stimuli.

Not surprisingly, scientists do not agree on what defines a pheromone, and attempts by chemists to identify such putative agents have failed. Among the many reasons for this failure is that the basic tenet of the concept - that one or a few hormone-like chemicals, specific to each species, are triggers of social behaviour - is wrong. In mammals, chemically mediated behaviours are rarely hard-wired, and most biochemicals involved in communication between members of the same species are not specific to that species and comprise many compounds, some of them affected by diet, stress and other factors.

In mammals, chemically mediated behaviours are rarely hard-wired

The two main classes of pheromones said to exist in mammals are "releaser" (biochemicals that elicit particular behavioural responses in others) and "primer" (biochemicals that alter endocrine function in others). In fact, nearly all phenomena attributed to releasers in mammals turn out to depend on learning, context, or novelty. Take mating preferences. When mice of strain A are fostered as babies with mice of strain B, they tend to prefer to mate with B mice rather than with A mice, their own genetic strain. Pheromones need not be invoked to account for this behaviour as it can be explained by the smell of the foster nest: the fostered mice mate mainly with mice that smell the same. The learning of smells can occur before birth, with adult offspring of a number of species, including humans, showing a stronger preference for foods and smells to which their pregnant mothers were exposed.

As for primer pheromones, in mammals most phenomena attributed to them turn out to reflect physiological and psychological responses to abnormal changes in the social and physical environment, such as stress. And when it comes to hormones and the endocrine system, those influences come from many sources.

Another problem with the pheromone concept is that it forces complex behaviours and stimuli into two categories - pheromonal and non-pheromonal, essentially innate and learned. Mutually exclusive categories cannot share attributes or features and so this false dichotomy precludes multiple categories or continua, and so too narrowly represents the diversity of mammalian behaviour.

The evolutionary biologist Ernst Mayr argues that the situation is even more complex, pointing out that the categories of innate and learned are not, in fact, mutually exclusive. In an article in American Scientist in 1974, Mayr infers the existence of "neural programs" that are to varying degrees open or closed to change according to experience - programs that are "translations" of genes. At one extreme are those programs, and the behaviours that go with them, which cannot be modified, and at the other are those which are totally open to modification.

Naturalist Konrad Lorenz thought along similar lines, suggesting that a continuum exists across species, with those at one end having extremely specialised instinctive behaviour patterns, and those at the other end having behaviour patterns much more open to purposive control. Not surprisingly, more intelligent species, such as mammals, fall into the latter category.

Among the most publicised claims for the existence of human pheromones is menstrual synchrony. After exposure to supposed pheromones, the menstrual cycles of close friends and room-mates are said to synchronise so at some point their periods overlap. No such pheromones have been identified, and on statistical grounds alone periods will overlap for a significant amount of time in women with slightly differing cycle lengths.

Anthropologist Clyde Wilson of the University of Missouri, Columbia, and biopsychologist Jeffrey Schank of the University of California, Davis, reported that the statistical analyses used in menstrual synchrony studies are flawed in many ways.

Neither is there any convincing biological or evolutionary basis for menstrual synchrony. As anthropologist Beverly Strassmann at the University of Michigan in Ann Arbor explained in a 1997 Current Anthropology article, pregnancy and lactation, not menstrual cycling, takes up most of the reproductive years of women in

societies where birth control is not typically practised (societies which presumably reflect the norm during the majority of human evolution).

In the Dogon of Mali, for example, women menstruate less than 130 times in a lifetime. As they are segregated while they menstruate they form an ideal study group. Using hormone profiles and other techniques to overcome the statistical problems, Strassmann found no evidence for synchrony in women who ate and worked together.

All in all, it looks as if "pheromonology" has become a modern-day phrenology, providing simple but false explanations for most chemically mediated social behaviours and endocrine responses, satisfying only those who seek simple answers to complex phenomena. Perhaps once the idea that mammals have pheromones is dispelled, we can work towards an appreciation of the real role chemicals play in their lives.

Profile *Richard L. Doty is director of the University of Pennsylvania's Smell and Taste Center. His awards include the US National Institutes of Health's James A. Shannon award (1996), and the Association for Chemoreception Sciences' Max Mozell award for outstanding achievement in the chemical senses (2005). This essay is based on his book, The Great Pheromone Myth (Johns Hopkins University Press)*

Giant Snake Preyed on Baby Dinosaurs

The huge, Cretaceous Era snake was found coiled inside a dinosaur nest, providing a first-ever glimpse into the feeding behavior of primitive snakes.

By Jennifer Viegas

THE GIST:

**** A new species of prehistoric snake fed on baby dinosaurs.***

**** A recently analyzed fossil shows the moment at which the snake was about to strike a hatchling titanosaur.***

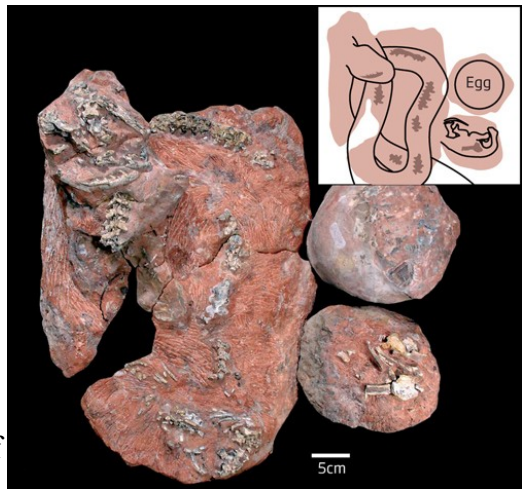
**** The massive snake lived during the Cretaceous and endured into early human history.***

Remains of an enormous snake have been discovered in a 67-million-year-old dinosaur nest, according to a new study. The snake was found coiled around a crushed dinosaur egg and next to what was left of a hatchling titanosaur.

This preserved moment in Cretaceous time provides the first direct evidence of the feeding behavior of a primitive snake, co-author Jason Head told Discovery News. Aside from this discovery, two other similar snake-egg pairings were also found at the site, located in what is now Gujarat in western India.

The 1.6-foot-long baby dinosaurs were probably defenseless when facing large snake predators. **Sculpture by Tyler Keillor; Original photography by Ximena Erickson; Image modified by Bonnie Miljour**

The 11.5-foot-long snake, described in the latest PLoS Biology, represents a new species, Sanajeh indicus, meaning "ancient-gaped one from the Indian subcontinent."



"It was not necessarily a specialized constrictor, but it clearly grabbed dinosaur hatchlings and gobbled them down," said Head, a paleontologist and assistant professor in the Department of Biology at the University of Toronto Mississauga.

"Sauropods laid their eggs in nests covering several hundred miles, so the newly hatched dinosaurs would have been like meatballs on a smorgasbord for the snakes," he added.

Dinosaur egg expert Dhananjay Mohabey from the Geological Survey of India first found the fossils in 1987. A formal agreement with the Government of India Ministry of Mines in 2004 allowed for additional study, fieldwork and other experts to come into the project. The best-preserved snake and nest set was brought to the University of Michigan Museum of Paleontology to facilitate analysis.

The snake, up to 3.5 metres long, was smothered by a landslide as it was about to prey on the baby sauropod, bottom right **(Image: Jeff Wilson/PLoS)**

"The eggs were laid in loose sands and covered by a thin layer of sediment," said Mohabey. "We think that the hatchling had just exited from its egg, and its movement attracted the snake."

Head added that, based on the geology of the site and the manner in which the fossils were preserved, a storm probably caused a sandy mudslide that buried the snake and remaining dinosaur hatchlings alive.

The parents, 70-foot-long titanosaur adults, were not present. "There was no evidence of parental care," Head said.

Even if these adult dinosaurs did encounter snakes, he doubts the lumbering plant-eating animals would have been very skillful at stomping out a fast moving snake.

He compared the scenario to modern sea turtles, which lay their eggs on the beach and then return to the ocean. When the turtle eggs hatch, "it's like a dinner bell for the ecosystem," Head said. The 1.6-foot-long baby dinosaurs would have been just as defenseless when facing large snake predators.

Snakes, therefore, probably helped to keep sauropod populations in check sometime after 100 million years ago, when snakes began to appear in the fossil record. The huge body of Sanajeh helped it to pack in such dinosaur meals.

"This points to an interesting evolutionary strategy for primitive snakes to eat large prey by increasing their body size," he explained.

As a species, Sanajeh was so successful that it actually survived the devastating mass extinction event 65.5 million years ago that wiped out all non-avian dinosaurs. In fact, this snake species lived on into early human history, according to Head.

A life-size reconstruction of the snake-eats-dinosaur scene, created by University of Chicago paleoartist Tyler Keillor, will be donated to the Geological Survey of India at a formal event in Mumbai on March 12.

Pterodactyls in Japan Hung Out With Birds

Five well-preserved trackways found in Japan reveal a relatively small pterosaur with hook-like claws on each foot.

By Jennifer Viegas

THE GIST:

**** The world's first known pterosaur tracks from Japan have been found.***
**** Scientists think the pterosaurs gathered to eat near a Cretaceous Era pond or lake.***
**** Bird tracks were also identified, suggesting that pterosaurs and birds might have enjoyed a relatively peaceful coexistence.***

The world's first pterosaur tracks from Japan, documented in a new study, suggest these Dinosaur-Age flying reptiles not only coexisted with birds, but that the two groups also hung out together when they weren't soaring the Cretaceous skies.

A reconstruction of Nemicolopterus crypticus, a small derived flying reptile that lived in China 120 million years ago. Newly analyzed tracks in Japan show small pterodactyls also roamed there and seemed to mingle with birds. **AP Photo/PNAS/National Academy of Sciences**

A lone siltstone slab contains the fossilized footprints, made by pterosaurs, birds and amphibians. It provides a literal slice of what prehistoric life was like in Japan around 127 million years ago.

"I think that a group of small pterosaurs was feeding together near a pond or near a lake," lead author Yuong-Nam Lee told Discovery News, adding "there are lots of feeding beak marks." Lee, a researcher at the Korea Institute of Geoscience and Mineral Resources, thinks "there were probably abundant food (sources) in the sediments" of what is now the Kitadani Dinosaur Quarry at Fukui Prefecture, Japan.

The quarry is well named, as the remains of several dinosaurs, such as Fukuiraptor kitadaniensis and Fukuisaurus tetoriensis, have been found at the site. A new, as-of-yet unnamed dromaeosaurid and a new sauropod were also recently excavated at the quarry, which is on the Sugiyama River within the city limits of Katsuyama. Remains of now-extinct fishes, turtles and relatives of crocodiles were discovered there too.

For the latest study, accepted for publication in the journal Cretaceous Research, Lee and his colleagues focused on the pterosaur tracks. The scientists identified a total of 64 imprints made by five to six individuals that "show a clear quadrupedal gait pattern" with feet bearing curved "hook-like sharp" claws.

"The high density of the tracks suggest gregarious behavior, but the random orientation of the trackways does not show that they were moving in the same direction as a herd," Lee said.

He and his team instead think the pterosaurs and birds randomly gathered to feed. The eating marks consist of "small round depressions on the slab," possibly where the animals repeatedly pecked away for food.

Since the tracks don't match up with any other known pterosaur prints, the researchers believe they were made by a new species, called Pteraichnus nipponensis. The only other evidence for pterosaurs in Japan is an incomplete spinal column bone and a single print set, not yet fully documented, from another location.

Nevertheless, this evidence and the siltstone slab prints suggest that multiple tiny pterosaurs called Japan home from at least 113 to 127 million years ago. Evidence for small pterosaurs at that time has also been found in Spain and Korea.

David Unwin, a senior researcher in paleobiology at the University of Leicester, told Discovery News that the slab "provides a fascinating and important insight into life in the mid Lower Cretaceous of eastern Asia."

Since the tracks are similar, yet appear to have been made by different sized individuals, Unwin said it is possible "that pterosaurs of widely differing growth stages visited/walked around in the same small area."

Unwin was also struck by the presence of the bird tracks. He indicated that scientists have long puzzled over the relationship between birds and pterosaurs, wondering if they enjoyed "a long peaceful coexistence, or protracted competition." The former now appears to be the case.

Pterosaur and bird tracks, along with dinosaur prints, were also recently found together at Hakou Formation in Gansu Province, northwest China. Those tracks also date to the Lower Cretaceous.

Some parents weigh 'hastening death' for children in extreme pain with terminal cancer

Researchers say parents need opportunity to discuss concerns with caregivers

BOSTON--A survey of parents who had a child die of cancer found that one in eight considered hastening their child's death, a deliberation influenced by the amount of pain the child experienced during the last month of life, report Dana-Farber Cancer Institute researchers in the March issue of Archives of Pediatrics & Adolescent Medicine.

The study, the first to explore this sensitive area, suggests that many parents worry that their children will suffer from uncontrollable pain, and that some parents might consider that an early death would be preferable. The researchers say the findings underscore the importance of managing patients' pain, and of communicating with parents about the tools available for easing progressive pain.

"The problem is that conversations about these family worries may not always happen," said senior author Joanne Wolfe, MD, MPH, Division Chief of Pediatric Palliative Care at Dana-Farber and Director of Palliative Care at Children's Hospital Boston. "Parents may not have the opportunity to express these feelings and considerations, and as clinicians, we may not be adequately enabling sufficient opportunity for them to talk about their concerns."

Wolfe, along with first author Veronica Dussel, MD, MPH, a Dana-Farber research fellow, undertook the research to gain an understanding of why some parents would consider a measure as extreme as intentionally ending a child's life.

The researchers interviewed 141 parents of children who had died of cancer and were treated at Dana-Farber, Children's Hospital, or Children's Hospitals and Clinics of St. Paul and Minneapolis, Minn.

The scientists queried parents about their behaviors and feelings leading up to their child's death and at the time the survey was conducted, which was a year or more after the death. The parents were also presented with hypothetical vignettes involving a terminally ill child with uncontrolled excruciating pain or who was in an irreversible coma.

One in eight (13 percent) of parents had considered asking caregivers about the possibility of ending their child's life, though only 9 percent reported having such a discussion. Five parents, or 4 percent, had requested that their child's death be hastened, and 3 parents said it had been carried out, using morphine. Wolfe commented, however, that "this may not reflect what actually happened, because morphine is used in increasing doses to manage worsening pain without the intent or the effect of ending life."

In response to the hypothetical vignettes, 50 percent of parents said they endorsed hastening death in situations of uncontrollable pain or if the child was in an irreversible coma. Parents were 40 percent more likely to approve hastening death for a child experiencing extreme pain than for a terminally ill child in a coma.

Wolfe said it is important to keep the findings in perspective. Only five parents reported having talked about hastening their child's death, and 19 said they considered it. Wolfe said it is her experience that parents are comforted by having conversations about pain management and that most are reassured by knowing what will be done to ease their child's suffering.

"We've come a long way, because we have a good palliative and supportive care program for children with cancer," said Wolfe, who is also an assistant professor of pediatrics at Harvard Medical School.

But she acknowledged, "I can never promise that their child will be pain free. We still have quite a way to go in figuring out the best way to ease suffering at the end of life." The gap exists in part, Wolfe said, because this area is not one given high priority for research funding agencies.

Other authors of the report are Steven Joffe, MD, MPH, and Jane Weeks, MD, MSc, of Dana-Farber; Joanne Hilden, MD, of the Peyton Manning Children's Hospital at St. Vincent in Indianapolis, Ind.; and Jan Watterson-Schaeffer of Children's Hospitals and Clinics, St. Paul, Minn.

The project was funded in large part by the Agency for Health Research and Quality and the National Cancer Institute.

Key player found for a cancer typical in Down syndrome

Over-expression of gene regulator spurs development of leukemia in babies with Down syndrome

Boston, Mass. – Between 5 and 10 percent of babies with Down syndrome develop a transient form of leukemia that usually resolves on its own. However, for reasons that haven't been clear, 20 to 30 percent of these babies progress to a more serious leukemia known as Down syndrome acute megakaryoblastic leukemia (DS-AMKL), which affects the blood progenitor cells that form red blood cells and platelets. Now, researchers at Children's Hospital Boston have found a gene regulator they believe to be a key player in DS-AMKL, advancing understanding of how the disease develops and how to treat it. The study findings, published in the March 1 issue of Genes and Development, may also help in understanding other forms of leukemia, the researchers say.

The gene regulator, miR-125b-2, belongs to a class of molecules known as microRNAs, which silence gene expression by halting the manufacturing of different proteins. While microRNAs are important to normal cell function, unusual amounts of them can lead to disease. "DS-AMKL has a very strong genetic basis," says senior investigator Stuart Orkin, MD, of the Division of Hematology/Oncology at Children's. "However, there aren't that many cancers in which a particular microRNA can be pointed to as contributing."

Because children with Down syndrome have three copies of chromosome 21 rather than the usual two copies, the researchers focused on the five microRNAs produced by this chromosome, and zeroed in on miR-125b-2.

"In human primary DS-AMKL cells, this microRNA is quite dramatically over-expressed," says Zhe Li, PhD, of Children's Division of Hematology/Oncology and first author of the paper. "We then went back and studied how over-expression or downregulation of this microRNA affects the phenotype of leukemia cells."

DS-AMKL is always associated with mutations in the gene GATA1, which helps make and regulate red blood cells and megakaryocytes (the cells that produce platelets). The increased incidence of this leukemia in children with Down syndrome convinced the researchers that a GATA1 mutation may be joining forces with some genetic factor on chromosome 21 – specifically, miR-125b-2. "GATA1 is always mutated, while miR-125b-2 is always over-expressed in leukemic cells," Li says. "Do they cooperate?"

The researchers experimented on genetically engineered mice that specifically expressed the mutant version of GATA1. Cells were taken from the fetal livers of these mice and induced into becoming blood progenitor cells that either made both red blood cells and megakaryocytes (MEP) or only made megakaryocytes (MP). The researchers then used a virus to over-express miR-125b-2 in these cells and compared them to MEP and MP cells without a GATA1 mutation.

Although over-expression of miR-125b-2 caused increased growth and replication of MEP and MP cells with or without the GATA1 mutation, the growth was further enhanced in the presence of the GATA1 mutation. But once the researchers down-regulated this microRNA in DS-AMKL leukemic cells, which have both GATA1 mutation and miR-125b-2 over-expression, the aberrant growth stopped. These observations support the notion that GATA1 mutation and over-expression of miR-125b-2 are both needed for DS-AMKL to develop.

Further tests on these cells suggested that over-expression of miR-125b-2 spurs the leukemia by silencing two genes: one for tumor-suppression, and another for producing other regulatory microRNAs. Genetic analyses of leukemia cells taken from DS-AMKL patients confirmed the results seen in the mouse models. The next step is for researchers to model DS-AMKL in vivo, using animal cells and, eventually, fetal cells.

Studying leukemia in Down syndrome patients may help scientists understand and treat other forms of the cancer, says Orkin. Past research has shown that other genes on chromosome 21 may be involved in other types of leukemia. "Learning more about the genetics of leukemia will then lead to some thoughts about other ways to interfere with the growth of the cells," Orkin says.

This research was funded by grants from the German National Academic Foundation, the Madelein Schickedanz Foundation, and the National Institutes of Health. Orkin, who is also Chairman of Pediatric Oncology at the Dana Farber Cancer Institute and the David G. Nathan Professor of Pediatrics at Harvard Medical School, is an Investigator of the Howard Hughes Medical Institute.

Citation: *Jan-Henning Klusmann, Zhe Li, Katarina Böhmer, Aliaksandra Maroz, Mia Lee Koch, Stephan Emmrich, Frank J. Godinho, Stuart H. Orkin, Dirk Reinhardt. miR-125b-2 is a potential oncomiR on human chromosome 21 in megakaryoblastic leukemia. Genes and Development March 1, 2010.*

Critical brain chemical shown to play role in severe depression

TORONTO, March 1 /CNW/ - The next advance in treating major depression may relate to a group of brain chemicals that are involved in virtually all our brain activity, according to a study published today in Biological Psychiatry. The study is co-authored by Drs. Andrea J. Levinson and Zafiris J. Daskalakis of the Centre for Addiction and Mental Health (CAMH). This study shows that compared to healthy individuals, people who

have major depressive disorder have altered functions of the neurotransmitter GABA (gamma-aminobutyric acid). In the study, individuals with the most treatment-resistant forms of illness demonstrated the greatest reductions of GABA levels in the brain.

This points to the possibility that medications which correct a GABA imbalance could advance the treatment of major depressive disorder. Approximately 4% of Canadians experience major depressive disorder each year.

Several current medications for mood disorders correct imbalances in neurotransmitters such as serotonin and dopamine. However, many patients do not benefit from these medications. "Our findings build on the idea that some current medications do not help many patients because those drugs don't affect the GABA-related brain chemistry," says study author Dr. Andrea Levinson.

Applying the brakes

The GABA neurotransmitter and its receptors are involved in many different brain functions. Imbalances in GABA also are relevant to bipolar disorder, schizophrenia, and anxiety disorder.

The GABA neurotransmitter and its receptors are critical to how humans think and act, Dr. Levinson adds. "We apply so many conscious and unconscious perceptions and judgments to our actions at every second, without even realizing that we are doing so," she says. "GABA is part of the brain system that allows us to fine-tune our moods, thoughts, and actions with an incredible level of detail."

"It's a little like driving a car. You need the accelerator, but at every stage you need the brakes to work. Some of our neurotransmitters apply the spark and the gas to the engine, and GABA supplies the brakes," she says. "GABA provides the necessary inhibitory effect that we need in order to block out excessive brain activity that in depression may lead to excessive negative thinking."

In addition, today's study points to the reason why electroconvulsive therapy is still the most efficacious therapy for major depressive disorder, Dr. Levinson adds. "Electroconvulsive therapy may act on GABA brain chemicals in a way that can reset the balance," she says.

Largest study to date

This study of 85 people is the largest such research effort on GABA and major depressive disorder to date. It compared four groups: 25 individuals with treatment-resistant depression, 16 with major depression who were unmedicated, 19 individuals with major depression who were successfully treated with medication and had normal mood, and a control group of 25 healthy individuals.

In all groups, a thumb twitch response to transcranial magnetic (brain) stimulation (TMS) was used to measure how GABA acts physiologically in the brain. GABA receptors were found to be dysfunctional in the three groups with major depressive disorder when compared to healthy subjects. In people who were the least responsive (treatment-resistant) to medications, the physiological effect of GABA in the brain was at its lowest.

Personalized medicine

"We are advancing the goal of a truly personalized medicine," says study co-author Dr. Daskalakis. "It is intriguing to think that we may soon be able to apply simple brain stimulation to identify which treatments are most likely to help the individual person, eliminating the guesswork. That is, through these findings we may be able to one day determine who is and who is not going to respond to traditional pharmacological approaches to depression."

The journal published a separate editorial to highlight the potential for an individualized approach to diagnosing depression, one that would include brain stimulation to identify low levels of the GABA neurotransmitters.

Dr. Daskalakis has international expertise in the electrophysiology of psychiatric disorders, particularly related to GABA.

This study was conducted at the Centre for Addiction and Mental Health, with coauthors in Melbourne, Australia. Funders of the study were the Ontario Mental Health Foundation, the Canadian Institutes of Health Research, and NARSAD.

ISU study proves conclusively that violent video game play makes more aggressive kids

AMES, Iowa -- Iowa State University Distinguished Professor of Psychology Craig Anderson has made much of his life's work studying how violent video game play affects youth behavior. And he says a new study he led, analyzing 130 research reports on more than 130,000 subjects worldwide, proves conclusively that exposure to violent video games makes more aggressive, less caring kids -- regardless of their age, sex or culture.

The study was published today in the March 2010 issue of the Psychological Bulletin, an American Psychological Association journal. It reports that exposure to violent video games is a causal risk factor for increased aggressive thoughts and behavior, and decreased empathy and prosocial behavior in youths.

"We can now say with utmost confidence that regardless of research method -- that is experimental, correlational, or longitudinal -- and regardless of the cultures tested in this study [East and West], you get the same effects," said Anderson, who is also director of Iowa State's Center for the Study of Violence. "And the effects are that exposure to violent video games increases the likelihood of aggressive behavior in both short-

term and long-term contexts. Such exposure also increases aggressive thinking and aggressive affect, and decreases prosocial behavior."

The study was conducted by a team of eight researchers, including ISU psychology graduate students Edward Swing and Muniba Saleem; and Brad Bushman, a former Iowa State psychology professor who now is on the faculty at the University of Michigan. Also on the team were the top video game researchers from Japan - Akiko Shibuya from Keio University and Nobuko Ihori from Ochanomizu University - and Hannah Rothstein, a noted scholar on meta-analytic review from the City University of New York.

Meta-analytic procedure used in research

The team used meta-analytic procedures -- the statistical methods used to analyze and combine results from previous, related literature -- to test the effects of violent video game play on the behaviors, thoughts and feelings of the individuals, ranging from elementary school-aged children to college undergraduates.

The research also included new longitudinal data which provided further confirmation that playing violent video games is a causal risk factor for long-term harmful outcomes.

"These are not huge effects -- not on the order of joining a gang vs. not joining a gang," said Anderson. "But these effects are also not trivial in size. It is one risk factor for future aggression and other sort of negative outcomes. And it's a risk factor that's easy for an individual parent to deal with -- at least, easier than changing most other known risk factors for aggression and violence, such as poverty or one's genetic structure."

The analysis found that violent video game effects are significant in both Eastern and Western cultures, in males and females, and in all age groups. Although there are good theoretical reasons to expect the long-term harmful effects to be higher in younger, pre-teen youths, there was only weak evidence of such age effects.

Time to refocus the public policy debate

The researchers conclude that the study has important implications for public policy debates, including development and testing of potential intervention strategies designed to reduce the harmful effects of playing violent video games.

"From a public policy standpoint, it's time to get off the question of, 'Are there real and serious effects?' That's been answered and answered repeatedly," Anderson said. "It's now time to move on to a more constructive question like, 'How do we make it easier for parents -- within the limits of culture, society and law -- to provide a healthier childhood for their kids?'"

But Anderson knows it will take time for the creation and implementation of effective new policies. And until then, there is plenty parents can do to protect their kids at home.

"Just like your child's diet and the foods you have available for them to eat in the house, you should be able to control the content of the video games they have available to play in your home," he said. "And you should be able to explain to them why certain kinds of games are not allowed in the house -- conveying your own values. You should convey the message that one should always be looking for more constructive solutions to disagreements and conflict."

Anderson says the new study may be his last meta-analysis on violent video games because of its definitive findings. Largely because of his extensive work on violent video game effects, Anderson was chosen as one of the three 2010 American Psychological Association Distinguished Scientist Lecturers. He will give a lecture at October's New England Psychological Association (NEPA) meeting in Colchester, Vt.

How the Men Reacted as the Titanic and Lusitania Went Under

By SINDYA BHANOO

Records from two nearly 100-year-old shipwrecks, the Titanic and the Lusitania, have given researchers new insight into human selfishness - and altruism.

On one boat, it seems, the men thought only of themselves; on the other, they were more likely to help women and children. This occurred for one key reason, researchers said: time. The Lusitania sank in about 18 minutes, while the Titanic took nearly three hours. Women and children fared much better on the Titanic.

“When you have to react very, very fast, human instincts are much faster than internalized social norms,” said Benno Torgler, an economics professor at Queensland University of Technology in Brisbane, Australia, and one of the authors of the study, published in the current issue of Proceedings of the National Academy of Sciences.

“It’s very nice to get a nice and controlled experiment,” he said. “You’re in the ship; you cannot go in and out. We were looking for shipwrecks that were very similar - similar structure, similar rates of survival, only a couple of years apart.”

The two ships fit the bill. The makeup of the passengers and crew on both of them was similar, and the sinkings happened relatively close in time, the Titanic in 1912 and the Lusitania in 1915.

In their analysis, the researchers studied passenger and survivor lists from both ships, and considered gender, age, ticket class, nationality and familial relationships with other passengers. The differences emerged after a closer look at the survival rates.

On the Titanic, the study found, children were 14.8 percent more likely to survive adults, while on the Lusitania they were 5.3 percent less likely to do so. And women on the Titanic were 53 percent more likely to survive than men, while on the Lusitania they were 1.1 percent less likely to do so. The implication, Dr. Torgler said, is that on the Titanic, male passengers went out of their way to help women and children.

The research is innovative, but there are still some unanswered questions, said Benigno Aguirre, a sociology professor at the University of Delaware who also works in the university's Disaster Research Center, and who was not involved in the study.

"The idea is an excellent idea - the sense of time in survival," Dr. Aguirre said. "My only concern is that as they do that they need to go back and look at group behaviors, counting the relationship within those groups."

In a study accepted for publication in Social Science Quarterly, Dr. Aguirre analyzed the records from a deadly nightclub fire in Rhode Island in 2003. He found that those who were at the club with friends, relatives or people they knew were less likely to survive than those who were there alone.

Although the researchers did consider parent-child relationships, Dr. Aguirre said he would like to see deeper analysis, looking into relationships of all sorts on the two ships, including family, friends, colleagues and acquaintances.

He said he had found that in life-or-death situations, those relationships can make a critical difference. Meanwhile, Dr. Torgler and his colleagues are studying the reactions to more recent disasters - namely in the use of text messages, including those sent by people trapped during the World Trade Center attacks on Sept. 11.

In texts sent in those situations, Dr. Torgler said, people seemed to convey their love to family members, tried to find closure with difficult issues and showed signs of faith in God.

A new generation of rapid-acting antidepressants?

Philadelphia, PA - Conventional antidepressant treatments generally require three to four weeks to become effective, thus the discovery of treatments with a more rapid onset is a major goal of biological psychiatry. The first drug found to produce rapid improvement in mood was the NMDA glutamate receptor antagonist, ketamine.

In a new issue of Biological Psychiatry, published by Elsevier, researchers from the National Institutes of Health report that another medication, scopolamine, also appears to produce replicable rapid improvement in mood. Scopolamine temporarily blocks the muscarinic cholinergic receptor, thought to be overactive in people suffering from depression.

Drs. Wayne Drevets and Maura Furey recruited outpatients with major depressive disorder who were randomly assigned to receive placebo and then scopolamine treatment, or vice versa, in a double-blinded design so that neither the researchers nor the patients knew which treatment they were receiving.

"Scopolamine was found to reduce symptoms of depression within three days of the first administration. In fact, participants reported that they experienced relief from their symptoms by the morning after the first administration of drug," explained Dr. Furey. "Moreover, one-half of participants experienced full symptom remission by the end of the treatment period. Finally, participants remained well during a subsequent placebo period, indicating that the antidepressant effects persist for at least two weeks in the absence of further treatment."

The efficacy of scopolamine is very interesting because the potent blockade of muscarinic receptors was a property of tricyclic antidepressant medications, the oldest type of antidepressants. With these medications, the muscarinic receptor blockade was mostly viewed as the cause of unwanted side effects, such as constipation, sedation, and memory impairments. Newer antidepressants, such as serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors, were explicitly designed to avoid blocking muscarinic receptors. Yet, the current data raise the possibility that this strategy may have increased safety and tolerability of these medications at the expense of providing effective and timely relief for depression symptoms.

Dr. John Krystal, Editor of Biological Psychiatry, commented that these findings "have the potential to raise expectations for new antidepressant treatments. Three-to-six weeks is a long time to wait for depression symptoms to be alleviated. Depressed people describe their emotional state using terms like 'agony' and others compare their condition to 'living in hell'. Further, depression is a life-threatening condition for some, preventing them from performing basic self-care functions or causing them to exhibit self-destructive behavior."

Although these findings open the door to a conceptually different approach to the treatment of depression, it remains to be seen whether rapid acting antidepressant effects will be viable clinically. One could imagine that

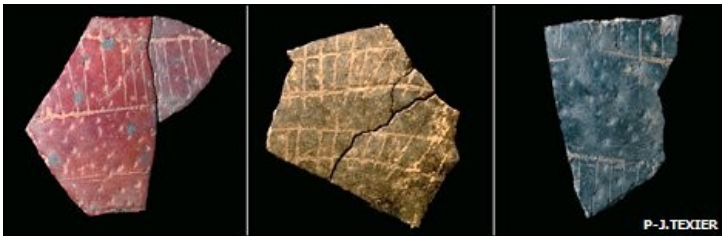
they might mitigate hospitalization in some patients and enhance the overall effectiveness of the treatment of depression. However, this possibility remains to be demonstrated empirically in studies that show that a rapid-acting antidepressant treatment can be smoothly transitioned to definitive long-term treatment for depression.

Notes to Editors: *The article is "Replication of Scopolamine's Antidepressant Efficacy in Major Depressive Disorder: A Randomized, Placebo-Controlled Clinical Trial" by Wayne C. Drevets and Maura L. Furey. The authors are affiliated with the Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland. The article appears in Biological Psychiatry, Volume 67, Issue 5 (March 1, 2010), published by Elsevier.*

Egg shells illustrate human story

By Jonathan Amos Science correspondent, BBC News

Inscribed ostrich shell fragments found in South Africa are among the earliest examples of the use of symbolism by modern humans, scientists say.



The etched shells from Diepkloof Rock Shelter in Western Cape have been dated to about 60,000 years ago.

Details are reported in the Proceedings of the National Academy of Sciences.

The researchers, who have investigated the material since 1999, argue that the markings are almost certainly a form of messaging - of graphic communication.

"The motif is two parallel lines, which we suppose were circular, but we do not have a complete refit of the eggs," explained Dr Pierre-Jean Texier from the University of Bordeaux, Talence, France.

"The lines are crossed at right angles or oblique angles by hatching. By the repetition of this motif, early humans were trying to communicate something. Perhaps they were trying to express the identity of the individual or the group," he told BBC News.

Symbolic thought - the ability to let one thing represent another - was a giant leap in human evolution, and sets our species apart from the rest of the animal world. Understanding when and where this behaviour first emerged is a key quest for scientists studying human origins.

Arguably the earliest examples of conceptual thought are the pieces of shell jewellery discovered at Skhul Cave in Israel and from Oued Djebbana in Algeria. These artefacts are 90,000-100,000 years old.

Shell beading from 75,000 years ago is also found at Blombos Cave in South Africa, as well as a number of ochre blocks that have engravings not dissimilar to those at Diepkloof.

However, the significance of the Diepkloof finds may lie in their number, which proves such markings could not have been simple doodlings. "What is extraordinary at Diepkloof is that we have close to 300 pieces of such engravings, which is why we are speaking of a system of symbolic representation," Dr Texier said.

The team, which includes Dr Guillaume Porraz from the University of Tubingen, tried themselves to recreate the markings using pieces of flint. "Ostrich egg shells are quite hard. Doing such engravings is not so easy. You have to pass through the outer layer to get through the middle layer," Dr Texier explained.

The team's experiments also suggest that the colouration of the fragments is natural and not the result of the application of pigments. The group was able to reproduce similar hues by baking pieces of shell near a fire.

Professor Chris Stringer, of London's Natural History Museum, said the find was important.

"Here we've got something that we can compare with later material that clearly does have important signalling value in the populations," he told BBC News.

"It's a very nice link between the Middle Stone Age, the later Stone Age and even recent population in South Africa. One question now is whether this is a special site, or as we excavate more sites will we find this material is more widespread?"

Darkness Increases Dishonest Behavior

Darkness can conceal identity and encourage moral transgressions; thus Ralph Waldo Emerson wrote in “Worship” in The Conduct of Life (1860), “as gaslight is the best nocturnal police, so the universe protects itself by pitiless publicity.” New research in Psychological Science, a journal of the Association for Psychological Science, shows that darkness may also induce a psychological feeling of illusory anonymity, just as children playing “hide and seek” will close their eyes and believe that other cannot see them, the experience of darkness, even one as subtle as wearing a pair of sunglasses, triggers the belief that we are warded from others’ attention and inspections.

Psychological scientists Chen-Bo Zhong, Vanessa K. Bohns (both of University of Toronto’s Rotman School of Management), and Francesca Gino (University of North Carolina at Chapel Hill) conducted three experiments to test whether darkness can license dishonest and self-interested behaviors. In the first experiment,

participants were placed in a dimly or well-lit room and received a brown envelope that contained $10 along with one empty white envelope. They were then asked to complete a worksheet with 20 matrices, each consisting of 12 three-digit numbers. The participants had five minutes to find two numbers in each matrix that added up to 10. The researchers left it up to the participants to score their own work and for each pair of numbers correctly identified they could keep $0.50 from their supply of money. At the end of the experiment, the participants were asked to place the remainder of their money into the white envelope on their way out. While there was no difference in actual performance, participants in the slightly dim room cheated more and thus earned more undeserved money than those in a well-lit room.

In the second experiment, some participants wore a pair of sunglasses and others wore clear glasses while interacting with an ostensible stranger in a different room (in actuality participants interacted with the experimenter). Each person had $6 to allocate between him-or herself and the recipient and could keep what he or she didn't offer. Participants wearing sunglasses behaved more selfishly by giving significantly less than those wearing clear glasses.

In the third experiment, the scientists replicated the previous experiment and then measured the extent to which participants felt anonymous during the experiment. Once again, those wearing sunglasses gave significantly less money and furthermore, those wearing sunglasses reported feeling more anonymous during the study.

Across all three experiments, darkness had no bearing on actual anonymity, yet it still increased morally questionable behaviors. The researchers suggest that the experience of darkness may induce a sense of anonymity that is disproportionate from actual anonymity in a given situation. Zhong explains, "Imagine that a person alone in a closed room is deciding whether to lie to a total stranger in an email. Clearly, whether the room is well-lit or not would not affect the person's actual level of anonymity. Nevertheless, darkness may license unethical behavior in such situations."

Hospices not deactivating defibrillators in patients

Implantable cardioverter defibrillators cause unnecessary suffering in end-of-life patients

Researchers from Mount Sinai School of Medicine have found that patients admitted to hospice care who have an implantable cardioverter defibrillator (ICD) are rarely having their ICDs deactivated and are receiving electrical shocks from these devices near the end of life. This first-of-its-kind study of hospice patients with ICDs is published in the March 2, 2010 issue of the Annals of Internal Medicine.

Mount Sinai researchers surveyed 900 hospices, 414 of which responded. Ninety-seven percent of the responding hospices admitted patients with ICDs. On average, nearly 60 percent of patients did not have the shocking function of the ICD deactivated. Only 20 percent of hospices had a question on their intake forms to identify patients with ICDs, and just 10 percent reported having a policy in place to discuss deactivation with patients and their families.

An ICD is a device programmed to detect cardiac arrhythmias and shock the heart back into normal rhythm. ICDs are effective in preventing sudden cardiac death in patients with recurrent arrhythmias, but for patients in hospice care they may cause unnecessary pain, and significant stress and anxiety for their family members who feel helpless in watching their loved one suffer.

"Hospices are the foremost experts at dealing with the complex communication issues surrounding end-of-life discussions with patients and their families," said Nathan Goldstein, MD, assistant professor, Hertzberg Palliative Care Institute, Brookdale Department of Geriatrics and Palliative Medicine, Mount Sinai School of Medicine. "The fact that so few organizations have a policy about deactivation shows how complicated these conversations are. Having a policy in place can improve communication and provide better quality of care for patients and their families."

ICD shocks may cause physical and psychological distress for patients and their caregivers. Patients report that receiving shocks from an ICD is comparable to being "kicked or punched" in the chest. Receiving ICD shocks has been associated with the development of adjustment disorders, depression, post-traumatic stress disorder, and panic disorder. Family caregivers who observe patients being shocked report feelings of fear, worry, and helplessness, and have been shown to have increased rates of depression and anxiety. For patients with advanced disease, an ICD may no longer prolong a life of acceptable quality, and cause needless discomfort.

"These data indicate that developing a policy to address concerns surrounding ICDs can be highly beneficial in reducing emotional and physical discomfort for hospice patients and their families," said Dr. Goldstein, whose team developed a model policy for ICDs in hospices based on feedback they received from several facilities. The policy includes the necessity for staff to be educated on how ICDs work, identification of patients with ICDs at the time of evaluation and admission, an informed consent discussion with the patient and family about the benefits and burdens of the device, and how to handle the device in an emergency situation.

"Many patients have had these devices for years and see them as a sign of stability. It's important to address this issue and emphasize the importance of the patient's comfort at end of life," Dr Goldstein explained.

The researchers received a list of 3,750 hospices from the National Hospice and Palliative Care Organization. From this list, the researchers generated a geographically weighted random sample of 100 hospices from each of the nine U.S. census regions. Survey response rate was 50 percent.

The sea squirt offers hope for Alzheimer's sufferers

New model for testing anti-Alzheimer's drugs: At a pier near you

Alzheimer's disease affects an estimated 27 million people worldwide. It is the most common form of age-related dementia, possibly the most feared disease of old age. There is no cure, and the available drugs only help to relieve symptoms without slowing progression of the disease. One of the characteristic changes in the brains of Alzheimer's patients is the accumulation of plaques and tangles; currently, the best hope for curing or at least slowing the disease lies in developing drugs that target this buildup. Some drugs are already in clinical trials, but there is still a pressing need for more research, and for more and better drugs directed against both known and novel targets.

One of the big problems in rapidly screening potentially useful drugs has been the lack of a good model system in which Alzheimer's plaques and tangles appear quickly. However, Mike Virata and Bob Zeller, scientists working at San Diego State University, California, have come up with a new, and perhaps unlikely candidate; the humble sea squirt, Ciona intestinalis. Sea squirts are tunicates, marine organisms protected by an outer hard tunic with a soft body inside. Adults spend their lives attached to one spot on underwater structures like the pilings of piers, sucking in water through one siphon, filtering out small plants to eat, and squirting the water back out through another siphon. However, as long ago as Darwin, it has been recognized that sea squirts may be our closest invertebrate relatives; in their immature, tadpole form, they resemble proper vertebrates, and they share about 80% of their genes with us.

Bob Zeller has been a fan of sea squirt tadpoles since starting work with them in the 1990s, when he helped develop a way of introducing foreign DNA into fertilized sea squirt eggs with almost 100% efficiency, opening the way for their use as model organisms. He and his colleague Mike Virata decided to see whether it would be possible to model Alzheimer's disease in the tiny animals, which share all the genes needed for the development of Alzheimer's plaques in humans. Incredibly, dosing the sea squirt tadpoles with a mutant protein found in human families with hereditary Alzheimer's resulted in aggressive development of plaques in the tadpoles' brains in only a day, and these, along with the accompanying behavioral defects seen in the tadpoles, could be reversed by treating with an experimental anti-plaque forming drug. This is an important breakthrough, as all other invertebrates tested have been unable to process the plaque-forming protein, and vertebrates take months or years to make plaques. These exciting results make it a real possibility that sea squirts are an excellent model for testing new drugs in the fight against Alzheimer's disease.

Hope for Alzheimer's sufferers from an unlikely source: the sea squirt is presented in the Research Article entitled 'Ascidians: an invertebrate chordate model to study Alzheimer's disease pathogenesis', written by Michael J. Virata and Robert W. Zeller, of San Diego State University, California. The study is published in Volume 3 Issue 5/6 of the research journal, Disease Models & Mechanisms (DMM), http://dmm.biologists.org/, published by The Company of Biologists, a non-profit organisation based in Cambridge, UK.

For Pennies, a Disposable Toilet That Could Help Grow Crops

By SINDYA N. BHANOO

A Swedish entrepreneur is trying to market and sell a biodegradable plastic bag that acts as a single-use toilet for urban slums in the developing world. Once used, the bag can be knotted and buried, and a layer of urea crystals breaks down the waste into fertilizer, killing off disease-producing pathogens found in feces.

BIODEGRADABLE Children in Kenya with the Peepoo, a single-use bag designed to convert waste into fertilizer while destroying disease-producing pathogens. **Camilla Wirseen and Niklas Palmklint/Peepoople**

The bag, called the Peepoo, is the brainchild of Anders Wilhelmson, an architect and professor in Stockholm.

"Not only is it sanitary," said Mr. Wilhelmson, who has patented the bag, "they can reuse this to grow crops."

In his research, he found that urban slums in Kenya, despite being densely populated, had open spaces where waste could be buried.

He also found that slum dwellers there collected their excrement in a plastic bag and disposed of it by flinging it, calling it a "flyaway toilet" or a "helicopter toilet."

This inspired Mr. Wilhelmson to design the Peepoo, an environmentally friendly alternative that he is confident will turn a profit. "People will say, 'It's valuable to me, but well priced,' " he said.

He plans to sell it for about 2 or 3 cents - comparable to the cost of an ordinary plastic bag.

In the developing world, an estimated 2.6 billion people, or about 40 percent of the earth's population, do not have access to a toilet, according to United Nations figures.

It is a public health crisis: open defecation can contaminate drinking water, and an estimated 1.5 million children worldwide die yearly from diarrhea, largely because of poor sanitation and hygiene. To mitigate this, the United Nations has a goal to reduce by half the number of people without access to toilets by 2015.

The market for low-cost toilets in the developing world is about a trillion dollars, according to Jack Sim, founder of the World Toilet Organization, a sanitation advocacy group.

As far as toilets go, "the people in the middle class have reached saturation in consumption," said Mr. Sim, who calls himself a fan of the Peepoo. "This has created a new need, urgently, of looking for a new customer."

Since 2001, his organization has held an annual World Toilet Summit, and Mr. Sims said he was excited that in recent years there had been an emergence of entrepreneurs devising low-cost solutions.

At the 2009 meeting, Rigel Technology of Singapore unveiled a $30 toilet that separates solid and liquid waste, turning solid waste into compost. Sulabh International, an Indian nonprofit and the host of the World Toilet Summit in 2007, is promoting several low-cost toilets, including one that produces biogas from excrement. The gas can then be used in cooking.

But Therese Dooley, senior adviser on sanitation and hygiene for Unicef, said that inculcating sanitation habits was no easy task. "It will take a large amount of behavior change," Ms. Dooley said.

She added that while "the private sector can play a major role, it will never get to the bottom of the pyramid."

A sizable population, poor and uneducated, will still be left without toilets, Ms. Dooley said, and nonprofits and governments will have to play a large role in distribution and education.

Meanwhile, Mr. Wilhelmson is pushing ahead with the Peepoo. After successfully testing it for a year in Kenya and India, he said he planned to mass produce the bag this summer.

Human Culture, an Evolutionary Force

By NICHOLAS WADE

As with any other species, human populations are shaped by the usual forces of natural selection, like famine, disease or climate. A new force is now coming into focus. It is one with a surprising implication - that for the last 20,000 years or so, people have inadvertently been shaping their own evolution.

The force is human culture, broadly defined as any learned behavior, including technology. The evidence of its activity is the more surprising because culture has long seemed to play just the opposite role. Biologists have seen it as a shield that protects people from the full force of other selective pressures, since clothes and shelter dull the bite of cold and farming helps build surpluses to ride out famine.

Because of this buffering action, culture was thought to have blunted the rate of human evolution, or even brought it to a halt, in the distant past. Many biologists are now seeing the role of culture in a quite different light.

Although it does shield people from other forces, culture itself seems to be a powerful force of natural selection. People adapt genetically to sustained cultural changes, like new diets. And this interaction works more quickly than other selective forces, "leading some practitioners to argue that gene-culture co-evolution could be the dominant mode of human evolution," Kevin N. Laland and colleagues wrote in the February issue of Nature Reviews Genetics. Dr. Laland is an evolutionary biologist at the University of St. Andrews in Scotland.

The idea that genes and culture co-evolve has been around for several decades but has started to win converts only recently. Two leading proponents, Robert Boyd of the University of California, Los Angeles, and Peter J. Richerson of the University of California, Davis, have argued for years that genes and culture were intertwined in shaping human evolution. "It wasn't like we were despised, just kind of ignored," Dr. Boyd said. But in the last few years, references by other scientists to their writings have "gone up hugely," he said.

The best evidence available to Dr. Boyd and Dr. Richerson for culture being a selective force was the lactose tolerance found in many northern Europeans. Most people switch off the gene that digests the lactose in milk shortly after they are weaned, but in northern Europeans - the descendants of an ancient cattle-rearing culture that emerged in the region some 6,000 years ago - the gene is kept switched on in adulthood.

Lactose tolerance is now well recognized as a case in which a cultural practice - drinking raw milk - has caused an evolutionary change in the human genome. Presumably the extra nutrition was of such great advantage that adults able to digest milk left more surviving offspring, and the genetic change swept through the population.

This instance of gene-culture interaction turns out to be far from unique. In the last few years, biologists have been able to scan the whole human genome for the signatures of genes undergoing selection. Such a signature is formed when one version of a gene becomes more common than other versions because its owners are leaving more surviving offspring. From the evidence of the scans, up to 10 percent of the genome - some 2,000 genes - shows signs of being under selective pressure.

These pressures are all recent, in evolutionary terms - most probably dating from around 10,000 to 20,000 years ago, in the view of Mark Stoneking, a geneticist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Biologists can infer the reason for these selective forces from the kinds of genes that are tagged by the genome scans. The roles of most of the 20,000 or so genes in the human genome are still poorly understood, but all can be assigned to broad categories of likely function depending on the physical structure of the protein they specify.

By this criterion, many of the genes under selection seem to be responding to conventional pressures. Some are involved in the immune system, and presumably became more common because of the protection they provided against disease. Genes that cause paler skin in Europeans or Asians are probably a response to geography and climate. But other genes seem to have been favored because of cultural changes. These include many genes involved in diet and metabolism and presumably reflect the major shift in diet that occurred in the transition from foraging to agriculture that started about 10,000 years ago.

Amylase is an enzyme in the saliva that breaks down starch. People who live in agrarian societies eat more starch and have extra copies of the amylase gene compared with people who live in societies that depend on hunting or fishing. Genetic changes that enable lactose tolerance have been detected not just in Europeans but also in three African pastoral societies. In each of the four cases, a different mutation is involved, but all have the same result - that of preventing the lactose-digesting gene from being switched off after weaning.

Many genes for taste and smell show signs of selective pressure, perhaps reflecting the change in foodstuffs as people moved from nomadic to sedentary existence. Another group under pressure is that of genes that affect the growth of bone. These could reflect the declining weight of the human skeleton that seems to have accompanied the switch to settled life, which started some 15,000 years ago.

A third group of selected genes affects brain function. The role of these genes is unknown, but they could have changed in response to the social transition as people moved from small hunter-gatherer groups a hundred strong to villages and towns inhabited by several thousand, Dr. Laland said. “It’s highly plausible that some of these changes are a response to aggregation, to living in larger communities,” he said.

Though the genome scans certainly suggest that many human genes have been shaped by cultural forces, the tests for selection are purely statistical, being based on measures of whether a gene has become more common. To verify that a gene has indeed been under selection, biologists need to perform other tests, like comparing the selected and unselected forms of the gene to see how they differ.

Dr. Stoneking and his colleagues have done this with three genes that score high in statistical tests of selection. One of the genes they looked at, called the EDAR gene, is known to be involved in controlling the growth of hair. A variant form of the EDAR gene is very common in East Asians and Native Americans, and is probably the reason that these populations have thicker hair than Europeans or Africans.

Still, it is not obvious why this variant of the EDAR gene was favored. Possibly thicker hair was in itself an advantage, retaining heat in Siberian climates. Or the trait could have become common through sexual selection, because people found it attractive in their partners.

A third possibility comes from the fact that the gene works by activating a gene regulator that controls the immune system as well as hair growth. So the gene could have been favored because it conferred protection against some disease, with thicker hair being swept along as a side effect. Or all three factors could have been at work. “It’s one of the cases we know most about, and yet there’s a lot we don’t know,” Dr. Stoneking said.

The case of the EDAR gene shows how cautious biologists have to be in interpreting the signals of selection seen in the genome scans. But it also points to the potential of the selective signals for bringing to light salient events in human prehistory as modern humans dispersed from the ancestral homeland in northeast Africa and adapted to novel environments. “That’s the ultimate goal,” Dr. Stoneking said. “I come from the anthropological perspective, and we want to know what the story is.”

With archaic humans, culture changed very slowly. The style of stone tools called the Oldowan appeared 2.5 million years ago and stayed unchanged for more than a million years. The Acheulean stone tool kit that

succeeded it lasted for 1.5 million years. But among behaviorally modern humans, those of the last 50,000 years, the tempo of cultural change has been far brisker. This raises the possibility that human evolution has been accelerating in the recent past under the impact of rapid shifts in culture.

Some biologists think this is a possibility, though one that awaits proof. The genome scans that test for selection have severe limitations. They cannot see the signatures of ancient selection, which get washed out by new mutations, so there is no base line by which to judge whether recent natural selection has been greater than in earlier times. There are also likely to be many false positives among the genes that seem favored.

But the scans also find it hard to detect weakly selected genes, so they may be picking up just a small fraction of the recent stresses on the genome. Mathematical models of gene-culture interaction suggest that this form of natural selection can be particularly rapid. Culture has become a force of natural selection, and if it should prove to be a major one, then human evolution may be accelerating as people adapt to pressures of their own creation.

Ice deposits found at Moon's pole

By Paul Rincon Science reporter, BBC News, The Woodlands, Texas

A radar experiment aboard India's Chandrayaan-1 lunar spacecraft has identified thick deposits of water-ice near the Moon's north pole.

The US space agency's (Nasa) Mini-Sar experiment found more than 40 small craters containing water-ice. But other compounds - such as hydrocarbons - are mixed up in lunar ice, according to new results from another Moon mission called LCROSS. The findings were presented at a major planetary science conference in Texas.

The craters with ice range from 2km to 15km (one to nine miles) in diameter; how much there is depends on its thickness in each crater. But Nasa says the ice must be at least a couple of metres thick to give the signature seen by Chandrayaan-1.

Dr Paul Spudis, from the Lunar and Planetary Institute in Houston, estimated there was at least 600 million metric tonnes of water-ice held within these impact craters.

The equivalent amount, expressed as rocket fuel, would be enough to launch one space shuttle per day for 2,200 years, he told journalists at the 41st Lunar and Planetary Science Conference.

What all these craters have in common are large areas of their interiors that never see sunlight.

Extreme cold

Temperatures in some of these permanently darkened craters can drop as low as 25 Kelvin (-248C; -415F) - colder than the surface of Pluto - allowing water-ice to remain stable. "It is mostly pure water-ice," said Dr Spudis. "It could be under a few tens of centimetres of dry regolith (lunar soil)." This protective layer of soil could prevent blocks of pure ice from vaporising even in some areas which are exposed to sunlight, he explained.

In February, President Barack Obama cancelled the programme designed to return Americans to the Moon by 2020.

However, Dr Spudis said: "Now we can say with a fair degree of confidence that a sustainable human presence on the Moon is possible. It's possible using the resources we find there. "The results from these missions, that we have seen in the last few months, are totally revolutionising our view of the Moon."

Chandrayaan-1 was India's contribution to the armada of unmanned spacecraft to have been launched to the Moon in recent years. Japan, Europe, China and the US have all sent missions packed with instruments to explore Earth's satellite in unprecedented detail.

In Nasa's LCROSS mission, a rocket and a probe were smashed into a large crater at the lunar south pole, kicking up water-ice and water vapour.

Spectral measurements of material thrown up by the LCROSS impact indicate some of the water-ice was in a crystalline form, rather than the "amorphous" form in which the water molecules are randomly arranged.

Water source

"There's not one flavour of water on the Moon; there's a range of everything from relatively pure ice all the way to adsorbed water," said the mission's chief scientist Anthony Colaprete, from Nasa's Ames Research Center. "And here is an instance inside Cabeus crater where it appears we threw up a range of fine-grained particulates of near pure crystalline water-ice."

Overall, results from recent missions suggest there could be several sources for lunar ice.

One important way for water to form is through an interaction with the solar wind, the fast-moving stream of particles that constantly billows away from the Sun.

Space radiation triggers a chemical reaction in which oxygen atoms already in the soil acquire hydrogen nuclei to make water molecules and the simpler hydrogen-oxygen (OH) molecule. This "adsorbed" water may be present as fine films coating particles of lunar soil.

In a cold sink effect, water from elsewhere on the lunar surface may migrate to the slightly cooler poles, where it is retained in permanently shadowed craters.

Scientists have also reported the presence of hydrocarbons, such as ethylene, in the LCROSS impact plume. Dr Colaprete said any hydrocarbons were likely to have been delivered to the lunar surface by comets and asteroids - another vital source of lunar water. However, he added, some of these chemical species could arise through "cold chemistry" on interstellar dust grains accumulated on the Moon.

In addition to water, researchers have seen a range of other "volatiles" (compounds with low boiling points) in the impact plume, including sulphur dioxide (SO2) and carbon dioxide (CO2).

The results from the Mini-Sar instrument are due to be published in the journal Geophysical Research Letters. The team is currently analysing results for craters at the Moon's south pole.

Basics

Bringing New Understanding to the Director's Cut

By NATALIE ANGIER

And now, just in time for Oscar junkies, comes a new statistical mincing of the movies that may someday yield an award category of its own: best fit between a movie's tempo and the natural rhythms of the brain.

Reporting in the journal Psychological Science, James E. Cutting of Cornell University and his colleagues described their discovery that Hollywood filmmakers, whether they know it or not, have become steadily more adroit at shaping basic movie structure to match the pulsatile, half-smooth, half-raggedy way we attend to the world around us. This mounting synchrony between movie pace and the bouncing ball of the mind's inner eye may help explain why today's films manage to seize and shackle audience attention so ruthlessly and can seem more lifelike and immediate than films of the past, even when the scripts are lousier and you feel cheap and used afterward, not to mention vaguely sick from the three-quart tub of popcorn and pack of Twizzlers you ate without realizing it.

According to the new report, the basic shot structure of the movies, the way film segments of different lengths are bundled together from scene to scene, act to act, has evolved over the years to resemble a rough but recognizably wave-like pattern called 1/f, or one over frequency - or the more Hollywood-friendly metaphor, pink noise. Pink noise is a characteristic signal profile seated somewhere between random and rigid, and for utterly mysterious reasons, our world is ablush with it. Start with a picture of Penélope Cruz, say, or a flamingo on a lawn, and decompose the picture into a collection of sine waves of various humps, dives and frequencies. However distinctive the original images, if you look at the distribution of their underlying frequencies, said Jeremy M. Wolfe, a vision researcher at Brigham and Women's Hospital, "they turn out to have a one over f characteristic to them."

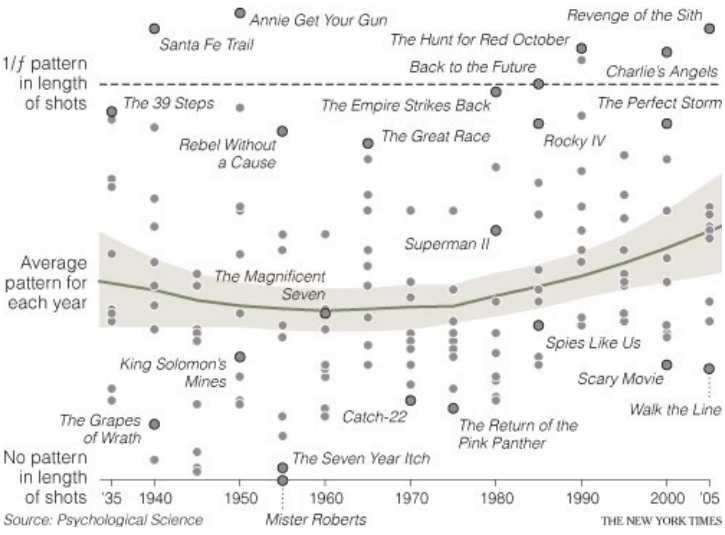
So, too, for many features of our natural and artifactual surroundings. Track the pulsings of a quasar, the beatings of a heart, the flow of the tides, the bunchings and thinnings of traffic, or the gyrations of the stock market, and the data points will graph out as pink noise. Much recent evidence from reaction-time experiments suggests that we think, focus and refocus our minds, all at the speed of pink. If you're sitting at a task, Dr. Cutting said, "sometimes you're good at it, sometimes your mind wanders, sometimes you're fast, sometimes you're slow, and the oscillating patterns that occur are generally one over f." His questions: Does Hollywood play pink? Are movies structured to appeal to this most basal of beats?

To address the problem, the psychologists analyzed 150 popular movies released from 1935 through 2005. They counted and measured all the separate shots, the bits of movie that are taken from different camera angles and that are spliced together by cuts, fades or wipes. They used computers, and they used eyeballs.

"For two days straight, I went through the movie, 'Spies Like Us,' with Dan Aykroyd and Chevy Chase," said Christine E. Nothelfer, who worked on the project as an undergraduate intern. "I went through

Studying the Pacing of Movie Shots

Researchers who analyzed the lengths of every shot in 150 Hollywood movies found that directors were increasingly using clusters of shots of similar length. Action movies in particular tend to use groups of quick shots in action sequences and groups of long shots in dialogue sequences. The researchers predict that the average pattern will eventually approach 1/*f*, a ratio thought to be related to attention and other mental processes.



it frame by frame, I knew where every single cut was." She added, "I still haven't seen the movie as a real filmgoer."

Some movies had fewer than 300 separate shots, others more than 3,000. Shot lengths varied enormously, as well, from the frenetically paced "Quantum of Solace," with an average shot length of 1.7 seconds, to some of the older movies where shots occasionally linger a minute or more.

The researchers then analyzed intershot relationships, performing extensive statistical comparisons of ever-thickening bundles of frames. "We'd ask, given that you've seen one shot with length X, how predictable is the shot length of the next shot?" Dr. Cutting said. Was the distribution of shot times entirely random, or were there any local or global patterns to descry: longies with longies, middies alternating with shorties, etc.?

Plot synopsis: Movies today are, on average, much pinker than the films of half a century ago. Their shot structure has greater coherence, a comparatively firmer grouping together of similarly sized units that ends up lending them a frequency distribution ever more in line with the lab results of human reaction and attention times. "Roughly since 1960," Dr. Cutting said, "filmmakers have been converging on a pattern of shot length that forces the reorientation of attention in the same way we do it naturally."

To cite a particularly slick example, the scenes in "Rocky IV" that show Rocky Balboa training for the big match not only alternate tidily with training scenes of his rival, Drago the Russian, but each back-and-forth sequence is also divvied up into shots of equivalent length. "That kind of pacing and clustering of similar shots is going to contribute to a one over f pattern," Dr. Cutting said.

Fun facts: The movie with the most pink-shaped distribution profile in the bunch was "Back to the Future," and those with the lowest scores - indicating pretty much a random distribution of shot lengths - were two comedies from 1955: John Ford's "Mister Roberts" and Billy Wilder's "The Seven Year Itch," although I doubt that even "Rocky"-style splicing would have made me chuckle at the sight of Marilyn Monroe's skirt being blown upward in public.

Dr. Cutting emphasized that there was much more to a movie than shot lengths and shot clusters. Cinematography, acting, directing, narrative, character development, makeup, costumes, special effects, catering service and more all play roles in distinguishing "The Godfather" from "The Godfather: Part III." Nor did the researchers find any correlation between the relative pinkness of a movie's cut structure and its popularity among viewers or critics.

Why our attention flits about in a pulsatile fashion that resembles heart beats and star beats and the fluctuating pitches of speech, nobody can say. "It depends on whether you think it's telling you something very deep about the general organizational principles of natural systems, or not," said David L. Gilden, a professor of psychology at of the University of Texas. As he sees it, complex systems are characterized by something called self-organized criticality. "They tend to migrate to the point where they are partially ordered, partially disordered," he said. "They're at the melting point between order and disorder."

A teeter-totter between stability and collapse? That sure sounds like life. Care to take in a flick?

Really?

The Claim: Fruit Juice Can Prevent Kidney Stones

By ANAHAD O'CONNOR

THE FACTS Kidney stones strike more than a million Americans every year, sometimes causing enough pain to bring them literally to their knees.

Along with medication to discourage the formation of kidney stones, sufferers are often encouraged to make dietary changes, among them drinking more citrus juices. Citrate in the fruit reduces the formation of calcium oxalate stones (the most common type) and lowers urine acidity, much like the kidney stone medication potassium citrate.

But not all juices have the same effect. Lemonade or diluted lemon juice is the usual recommendation for people with calcium stones. But a study financed by the National Institutes of Health in 2006 compared lemonade with orange juice in patients with calcium stones and found that three cups of orange juice a day - along with other standard dietary changes for kidney stone patients - did a better job of raising citrate levels and decreasing urine acidity than lemonade or distilled water.

Then there are cranberry and apple juices, which, according to studies. are good for some stones and bad for others. They raise the recurrence risk of calcium stones, but help prevent a far less common subset of kidney stones called brushite. Grapefruit juice, in contrast, raises the risk across the board. One large study in The Annals of Internal Medicine found that a daily cup of grapefruit juice raised the risk of stone formation as much as 44 percent.

THE BOTTOM LINE Some fruit juices protect against kidney stones; others raise the risk of recurrence.

Extremes of sleep related to increased fat around organs

WINSTON-SALEM, N.C. – Not getting enough sleep does more damage than just leaving you with puffy eyes. It can cause fat to accumulate around your organs – more dangerous, researchers say, than those pesky love handles and jiggly thighs.

A new study by researchers at Wake Forest University School of Medicine reveals how extremes of sleep - both too much and too little – can be hazardous to your health – especially for young minority women, a group most affected by obesity and chronic metabolic disease. The findings also indicate that there's more to "fat" than what we choose to eat – social factors such as the need to work three jobs in a bad economy – could be causing dangerous fat deposition around vital organs.

"We put a lot of stock in diet," said Kristen G. Hairston, M.D., M.P.H., an assistant professor of endocrinology and metabolism and lead author on the study. "But this study brings up some interesting questions about the way we live. We may need to start looking at other behaviors – besides daily food choices – that could be contributing to the obesity epidemic in younger age groups."

In individuals under 40, the study showed a clear association between averaging five hours or less of sleep each night and large increases in visceral fat, or fat around the organs. Of the study participants under 40, Hispanic men and black women were the largest groups to report getting such little sleep.

Short sleep has become more common in the United States and minorities are disproportionately affected, said Hairston, an affiliate of the Maya Angelou Center for Health Equity, part of the School of Medicine. They are also more prone to metabolic conditions, including increased rates of obesity, insulin resistance and type 2 diabetes. The study suggests that part of the explanation for higher rates of metabolic disease in this population may lie in the association between sleep duration and fat deposition.

But sleeping the day away won't do much to better one's health, either. The researchers found that getting more than eight hours of sleep on average per night has a similar – though less pronounced – affect and is a problem most commonly seen in Hispanic women of all ages. Surprisingly, the connection between extremes of sleep and accumulation of visceral fat was seen only in patients under 40, Hairston said.

"We don't really know yet why this wasn't seen in participants over 40, but it was clear that, in individuals under 40, it is worse to get five or less hours of sleep on average each night than it is to get eight or more hours," Hairston said. "However, both may be detrimental and, in general, people should aim for six to eight hours of sleep each night."

The study appears in the March issue of Sleep, the journal of the Associated Professional Sleep Societies, LLC.

The study raised important social questions for researchers, Hairston said, such as why so little sleep is such a problem in black women under age 40 and what circumstances may be contributing to their sleep patterns and likely to obesity and chronic disease development?

"This was certainly just a starting point," Hairston said. "We definitely know that a relationship exists between sleep and obesity. Now we need to know how this relationship can be modified."

Hairston added that it will be important for future obesity research to consider sleep patterns and the effect they can have on outcomes. Until the connection is understood, physicians should consider gathering information about sleep patterns just as they do other vital information when seeing patients. This information is especially relevant when treating patients about to make or in the middle of life transitions, such as college, marriage and childbearing, because such times are often associated with sleep deprivation in younger years.

"That information may help a physician put into context other issues going on in the patient's life which may be affecting their overall health," Hairston said.

Coresearchers on the study, funded by the National Institutes of Health, were Donald W. Bowden, Ph.D., and Lynne E. Wagenknecht, Dr.P.H., both of the School of Medicine, Michael Bryer-Ash, of the University of Oklahoma School of Health Sciences, Jill M. Norris, M.P.H., Ph.D., of the University of Colorado School of Health Sciences, and Steven Haffner, M.D., M.P.H., of the University of Texas Health Science Center at San Antonio.

Learning helps keep brain healthy, UCI researchers find

Study suggests mental activity could stave off age-related cognitive and memory decline

UC Irvine neurobiologists are providing the first visual evidence that learning promotes brain health - and, therefore, that mental stimulation could limit the debilitating effects of aging on memory and the mind.

Using a novel visualization technique they devised to study memory, a research team led by Lulu Chen and Christine Gall found that everyday forms of learning animate neuron receptors that help keep brain cells functioning at optimum levels.

These receptors are activated by a protein called brain-derived neurotrophic factor, which facilitates the growth and differentiation of the connections, or synapses, responsible for communication among neurons. BDNF is key in the formation of memories.

"The findings confirm a critical relationship between learning and brain growth and point to ways we can amplify that relationship through possible future treatments," says Chen, a graduate researcher in anatomy & neurobiology. Study results appear in the early online edition of the Proceedings of the National Academy of Sciences for the week of March 1.

In addition to discovering that brain activity sets off BDNF signaling at the sites where neurons develop synapses, researchers determined that this process is linked to learning-related brain rhythms, called theta rhythms, vital to the encoding of new memories.

Theta rhythms occurring in the hippocampus involve numerous neurons firing synchronously at a rate of three to eight times per second. These rhythms have been associated with long-term potentiation, a cellular mechanism underlying learning and memory.

In rodent studies, the team found that both unsupervised learning and artificial application of theta rhythms triggered BDNF signaling at synapse creation sites.

"This relationship has implications for maintaining good brain health," says Gall, a professor of anatomy & neurobiology. "There is evidence that theta rhythms weaken as we age, and our discoveries suggest that this can result in memory impairment. On the other hand, they suggest that staying mentally active as we age can keep neuronal BDNF signaling at a constant rate, which may limit memory and cognitive decline."

Researchers are now exploring whether learning-induced growth signals decrease with age and, if so, whether this can be reversed with a new family of experimental drugs.

UCI psychiatry & human behavior professor Gary Lynch, postdoctoral fellow Christopher Rex, and undergraduate researchers Yas Sanaiha and Danielle Pham also worked on the study, which received support from the National Institutes of Health and the National Institute of Mental Health.

Re-Using Equipment Could Help Hospitals Go Green

Hospitals could save billions of dollars and tons of waste by reusing medical equipment, analysis shows.

By Jessica Marshall Tue Mar 2, 2010 07:06 AM ET

THE GIST:

**** U.S. hospitals generate over four billion pounds of waste each year.***

**** Many types of medical equipment can be reused, from oxygen sensors to elastic bandages.***

**** Reusing equipment could reduce waste and save billions annually, research shows.***

U.S. health care facilities generate over four billion pounds of waste each year, second only to the food industry in trash-making. But much of this waste could be avoided, according to a new study, by cleaning, testing and re-sterilizing many types of medical equipment after first use, including elastic bandages, finger oxygen sensors and tourniquet cuffs.

"It's clear to me from all the surgery I do that many of the supplies can be re-sterilized or refurbished when they play non-critical roles," said study author Marty Makary of Johns Hopkins School of Medicine in Baltimore.

"We estimate that reprocessing of open-but-never-used supplies alone can account for a one-billion-dollar savings in a system, not to mention the instruments that are used and are in perfect condition that can be reprocessed as well," he said. "There are billions of dollars of savings."

Certain health-care systems have already experienced over $1 million in savings over a single year, he said, by buying reprocessed equipment from companies approved by the FDA to collect items labeled by their original manufacturers as "single-use" and clean, test and resterilize them.

In 2008, according to Makary's study, one leading reprocessing service prevented 4.3 million pounds (2150 tons) of waste from reaching landfills, saving hospitals more than $138 million.

The reprocessing industry has been FDA-regulated since 2000.

"We have to prove to the FDA's satisfaction that our device will be as clean, as sterile and as functional as a new device," said Daniel Vukelich, president of the Association of Medical Device Reprocessors, an organization that represents the reprocessing industry, headquartered in Washington D.C.

"One thing that probably surprises patients is that they actually have a better track record when it comes to reprocessed devices than a new one," he said. "Devices tend to fail less when reprocessed because every product is individually tested."

The industry arose in the 1980s when medical device manufacturers started labeling many items that were once labeled reusable as single-use, Vukelich said. This may have been done for legal reasons or as a way to increase profits, Makary said.

Hospitals can reprocess items that are sold for multiple uses -- from gowns to surgical beds to scalpel handles and surgical clamps. But since the FDA regulations took effect, only licensed reprocessing companies can handle single-use devices -- even if they are unused.

Hospitals can buy these reprocessed items for an average of half what it costs to buy them new.

Only certain items are eligible for reprocessing. Perhaps the two most common items are the blood oxygen sensors that wrap around a finger or toe, and compression stockings used during surgery that periodically fill with air to promote circulation in the legs and prevent blood clots while the patient is lying flat.

Other commonly reprocessed items are drills, saw blades, gowns, scalpel handles, and surgery clamps. Because these items are labeled as reusable, hospitals can clean and sterilize them onsite. Knife blades, or permanent medical implants like knee replacements, pacemakers, or cataract lenses -- things for which a failure or malfunction would cause patient harm -- are never reused.

So far, about 25 percent of U.S. hospitals are buying reprocessed equipment, according to Makary's study, published in the journal Academic Medicine. "The places that have tried it, like it," said Makary, who has no financial ties to the industry. "It is simply a matter of health care institutions not being familiar with this service. After over a decade, there have been no patient safety concerns," he added.

Others agreed: "Separate certified reprocessing stations or companies that pass very rigorous FDA standards -- their stuff is as good as new," said T. Forscht Dagi of the Harvard-MIT Division of Health Sciences and Technology and head of an American College of Surgeons committee dealing with patient safety and well-being during surgery. "The FDA reprocessing companies do a very, very good job. No question."

Noone from AdvaMed, the industry organization that represents medical device manufacturers, was available to discuss reprocessing with Discovery News. However, they have posted several statements and press releases about reprocessing on their Web site.

Their 2004 position statement on reprocessing says that single use products were not designed for reuse and that it may not be possible to thoroughly clean these products or for these products to withstand the harsh conditions of reprocessing.

Shopping for happiness? Get a massage, forget the flat-screen TV

Money can't buy you love, but it can buy satisfaction – if you spend wisely.

Consumers found that satisfaction with "experiential purchases" – from massages to family vacations – starts high and increases over time. In contrast, spending money on material things feels good at first, but actually makes people less happy in the end, says Thomas Gilovich, Cornell University professor of psychology and Travis J. Carter, Cornell Ph.D. '10.

When it comes to material things, Gilovich and Carter found shoppers often second-guess their original buying decisions, comparing what they bought to other people's purchases – or to better deals they missed.

But buying experiences provides greater satisfaction as time goes on, in part because of selective memory and because a consumer's experience is highly subjective, making it much harder to make negative comparisons. Consumers also find it easier to decide on experiences, spending money on the first option that meets a set of expectations rather than painstakingly comparing all options.

Still, there is hope for makers of CDs and flat-screen televisions. The research found that how people view a purchase – as an expensive boxed-set or as hours of enjoyable music – also influenced their level of satisfaction.

The original paper, "The Relative Relativity of Material and Experiential Purchases," appeared in the January 2010 issue of the American Psychological Association's Journal of Personality and Social Psychology. Carter is now conducting post-doctoral work at the University of Chicago. The National Science Foundation funded the research.

Cow Dung, Urine as Medicine?

Borrowing from Hindu spiritual traditions, researchers in India are working on medicines based on the waste of these sacred animals.

content provided ***by Rupam Jain Nair***, AFP

THE GIST:

**** Research centers in India are developing a line of dung- and urine-based medicines.***

**** In Ahmedabad, the raw materials are generated on site from more than 300 cows.***

**** One company has even developed a soft drink based on cow urine which they believes could eclipse Coke and Pepsi.***

"God resides in cow dung," says Kesari Gumat, as he walks through his laboratory where researchers mix bovine excreta with medicinal herbs and monitor beakers of simmering cow urine.

The lab in the western Indian city of Ahmedabad is one of a growing number of research centers which have embraced the sacred status of cows in India and sought to push it to a new level.

Promoting the practical alongside the spiritual, they have developed a line of dung- and urine-based medicines which they say can cure a whole herd of ailments from bad breath to cancer.

"These formulas are not new," Gumat said. "They are contained in ancient Hindu holy texts. We are just making them with a scientific approach."

The raw materials are generated on site from more than 300 cows which roam the compound housing the center. Visitors must remove shoes and socks before entering and brave a barefoot walk across a carpet of semi-soft dung drying in the sunlight.

"Walking on fresh cowdung is very healthy," Gumat insisted. "It kills all the germs and bacteria and heals wounds. And dry cowdung is a great scrub to get rid of dead skin and improve blood circulation."

The list of derivative applications is, according to Gumat, an extremely lengthy one, stretching beyond medicines to toiletries like soap, shampoo and toothpaste, as well as incense sticks and mosquito coils.

The products have been applauded by Hindu nationalist groups, the largest of which, the Rashtriya Swayamsevak Sangh (RSS), unveiled its own urine-based soft drink last year as a "healthy" alternative to Coke and Pepsi.

"Gau Jal," or "cow water" was developed at the RSS Cow Protection Department, a research facility in the northern city of Haridwar on the banks of the holy river Ganges.

"This will end the market for carbonated fizzy drinks," predicted the facility's bullish director Om Prakash.

Gau Jal is currently awaiting government approval. In the meantime Prakash said his team was focusing on packaging, marketing, and preservation -- to prevent the drink spoiling in India's summer heat.

Cows are sacred to India's huge Hindu majority, precluding them from eating beef, but the animals' bodily waste falls into the same acceptable category as dairy products.

The dung is generally dried for over a week, then blended at a very high temperature to kill all harmful bacteria and germs. The final product, a dung powder, is mixed with variety of ingredients to make the medicines and toiletries. The urine meanwhile is distilled to remove any impurities.

Raghav Gandhi, who heads the cow nutrition department at another research center in Ahmedabad, stressed that the process begins long before the waste is harvested. "It might seem that all we do is collect cow excreta to make medicines but it is not so easy," Gandhi told AFP.

"We have to serve the cow on a minute-to-minute basis," said Gandhi who personally feeds his charges on grass dipped in milk, herbs with unrefined cane sugar and water containing essential salts.

He also sings to them.

"It's simple," Gandhi said. "What they eat is what they release. Cow dung stores all the vital nutrients and minerals. The urine is blessed with disinfectant properties."

Mainstream doctors are divided about the medical benefits, with some pointing out that the curative claims have never been validated by independent bodies. But others see no harm in patients consuming a product that they believe is helping them.

"I've read about the benefits of cow urine and dung," said Mayur Patel, an oncologist working at the Gujarat State Cancer Research Center. "My patients take it and I allow them to do so. It's an alternative form of medicine and it has no negative effects," Patel said.

Ahmedabad housewife Nila Parmar, 42, has been kickstarting her day with a shot of cow urine for years, and she has no doubts about its efficacy.

"Trust me. I tried allopathy and homeopathy to cure my liver disease but nothing worked," she told AFP.

"I kept changing doctors for over two years but it's gau mutra (cow urine) that did the trick."

Scientists discover cause of destructive inflammations

The signaling molecule CD95L, known as "death messenger," causes an inflammatory process in injured tissue after spinal cord injuries and prevents its healing. This discovery was published by scientists of the German Cancer Research Center. In mice, the researchers found out that if they switch off CD95L, the injured spinal cord heals and the animals regain better ability to move. Therefore, substances which block the death messenger might offer a new approach in the treatment of severe inflammatory diseases.

A couple of years ago, Dr. Ana Martin-Villalba of the German Cancer Research Center already succeeded in reducing the effects of spinal cord injuries in mice. She was able to improve the animals' ability to move by neutralizing the signaling molecule CD95L. In her research work now published, Martin-Villalba and her team were studying the question of how CD95L exerts its harmful effect in injured nerve tissue.

So far, scientists had assumed that the CD95L molecule, which is also known as 'death messenger', attaches to the death receptor, CD95, on the surface of neurons, thus triggering programmed cell death, or apoptosis, and further damaging injured nerve tissue. After the recent discoveries, this view needs to be revised.

Martin-Villalba's team observed in mice that after spinal cord injuries there is a prolonged inflammatory reaction in the surrounding tissue. Within 24 hours after an injury, large numbers of white blood cells migrate to the affected site in the spinal cord. These are primarily cells of what is called the innate immunity –

macrophages and neutrophils. Researchers found out that during the same time the amount of CD95L on the cell surface of white blood cells in the blood stream increases significantly – apparently as a result of a still unidentified chemical signal sent out by the injured tissue.

In their latest study, Martin-Villalba's team has proven that the signaling molecule CD95L is responsible for the migration of immune cells to the injury site. When the investigators blocked the death messenger using specific agents, the migration came to an end. The researchers identified a previously unknown signaling pathway by which CD95L activates immune cells to become mobile and migrate from the blood stream into the injured spinal cord. This mobilization is not restricted to the inflammatory reaction in spinal cord injuries; in mice with severe peritonitis, the researchers also found CD95L mediated migration of immune cells into the affected tissue.

CD95L promotes tissue-damaging inflammatory reactions

What does CD95L cause in injured spinal cord tissue? To explore this question, the DKFZ researchers investigated genetically modified mice whose immune cells are unable to form CD95L. If the spinal cord of such animals is injured, their neurons are protected from death; the mice recover and perform better in subsequent mobility tests than normal mice.

It seems that the migrated immune cells boost the tissue-damaging inflammatory reaction. When the researchers switched off the CD95L molecule on immune cells and subsequently studied the gene activity in the injured tissue, they observed a decrease in the activity of genes promoting cell death and inflammation. In contrast, more genes which promote neuronal growth were active.

Does death messenger CD95L really exert its harmful effect in injured spinal cord by causing programmed cell death (apoptosis)? The investigators explored this question in mice whose neurons lack the CD95 receptor, i.e. the docking site for death messenger CD95L. In these animals it became obvious that CD95L contributes to the demise of neurons by recruiting inflammation-promoting immune cells to the injured spinal cord and not by programmed cell death.

Blocking CD95L as a new treatment approach for inflammatory diseases

"We assume that CD95L causes harmful inflammatory reactions in the human body, too," said project leader Ana Martin-Villalba. An analysis of blood samples from patients with spinal cord injuries showed that here, too, the amount of CD95L on immune cells rises within a few hours after the injury.

This is an encouraging indication suggesting that blocking CD95L might be a promising treatment approach for severe inflammatory diseases such as autoimmune disorders, e.g. rheumatoid arthritis or multiple sclerosis. An agent acting against the death messenger would prevent the migration of inflammation-promoting immune cells into the affected tissue and the resulting intensification of the tissue damage. Most recent research results even suggest that inflammatory reactions promote the invasive capability of cancer cells, so that using a CD95L blocker could be helpful in such cases, too.

Such an agent might soon be available. On the basis of inventions from DKFZ, a biotech company is already developing an inhibitor which specifically switches off the human CD95L molecule.

Elisabeth Letellier, Sachin Kumar, Ignacio Sancho-Martinez, Stefanie Krauth, Anne Funke-Kaiser, Sabrina Laudenklos, Katrin Konecki, Stefan Klussmann, Nina S. Corsini, Susanne Kleber, Natalia Drost, Andreas Neumann, Matthieu Lévi-Strauss, Benedikt Brors, Norbert Gretz, Lutz Edler, Carmen Fischer, Oliver Hill, Meinolf Thiemann, Bahram Biglari, Saoussen Karray and Ana Martin-Villalba: CD95-Ligand on Peripheral Myeloid Cells Activates Syk Kinase to Trigger Their Recruitment to the Inflammatory Site. Immunity 2010, DOI 10.1016/j.immuni.2010.01.011

Vitamin D Lifts Mood During Cold Weather Months

Loyola Researchers to Study Nutrient in Depression and Diabetes Patients

MAYWOOD, ILL. -- A daily dose of vitamin D may just be what Chicagoans need to get through the long winter, according to researchers at Loyola University Chicago Marcella Niehoff School of Nursing (MNSON). This nutrient lifts mood during cold weather months when days are short and more time is spent indoors.

“Vitamin D deficiency continues to be a problem despite the nutrient’s widely reported health benefits,” said Sue Penckofer, PhD, RN, professor, MNSON. “Chicago winters compound this issue when more people spend time away from sunlight, which is a natural source of vitamin D.”

Diet alone may not be sufficient to manage vitamin D levels. A combination of adequate dietary intake of vitamin D, exposure to sunlight, and treatment with vitamin D2 or D3 supplements can decrease the risk of certain health concerns. The preferred range in the body is 30 - 60 ng/mL of 25(OH) vitamin D.

Loyola faculty members plan to take vitamin D research a step further by evaluating whether weekly vitamin D supplements improve blood sugar control and mood in women with diabetes. Depression is associated with increased insulin resistance, so people with diabetes have a greater risk for the disease than those without

depression. Women also tend to have greater rates of depression and poorer blood sugar control than men with diabetes.

“There is evidence to suggest that vitamin D supplementation may decrease insulin resistance,” said Dr. Penckofer. “If we can stabilize insulin levels, we may be able to simply and cost effectively improve blood sugar control and reduce symptoms of depression for these women.”

Loyola is currently enrolling women in this clinical trial. In order to enter the study, they must be 18 to 70 years of age, have stable type 2 diabetes, signs of depression and no other major medical illness. Eighty women with type 2 diabetes and signs of depression will be given a weekly dose of vitamin D (50,000 IU) for a period of six months. Study participants will be evaluated at three points during this time.

"Vitamin D has widespread benefits for our health and certain chronic diseases in particular," Dr. Penckofer said. "Our research may shed greater light on the role this nutrient plays in managing two conditions that impact millions of Americans. If proven to be successful, vitamin D may an important addition to care for diabetes and depression."

Hangover-Free Booze? Increasing Dissolved Oxygen Concentrations in Alcohol May Reduce Negative Side Effects

Oxygen for ethanol oxidation is supplied through breathing, the stomach, and the skin. There is a great deal of genetic and environmental variability in the pharmacokinetics of alcohol absorption, distribution, metabolism, and elimination. A new study has found that increasing dissolved oxygen concentrations in alcohol may help to reduce alcohol-related side effects and accidents. Results will be published in the May 2010 issue of Alcoholism: Clinical & Experimental Research and are currently available at Early View.

"Ethanol is oxidized to acetaldehyde, then further oxidized to water and carbon dioxide in the body after consumption," explained Kwang-il Kwon, a professor in the college of pharmacy at Chungnam National University and corresponding author for the study. "These oxidation reactions occur primarily via hepatic oxidation and are governed by the catalytic properties of alcohol-metabolizing enzymes, including the microsomal ethanol oxidizing system (MEOS), alcohol dehydrogenase (ADH), and aldehyde dehydrogenase (ALDH). Ethanol oxidation by ADH, ALDH, and MEOS requires oxygen, and a higher oxygen uptake increases the rate of ethanol oxidation."

"Several studies have indicated that high-oxygen water can enhance the survival ability of mice, fatigue recovery, and anoxia endurance function," added Hye Gwang Jeong, a professor in the department of toxicology in the college of pharmacy at Chungnam National University. "It can also increase energy storage. However, the influence of dissolved oxygen concentration on alcohol pharmacokinetics has not previously been described. This manuscript is the first to investigate the influence of dissolved oxygen concentrations on the pharmacokinetics of alcohol in healthy human subjects."

Kwon and his colleagues performed three experiments with 49 healthy volunteers (30 men, 19 women), with a mean age of 27.2 years. Experiment one compared 8 ppm and 20 ppm dissolved oxygen concentrations in 240 ml of 19.5 percent alcoholic beverage. Experiment two compared 8 ppm and 20 ppm dissolved oxygen concentrations in 360 ml of 19.5 percent alcoholic beverage. Experiment three compared 8 ppm and 25 ppm dissolved oxygen concentrations in 360 ml of 19.5 percent alcoholic beverage.

Results showed that elevated, dissolved oxygen concentrations in alcoholic drinks can accelerate the metabolism and elimination of alcohol. For example, the time to reach 0.000 percent blood alcohol concentration (BAC) for the 240 ml of 19.5 percent alcoholic beverage with 20 ppm dissolved oxygen concentration was 20.0 min faster than with 8 ppm (257.7 min). The time to reach 0.000 percent BAC for the 360 ml of 19.5 percent alcoholic beverage with 20 ppm (334.5 min) and 25 ppm (342.1 min) dissolved oxygen concentration was 23.3 min and 27.1 min faster than with 8 ppm, respectively.

"The oxygen-enriched alcohol beverage reduces plasma alcohol concentrations faster than a normal dissolved-oxygen alcohol beverage does," said Kwon. "This could provide both clinical and real-life significance. The oxygen-enriched alcohol beverage would allow individuals to become sober faster, and reduce the side effects of acetaldehyde without a significant difference in alcohol's effects. Furthermore, the reduced time to a lower BAC may reduce alcohol-related accidents."

Both Kwon and Jeong noted that alcoholic drinks with a higher oxygen concentration already exist in Korea, but they lack scientific support. "It seems that these drinks can maintain a high dissolved-oxygen concentration for about 10 to 20 days before the stopper is removed, and for 70 minutes after removing the stopper, respectively, at room temperature," said Kwon. Both scientists suggested that future studies look closer at dissolved-oxygen concentrations on specific enzymes of alcohol metabolism, such as ADH, ALDH, and MEOS.

New way to control disease-spreading mosquitoes: Make them hold their urine

ITHACA, N.Y. - Cornell researchers have found a protein that may lead to a new way to control mosquitoes that spread dengue fever, yellow fever and other diseases when they feed on humans: Prevent them from urinating as they feed on blood.

The work may lead to the development of new insecticides to disrupt the mosquito's renal system, which contributes to a mosquito's survival after feeding on blood.

Aedes aegypti mosquitoes transmit the virus that causes dengue fever, putting 40 percent of the world's population at risk of catching the disease, and causing 50 million to 100 million infections (22,000 deaths) annually. They pick up diseases when feeding on infected hosts and can then infect new hosts when they feed again. Currently, no vaccine or treatment protects against dengue, so the only way to stop its spread is by controlling mosquitoes.

But now, a Cornell study published in the March 4, 2010 issue of the American Journal of Physiology – Regulatory, Integrative and Comparative Physiology has identified a protein from the renal tubules of Aedes aegypti mosquitoes that appears to be involved in promoting urination as they feed on blood. When mosquitoes consume and process blood meals, they must urinate to prevent fluid and salt overloads that can kill them.

Also, "they have to undergo rapid urination when feeding, or they can't fly away," said Peter Piermarini, the paper's lead author and a postdoctoral research associate in the lab of Klaus Beyenbach, a professor of biomedical sciences in Cornell's College of Veterinary Medicine and the paper's senior author. "Too much weight will impair the mosquito's flight performance, like an aircraft with too much payload. [If they get too heavy,] they may become more susceptible to being swatted by their host or eaten by a predator," said Piermarini.

The researchers discovered a key protein expressed in the mosquito's renal system that contributes to urination. In lab experiments, Piermarini, Beyenbach and colleagues demonstrated that blocking the protein's function in the renal tubules with a drug reverses the enhanced rates of urination that would occur during blood feeding.

"Thus, blocking the function of this protein in natural populations of mosquitoes may limit their ability to survive the physiological stresses of a blood meal and to further transmit viruses," said Piermarini.

The Aedes aegypti renal system also serves as a valuable model for parts of the mammalian kidney, with similar cells in each system and possibly similar proteins, said the authors.

Co-authors include Laura Grogan, a participant in the Leadership Program for Veterinary Scholars at Cornell in 2007; Kenneth Lau '08, a former research technician in the Department of Biomedical Sciences; and Li Wang '10, an honors student in physiology. The National Institutes of Health and the National Science Foundation funded the study.

Dinosaur's oldest relative found

By Victoria Gill Science reporter, BBC News

Scientists have discovered a dinosaur-like creature 10 million years older than the earliest known dinosaurs.

Asilisaurus kongwe is a newly discovered herbivore that lived during the middle Triassic period - about 245 million years ago. The scientists say that its age suggests that dinosaurs were also on the Earth earlier than previously thought. They described their findings in the journal Nature.

The study was led by Dr Sterling Nesbitt from the University of Texas at Austin in the US. He said: "This new evidence suggests that [dinosaurs] were really only one of several large and distinct groups of animals that exploded in diversity in the Triassic period, including silesaurs [like this one], pterosaurs, and several groups of crocodilian relatives."

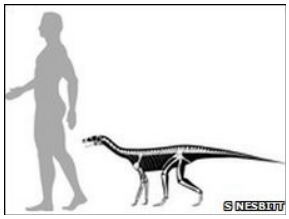
Dr Randall Irmis from the Utah Museum of Natural History in the US was also involved in the study. He said that this group of creatures - the silesaurs - were the "closest relative of the dinosaurs". "It was to dinosaurs much like chimps are to humans - kind of cousins," he told BBC News.

Reconstruction of Asilisaurus kongwe, a close dinosaur relative, from the Middle Triassic of Africa
Asilisaurus kongwe was a very close relative of the dinosaurs

Since we have one line of the family tree, the other branch must have existed at the same time. So this suggests there are other very early dinosaurs that we haven't found yet."

He also said that the creature was not what the researchers expected an early dinosaur cousin to look like. "It was a weird little creature," he said. "We always thought the earliest relatives were small, bipedal, carnivorous animals. "These walked on four legs and had beaks and herbivore-like teeth."

'Failed experiment'



Dr Paul Barrett, a palaeontologist from the Natural History Museum in London said that the finding provided scientists with important information about how dinosaurs evolved. "The creatures share a lot of features with dinosaurs," he said. "They show us an intermediate step between more primitive reptiles and the more specialised dinosaurs."

The fossil record indicates that this group of primitive creatures went extinct approximately 45 million years after they emerged. The dinosaurs, on the other hand, were far more successful and walked the Earth for about 165 million years.

Asilisaurus stood up to 1m tall and walked on all fours

Dr Barrett said: "[Silesaurids] were like a failed experiment in how to build a dinosaur."

Safety data favor norepinephrine over dopamine for shock

ATLANTA - Physicians treating patients with shock should consider norepinephrine instead of dopamine as a tool for stabilizing blood pressure, according to an editorial in the March 4, 2010, issue of the New England Journal of Medicine (NEJM). Jerrold Levy, MD, FAHA, professor and deputy chair for research, Department of Anesthesiology, Emory University School of Medicine, and co-director of cardiothoracic anesthesiology, Emory Healthcare, authored the editorial.

The editorial accompanies a report in the same issue of NEJM on a European clinical trial evaluating dopamine and norepinephrine in shock patients. The randomized trial, led by Daniel De Backer, MD, PhD, at Erasme University Hospital in Belgium, compared 28-day mortality in 1679 patients treated for shock with dopamine or norepinephrine in Austria, Belgium and Spain between 2003 and 2007.

"Dopamine has been commonly used as a first-line therapy for shock at many hospitals for years, partially because of the widespread perception that norepinephrine is associated with adverse events," Levy says. "The current study supports the concept that shock from any cause carries a high risk of death, and raises significant concerns about the safety of dopamine."

Shock, or dangerously low blood pressure, can occur as a result of sepsis (severe inflammation resulting from bacterial infection), heart failure (cardiogenic), hemorrhage (severe blood loss) or anaphylaxis. Most of the patients (62.2 percent) in the European trial had septic shock, 16.7 percent had heart failure and 15.7 percent hemorrhage.

The authors of the clinical study reported no overall difference in death rates at 28 days. However, heart arrhythmias were almost twice as common in the dopamine group (24.1 percent vs 12.4 percent) and mortality was higher for patients with cardiogenic shock treated with dopamine.

A previous observational study showed that dopamine's use in intensive care units added to the risk of death, and rapid heart rate is known to be a frequent side effect of dopamine, Levy notes.

Norepinephrine has been used to stabilize patients' blood pressure during cardiac and non cardiac surgery, and in intensive care units after surgery. Vasopressin, although not studied in the European clinical trial, is also a viable alternative treatment for shock, Levy says.

The hormones dopamine and norepinephrine have functions in the brain, helping neurons communicate, as well as in the body to maintain vascular tone. In an emergency situation, they both can increase blood pressure by constricting blood vessels. Dopamine is the precursor to norepinephrine in the sympathetic nervous system, and thus acts indirectly.

"The data challenge consensus guidelines that recommend dopamine as the initial vasopressor for increasing arterial pressure in the case of septic shock or cardiogenic shock," Levy writes in the editorial.

"In addition, norepinephrine needs to be considered as an initial therapeutic agent for patients in circulatory shock. … The results of the study by De Backer et al should also put an end to the outdated view that the use of norepinephrine increases the risk of death."

Possible vaccine for mesothelioma proven safe

Researchers have demonstrated the safety of a potential vaccine against mesothelioma, a rare cancer associated primarily with asbestos exposure. The vaccine, which infuses uses a patient's own dendritic cells (DC) with antigen from the patient's tumor, was able to induce a T-cell response against mesothelioma tumors.

"[This] is the first human study on DC-based immunotherapy in patients with mesothelioma," wrote Joachim G Aerts M.D., Ph.D., a pulmonary physician at Erasmus Medical Center in the Netherlands.

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

The U.S. and other developed countries have prohibited the use of asbestos for decades, but the time between asbestos exposure and diagnosis of mesothelioma can up to 50 years. The incidence of mesothelioma,

therefore, is still on the rise and expected to continue to increase until 2020. Once diagnosed, mesothelioma has a median survival time of 12 months. The standard chemotherapeutic treatment only improves survival time by about three months.

The anticipated increase in the incidence of mesothelioma, together with the paucity of treatment options, has spurred considerable interest in the development of new therapies. Immunotherapy, which uses the body's own immune system to target and destroy cancer cells, has been shown to have some promise.

"The possibility to harness the potency and specificity of the immune system underlies the growing interest in cancer immunotherapy," said Dr. Aerts. "One such approach uses the patient's own DC to present tumor-associated antigens and thereby generate tumor-specific immunity."

Building upon their previous research which demonstrated that DC vaccinations induced anti-tumor immunity and conferred a survival benefit in mice, Dr. Aerts and colleagues sought to test the clinical relevance of their finding. After recruiting 10 human patients recently diagnosed with malignant pleural mesothelioma of the epithelial subtype, they cultured immature DC from their blood and exposed the DC to the antigen produced by the patients' tumors. The DC were also exposed to keyhole limpet hemocyanin (KLH), which was used as a surrogate marker to show an immune response. The DC were then matured and injected back into the patients in three doses over a two-week interval.

Serum samples from all patients showed a significant increase of pre- versus post-vaccine antibodies to KLH. In the four patients whose tumor material was sufficient for testing, there was clear induction of cytotoxicity against their own tumors after vaccination. Three patients showed signs of tumor regression, though this could not be conclusively or directly attributed to the vaccine.

Encouragingly, while eight of the patients developed flu-like symptoms in response to the vaccinations, the symptoms normalized after one day in all but one of the patients. There were no signs of autoimmune diseases in the patients provoked by the vaccination, nor other serious side effects.

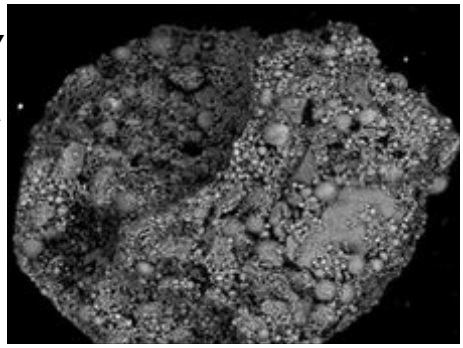
"The major problem in mesothelioma is that the immunosuppressive environment caused by the tumor will negatively influence our therapy so we are now working on a method to lower this immunosuppressive environment," said Dr. Aerts. "We hope that by further development of our method it will be possible to increase survival in patients with mesothelioma and eventually vaccinate persons who have been in contact with asbestos to prevent them from getting asbestos related diseases."

Link to original article: ***http://www.thoracic.org/newsroom/press-releases/resources/Aerts_Mesothelioma.pdf***

Clues to Antarctica space blast

By Paul Rincon Science reporter, BBC News, The Woodlands, Texas

A large space rock may have exploded over Antarctica thousands of years ago, showering a large area with debris, according to new research.



The team's findings could help in the search for other ancient "airbursts"

The evidence comes from accumulations of tiny meteoritic particles and a layer of extraterrestrial dust found in Antarctic ice cores. Details of the work were presented at a major science conference in Texas.

The event would have been similar to the Tunguska event, which flattened a large area of Siberian forest in 1908. It is thought to have been a so-called "airburst" in which a space rock does not reach the ground, but rather explodes in the atmosphere.

The research is based on a study of extraterrestrial debris found in granite from Miller Butte, in the Transantarctic Mountains, and a layer of cosmic dust represented in two Antarctic ice cores.

The debris from the mountains includes micrometeorites and tiny particles called spherules. The study's authors think these spherules could be material eroded from a stony meteorite as it was heated up on its way through our atmosphere. The spherules could potentially provide a signature to look for evidence of "airbursts" in the geological record.

Wide area

The results were the subject of a presentation at the Lunar and Planetary Science Conference (LPSC) in The Woodlands, Texas. A layer of extraterrestrial dust has been found in both the Dome C and Dome Fuji ice cores from Antarctica. The dust in both cores is dated to about 481,000 years ago - and is therefore likely to derive from the same event.

The team, comprising Luigi Folco and Matthias van Ginneken from the University of Siena, Italy, and Phil Bland from Imperial College London, UK, now conclude that the Dome C and Dome Fuji dust layers are also paired with debris from the Transantarctic Mountains.

They point to strong similarities in the texture and composition of the debris found in the ice cores and that found in the granite. However, the sites are more than 2,900km apart. For cosmic debris to be spread over such a wide area, the researchers propose that an airburst is the most likely explanation. They estimate that it could have been caused by an object weighing 100,000 tonnes. "We've got similar material spread over a very large area. It's difficult to do that with any other mechanism," said co-author Dr Bland.

The Tunguska impact was caused by a space rock some tens of metres across that detonated 5-10km above the ground. The blast flattened some 2,000 sq km of Siberian forest, knocking people to the ground about 60km from the epicentre.

Airbursts on the scale of the Tunguska event are thought to occur every 500-1,000 years on Earth. This figure is based on computer modelling by Dr Bland and his colleagues. These results are consistent with an analysis of airbursts in the atmosphere gathered by US Department of Defense satellites from the 1960s onwards.

"These events are tricky to spot after they happen. If you go to Tunguska now, you've really got your work cut out trying to find any trace of that event - and that was 1908," Dr Bland told BBC News.

"What makes [the] work so exciting is that it may give us a way of spotting these events in the geological record. If these spherules are the signature, we know what to look for in future."

Organic pesticide doubles up as worm killer

* 11:09 04 March 2010 **by Peter Aldhous**

A common organic pesticide could do double duty as a cure for intestinal worms, and drag hundreds of millions of people out of poverty – provided cash can be found for human trials.

More than 1 billion people, almost all of them living below the World Bank's poverty line of $1.25 a day, are plagued by nematodes. While the worms don't usually kill, they stunt growth, cause anaemia and impair cognitive development. All this helps to "trap the 'bottom billion' in poverty", says Peter Hotez, a specialist in tropical diseases at George Washington University in Washington DC. Existing treatments don't work well on all types of worms – and resistance is emerging.

Now Raffi Aroian at the University of California, San Diego, and colleagues have shown that the protein Cry5B, produced by the bacterium Bacillus thuringiensis and used as a crop pesticide, could act as an effective drug. An oral dose cleared around 70 per cent of the worms from infected mice.

Acid protection

Molecule for molecule, Cry5B is about three times as effective as tribendimidine, the other leading drug in development. And Aroian is confident of obtaining better results still.

Cry5B is largely broken down in the stomach before reaching the intestine, so his team is now working with SRI International of Menlo Park, California, to develop coatings to protect the drug from stomach acids and get higher doses to the intestine where the worms live.

The protein is known to be safe – it is one of the few pesticides used by organic farmers. The main obstacle is a dearth of funding to push the drug through human trials and begin mass treatment in the world's poorest countries. "If we don't get money this year, we will have to stop the project," Aroian warns.

Even the Drugs for Neglected Diseases initiative, launched by Médicines Sans Frontières and other partners in 2003, has not yet made intestinal worms a priority. Instead, it is concentrating on killers including malaria and sleeping sickness. "Somebody's got to step into this space," says Hotez.

Journal Reference: PLoS Neglected Tropical Diseases, DOI: 10.1371/journal.pntd.0000614.t002

Drug flop is blow to immune theory of dementia

Ewen Callaway, reporter

A hay fever medicine that showed early promise as a treatment for Alzheimer's disease does nothing to stave off dementia, a large clinical trial concludes. The results are a blow to the start-up that manufactures the drug, an antihistamine called Dimebon, and its partner Pfizer: shares of the start-up, called Medivation, were down two-thirds on Wednesday, according to The New York Times.

But the failure also calls into question whether other anti-inflammatory drugs will work, and whether the disease is caused by a dysfunctional immune system, a theory that had been gaining traction recently.

A previous trial of Dimebon showed that it improves cognitive function in patients. But how the drug worked was never clear, The New York Times reports.

Now Pfizer has announced the results of a phase III trial of 598 people with mild to moderate Alzheimer's. The company found that there was no difference in cognitive function between people with Alzheimer's who took the drug, compared with people who received a placebo.

Last year, we described how increasing evidence is suggesting that immune dysfunction could be an underlying cause of Alzheimer's disease, not just the protein plaques and tangles that build up in the brains of patients:

"This could help steer Alzheimer's research towards drugs that maintain the health of immune and vascular systems, while prevention strategies might include eating a low-fat, vegetable-rich diet and exercising."

Maybe so, but according to the Fisher Center for Alzheimer's Research Foundation, clinical studies on prescription and non-prescription anti-inflammatory drugs have returned decidedly mixed results.

The inflammation theory isn't dead yet. According to the Alzheimer Research Forum, clinical trials for several immune-dampening medicines are still under way. But the latest Dimebon results make these trials all the more interesting.

30 years later, what killed the dinosaurs is revisited

Scripps researcher among dozens making the case with new evidence that an asteroid impact caused a mass extinction 65.5 million years ago

Scripps Institution of Oceanography, UC San Diego, paleoceanographer Richard Norris is one of 41 scientists presenting evidence that an asteroid impact really did kill off dinosaurs and myriad other organisms 30 years after the theory was first proposed.

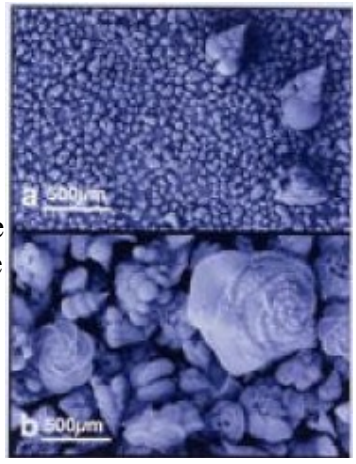
The researchers are authors of a review paper being released Friday in the journal Science that represents a new salvo in an ongoing controversy over the cause of the mass extinction. Norris' contribution to the paper was evidence in seafloor sediment records that indicate how deep-sea life was profoundly reshaped by the impact.

"The story is a lot stronger now than 30 years ago, when it was admittedly a little more speculative," said Norris. "Since 1980, we have accumulated an overwhelming amount of evidence that there was an impact. We also think the evidence is overwhelming that there was a mass extinction as a direct result of this event."

An asteroid impact 65.5 million years ago left a clear band between light colored Cretaceous sediment (left) and dark-colored, Paleocene sediment (right) recovered from the seafloor off South America. The abrupt shift in sediment color that reflects the instantaneous drop in ocean biological productivity, fossil numbers, and species. **Scripps Institution of Oceanography, UC San Diego**

In that year, father and son researchers Luis and Walter Alvarez first proposed the notion that an asteroid impact killed off the dinosaurs. They had discovered that high levels of iridium, an element rare on Earth but common on extraterrestrial objects like meteors, were uniformly present in sedimentary samples that could be dated back to the extinction event, which marked the transition between two geologic periods.

At the time, they did not know where on Earth that impact might have taken place. It would be another 11 years before researchers Alan Hildebrand and Glen Penfield suggested that a crater left behind by an asteroid impact was buried on the Yucatan peninsula. With the crater nearly 200 kilometers (125 miles) in diameter, the impact was one large enough to have caused the mass extinction in agreement with the Alvarez hypothesis.



The force of the impact itself - there is evidence of giant earthquakes and tsunami waves more than 1,000 feet tall being generated in the immediate aftermath - and the following profound atmospheric changes combined to make the planet uninhabitable for between 40 and 70 percent of all life forms on Earth.

But rival explanations, though outside the mainstream, have continued to proliferate in high-profile fashion. One theory that has gained widespread attention attributes the mass extinction to a volcanic event in India that took place at roughly the same time as the impact. Another faction of researchers acknowledges that the asteroid did strike but that its effects were not enough to cause the mass extinction.

The sizes of deep sea foraminifera fossils from just after the impact (a) and immediately before the impact. The scale bar in both pictures is 500 microns (half a millimeter). **Scripps Institution of Oceanography, UC San Diego**

Norris notes that an inspection of ancient layers of seafloor sediment around the world show a clear record of the event contained in a red or green band composed of materials ejected from the blast. These include pieces of rock like those on the Yucatan, glassy droplets that represent melted rock, microscopic diamonds made under the very high pressures produced by the impact and meteoric debris.

"There are also monster submarine landslides along the entire East Coast of the U.S. from the massive earthquake triggered by the impact," he said.

Norris points to several pieces of evidence from the deep sea that support a tight link between the impact and the mass extinction. In most places in the deep ocean, the impact debris layer is associated with an abrupt decrease in the size of fossils - the appearance of a dwarfed "disaster" fauna. Abrupt environmental changes throughout history such as the impact tend to favor smaller organisms that have more rapid lifecycles and fewer

resource needs than larger organisms. Biological productivity plummets in many parts of the oceans immediately after the impact. The drop in productivity is partly reflected by a change in the color of deep-sea sediments - from creamy white to brown or grey - as light-colored fossil shells abruptly decreased in number.

Individually, the decrease in fossil size, the appearance of a "disaster fauna" and the plummet in ocean productivity are unusual, and together with an impact debris layer, are unique in the deep-sea sediment record.

"This is not a 'smoking gun,'" said Norris, "it's a 'smoking cannon.'"

Researchers find further evidence linking Epstein-Barr virus and risk of multiple sclerosis

First long-term study among individuals not infected with EBV suggests EBV infection likely to be a cause of MS, not a consequence

Boston, MA – Researchers from the Harvard School of Public Health, Walter Reed Army Institute of Research, and a team of collaborators have observed for the first time that the risk of multiple sclerosis (MS) increases by many folds following infection with the Epstein-Barr virus (EBV). This finding implicates EBV as a contributory cause to multiple sclerosis. The study appears in an advance online edition of the journal Annals of Neurology and will appear in a later print edition.

Hundred of thousands of individuals not infected with EBV were followed up for several years through repeated blood samples collections. Researchers were then able to determine the time when individuals developed an EBV infection and its relation to MS onset. "The recruitment of individuals before they were infected with EBV and following up with them for several years is the critical methodological aspect that makes this study qualitatively different from all previous work," said Alberto Ascherio, senior author of the study and professor of epidemiology and nutrition at Harvard School of Public Health and professor of medicine at Harvard Medical School.

MS is a chronic degenerative disease of the central nervous system. Women are more likely than men to get the disease and it is the most common neurologically disabling disease in young adults. Although genetic predisposition plays an important role in determining susceptibility, past studies have shown that environmental factors are equally important.

EBV is a herpes virus and one of the most common human viruses worldwide. Infection in early childhood is common and usually asymptomatic. Late age at infection, however, often causes infectious mononucleosis. In the U.S., upwards of 95% of adults are infected with the virus, but free of symptoms. EBV has been associated with some types of cancer and can cause serious complications when the immune system is suppressed, for example, in transplant recipients. There is no effective treatment for EBV.

This is the first study based on the longitudinal follow-up of several thousand individuals who were not infected with EBV at the time of recruitment. The study population was made up of active-duty US Army, Navy, and Marines personnel who have at least one blood sample in the Department of Defense Serum Repository. The electronic databases of the Physical Disability Agencies of the US Army and Navy were then searched for individuals whose records indicated a possible diagnosis of MS reported between 1992 and 2004.

The researchers selected 305 individuals diagnosed with MS and who had blood specimens collected before the date of their diagnosis. Two controls for each case were then selected from the serum database and matched by branch of service, sex, date of blood collection, and age at time of blood collection.

The study found that MS risk is extremely low among individuals not infected with EBV, but it increases sharply in the same individuals following EBV infection.

"The observation that MS occurred only after EBV is a big step forward," said Alberto Ascherio. "Until now we knew that virtually all MS patients are infected with EBV, but we could not exclude two non-causal explanations for this finding: that EBV infection is a consequence rather than a cause of MS, and that individuals who are EBV negative could be genetically resistant to MS. Both of these explanations are inconsistent with the present findings," said Ascherio.

"The evidence is now sufficiently compelling to justify the allocation of more resources to the development of interventions targeting EBV infection, or the immune response to EBV infection, as these may contribute to MS prevention," he said.

The study was supported by a grant from the National Institute of Neurological Disorders and Stroke.

"Primary Infection with the Epstein-Barr Virus and Risk of Multiple Sclerosis," Lynn I. Levin, Kassandra L. Munger, Eilis J. O'Reilly, Kerstin I. Falk, Alberto Ascherio, Annals of Neurology, online January 20, 2010

For a long life, smile like you mean it

* 13:26 05 March 2010 **by Ewen Callaway**

If you want to live to a grand old age, then smile – and make sure you mean it. Pro baseball players in the 1950s who genuinely beamed in their official photographs tended to outlive more sullen-looking sportsmen and those who put on fake smiles.

Players from the US major league with honest grins lived an average of seven years longer than players who didn't smile for the camera and five years longer than players who smiled unconvincingly, conclude Ernest Abel and Michael Kruger at Wayne State University in Detroit, Michigan.

It's known that happy people tend to be healthy too. Kruger and Abel wondered whether this relationship would be reflected in the smiles and longevity of baseball players.

Genuine smiles are known as Duchenne smiles after the 19th-century neurologist who defined them in detail. They engage muscles both near the corners of the mouth and around the eyes – the zygomatic major and the orbicularis oculi respectively. Fake, "non-Duchenne" smiles exercise only mouth muscles.

Duchenne or not Duchenne? (Image: Archive Holdings Inc./Getty)

Smile survival

With training, these muscles are easy to recognise in photographs. So Abel and four colleagues who were not aware of what the study was investigating, but were trained to analyse smiles, looked at vintage photographs of 230 major leaguers who played in the 1952 season. The researchers classified them as non-smilers, Duchenne smilers or non-Duchenne smilers. Then they looked up the lifespans of the 184 players who had already died.

They found that out of the dead players, Duchenne smilers had tended to live the longest, followed by non-Duchenne smilers. And after accounting for other factors that tend to predispose people to longevity, such as a university education and good health, they found an even firmer link between strength of smile and length of life.

People who didn't smile had just a 50 per cent chance of surviving to 80, all other things being equal, whereas those with Duchenne smiles had about a 70 per cent chance of surviving to this age. Overall, 35 per cent of the differences in lifespan correlated with smile intensity.

Abel and Kruger conclude that people who smile genuinely in photographs "may be basically happier than those with less intense smiles", making them more likely to experience the health benefits of happiness, which has been linked with lower levels of stress hormones and a protein implicated in heart disease.

Conscientious smiler

Is a smile in a photograph really a good measure of overall happiness? Not necessarily, but the results don't come out of left field, say Wallace Friesen and Deborah Danner, psychologists at Sanders Brown Center on Aging in Lexington, Kentucky: previous studies have found links between genuine smiles in photographs and overall happiness and marital satisfaction.

Matt Hertenstein, a psychologist at DePauw University in Greencastle, Indiana, adds that smiling in a photo may not simply reflect happiness: people who are conscientious might be more willing to heed a photographer's request to "say cheese", and conscientiousness has also been linked to longevity.

Alternatively, players who smiled could be more sociable than others. "A long line of work indicates that greater and deeper social networks increase well-being and longevity in life," he says.

Increased conscientiousness and stronger social networks could also explain why non-Duchenne smilers – those who made an effort to smile, albeit unconvincingly – lived longer than those who didn't smile at all.

Journal reference: Psychological Science, DOI: 10.1177/0956797610363775

Scientists find signs of 'snowball Earth' amidst early animal evolution

New evidence hints at global glaciation 716.5 million years ago

Geologists have found evidence that sea ice extended to the equator 716.5 million years ago, bringing new precision to a "snowball Earth" event long suspected to have taken place around that time.

Funded by the National Science Foundation (NSF) and led by scientists at Harvard University, the team reports on its work this week in the journal Science.

The new findings--based on an analysis of ancient tropical rocks that are now found in remote northwestern Canada--bolster the theory that our planet has, at times in the past, been ice-covered at all latitudes.

"This is the first time that the Sturtian glaciation has been shown to have occurred at tropical latitudes, providing direct evidence that this particular glaciation was a 'snowball Earth' event," says lead author Francis Macdonald, a geologist at Harvard University.

"Our data also suggest that the Sturtian glaciation lasted a minimum of five million years."

According to Enriqueta Barrera, program director in NSF's Division of Earth Sciences, which supported the research, the Sturtian glaciation, along with the Marinoan glaciation right after it, are the greatest ice ages

known to have taken place on Earth. "Ice may have covered the entire planet then," says Barrera, "turning it into a 'snowball Earth.'"

The survival of eukaryotes--life forms other than microbes such as bacteria--throughout this period suggests that sunlight and surface water remained available somewhere on Earth's surface. The earliest animals arose at roughly the same time.

Even in a snowball Earth, Macdonald says, there would be temperature gradients, and it is likely that sea ice would be dynamic: flowing, thinning and forming local patches of open water, providing refuge for life.

"The fossil record suggests that all of the major eukaryotic groups, with the possible exception of animals, existed before the Sturtian glaciation," Macdonald says. "The questions that arise from this are: If a snowball Earth existed, how did these eukaryotes survive? Did the Sturtian snowball Earth stimulate evolution and the origin of animals?"

"From an evolutionary perspective," he adds, "it's not always a bad thing for life on Earth to face severe stress."

The rocks Macdonald and his colleagues analyzed in Canada's Yukon Territory showed glacial deposits and other signs of glaciation, such as striated clasts, ice-rafted debris, and deformation of soft sediments.

The scientists were able to determine, based on the magnetism and composition of these rocks, that 716.5 million years ago the rocks were located at sea-level in the tropics, at about 10 degrees latitude.

"Climate modeling has long predicted that if sea ice were ever to develop within 30 degrees latitude of the equator, the whole ocean would rapidly freeze over," Macdonald says. "So our result implies quite strongly that ice would have been found at all latitudes during the Sturtian glaciation."

Scientists don't know exactly what caused this glaciation or what ended it, but Macdonald says its age of 716.5 million years closely matches the age of a large igneous province--made up of rocks formed by magma that has cooled--stretching more than 1,500 kilometers (932 miles) from Alaska to Ellesmere Island in far northeastern Canada.

This coincidence could mean the glaciation was either precipitated or terminated by volcanic activity.

Macdonald's co-authors on the Science paper are Phoebe A. Cohen, David T. Johnston, and Daniel P. Schrag at Harvard; Mark D. Schmitz and James L. Crowley of Boise State University; Charles F. Roots of the Geological Survey of Canada; David S. Jones of Washington University in St. Louis; Adam C. Maloof of Princeton University; and Justin V. Strauss.

Virus infections may be contributing factor in onset of gluten intolerance

Recent research findings indicate a possible connection between virus infections, the immune system and the onset of gluten intolerance, also known as coeliac disease. A research project in the Academy of Finland's Research Programme on Nutrition, Food and Health (ELVIRA) has brought new knowledge on the hereditary nature of gluten intolerance and identified genes that carry a higher risk of developing the condition. Research has shown that the genes in question are closely linked with the human immune system and the occurrence of inflammations, rather than being connected with the actual breakdown of gluten in the digestive tract.

"Some of the genes we have identified are linked with human immune defence against viruses. This may indicate that virus infections may be connected in some way with the onset of gluten intolerance," says Academy Research Fellow Päivi Saavalainen, who has conducted research into the hereditary risk factors for gluten intolerance.

Saavalainen explains that the genes that predispose people to gluten intolerance are very widespread in the population and, as a result, they are only a minor part of the explanation for the way in which gluten intolerance is inherited. However, the knowledge of the genes behind gluten intolerance is valuable in itself, as it helps researchers explore the reasons behind gluten intolerance, which in turn builds potential for developing new treatments and preventive methods. This is essential, because the condition is often relatively symptom-free, yet it can have serious complications unless treated.

Researchers have localised the risk genes by using data on patients and on entire families. The material in the Finnish study is part of a very extensive study of thousands of people with gluten intolerance and control groups in nine different populations. The research will be published in a coming issue of Nature Genetics.

Research into hereditary conditions has made great progress over the past few years. Gene researchers now face their next challenge, as a closer analysis is now needed of the risk factors in the genes that predispose people to gluten intolerance. It is important to discover how they impact on gene function and what part they play in the onset of gluten intolerance.

Gluten intolerance is an autoimmune reaction in the small intestine. Roughly one in a hundred Finns suffer from this condition. The gluten that occurs naturally in grains such as wheat, barley and rye causes damage to the intestinal villi, problems with nutrient absorption and potentially other problems too. Gluten intolerance is an inherited predisposition, and nearly all sufferers carry the genes that play a key part in the onset of the condition. The only known effective treatment is a lifelong gluten-free diet.

Why it is important for media articles to link to scientific papers

Posted on: March 3, 2010 1:09 AM, **by Coturnix**

You may be aware that, as of recently, one of my tasks at work is to monitor media coverage of PLoS ONE articles. This is necessary for our own archives and monthly/annual reports, but also so I could highlight some of the best media coverage on the everyONE blog for everyone to see. As PLoS ONE publishes a large number of articles every week, we presume that many of you would appreciate getting your attention drawn to that subset of articles that the media found most interesting.

So, for example, as I missed last week due to my trip to AAAS, I posted a two-week summary of media coverage this Monday. And that took far more time and effort (and some silent cursing) than one would expect. Why?

I don't think I am a slouch at googling stuff. Some people joke that the entire Internet passes through my brain before it goes to the final audience. After all, I have been monitoring the Web for mentions of 'PLoS' and 'Public Library of Science' on blogs, Twitter, FriendFeed, Facebook and elsewhere for a few years now. If I don't catch a mention within minutes of it being posted, you can bet one of my many online friends/followers/subscribers is bound to quickly let me know by e-mail or Direct Messaging somewhere. If someone says something nice about PLoS, I am quick to post a ThankYou note. If someone asks a question, I try to answer or to connect the person with the appropriate member of the PLoS staff. If someone is publicly musing about submitting a manuscript to one of our journals, I am right there to give encouragement. If someone makes a factual error, I gently correct it. It is very, very rare that I need to raise the Immense Online Armies because someone is wrong on the Internet ;-)

So, why is it difficult then to compile a collection of weekly media coverage? Let me walk you through the process....

First, as you probably already know, PLoS makes no distinction between Old and New media. We have bloggers on our press list who apply/sign-up in the same way and abide by the same rules as traditional journalists (and, unlike mainstream media, bloggers NEVER break embargos, not once in the past three years since we started adding bloggers to our press list). For the kind of coverage we prefer to see, we point bloggers to the ResearchBlogging.org criteria. In return, bloggers can send trackbacks to our articles, their work is showcased side-by-side with the traditional outlets in our weekly posts, they can be discovered via Google Blogsearch, Postgenomic and ResearchBlogging.org links directly from each article, and one blogger per month wins a t-shirt and special recognition.

So, I start with blog posts first. The first thing I do is take a look at ResearchBlogging.org. Those are the best of the best posts - not merely mentioning our articles, but adding analysis, commentary, critique, context and additional information. How do I find them? I just search the site for the phrase 'journal.pone'. That search brings up every single post that mentions a PLoS ONE article because that phrase is a part of every possible form of the URL of the article (including the shortest one, which includes just the DOI). If a post links to our article (and that is the only way to get aggregated on ResearchBlogging.org) I will find it this way. Needless to say, this process takes just a few minutes per week.

Knowing that there are some good blogs out there that are not registered at ResearchBlogging.org (which is strange and unfathomable why - RB.org is a 'stamp-of-approval' place for science blogs recognized by the outside world of journals and media, as well as a nice way to get extra recognition and traffic, and even awards), I then repeat the same search - for 'journal.pone' - on Google Blogsearch. This may bring up a few more posts that I did not catch yet. Occasionally, some of these are good. Another couple of minutes. Blogs are now done. Move on to traditional media....

And this is where the Hell starts. Try searching Google News for 'journal.pone'...?! All I get are a couple of prominent blogs that I have already counted, e.g., those blogs that are listed by Google News (scienceblogs.com blogs, Ars Technica, Wired blogs, etc.). Where are the others?

The problem is, nobody in the mainstream media links to papers.

So I have to search for PLoS and for Public Library Of Science and then figure out which ones are covering specifically PLoS ONE articles (sometimes they don't specify, sometimes they name the wrong journal - last week an article on PLoS Current-Influenza was reported to be in PLoS ONE by a number of outlets copying the error from each other). Then I have to search for keywords for individual articles I suspect may have received some coverage. Last week, for example, I searched for "swallows+antioxidants" and "St. Birgitta", among many others. This lasts for hours! And at the end I am still not 100% sure I caught everything. How frustrating!

Not just is there a big difference in time and effort spent between finding blog posts and finding media articles, but there is an even bigger disparity when one considers what results come out of these searches. I have been doing this for a month now. I expected that there would be poor blog posts and poor media articles, that

there would be good blog posts and good media articles, and that there would occasionally be some excellent blog posts and excellent media articles. So far, that is true.... except I have yet to discover an excellent media article. As a rule, the very best coverage of every paper in the past month was done by a blogger or two or three. Then there are some other, good pieces of coverage in both the New and Old media, and then there are some really bad pieces in both realms as well (not all blog posts I count here are really bad - they may just be too detailed, technical and dry for lay audience because the blogger is intentionally targeting scientific peers as audience, which is fair thing to acknowledge).

So, every week, it takes me a few minutes to find the very best coverage (which is on blogs, usually those aggregated on ResearchBlogging.org). And then I spend hours looking for remnants, in the traditional media, which turn out to be so-so, some OK, some not so good, some horrible. If I wasn't paid to do this, I would not do it - it cannot be good for my long-term mental health.

The resistance to post links is an atavism, a remnant of an old age before the Web. I know (because I asked many times) many good science journalists keep trying to add links, but the editors say No. The traditional media has still not caught on to the Ethic of the Link, which is an essential aspect of ethics of online communication.

I can think, off the top of my head, of three good reasons why everyone who publishes online should include a link to the scientific paper described in the article (just post the DOI link that comes with the press release if you are on the press list - if it does not resolve immediately, it is not your fault, you can always blame the journals for being slow on it - though this should never happen with PLoS articles):

Reason One: I will not go crazy every week. I am assuming that every scientific publisher has people on the staff whose task is to monitor media coverage and each one of these people is cussing and cursing YOU, the Media, every day. Try to make friends with people who provide you with source material on a regular basis.

Reason Two: Media coverage is one of the many elements of article-level metrics. Furthermore, links from the media affect the number of views and downloads of the article, and those are also elements of article-level metrics. Number of views/downloads then, in the future, affects the number of citations the work gets which is also and element of article-level metrics. Thus omitting the link skewes the ability of readers and observers to evaluate the papers properly.

The current ecosystem of science communication has a scientific paper at its core, additions to the paper (e.g., notes, comments and ratings, as well as Supplemental materials, videos posted on Scivee.tv, etc) as a shell, and incoming and outgoing links - trackbacks, cited papers, citing papers, links to other papers in the same Collection, links to other papers with the same keywords, and yes, incoming links from the media - as connections building a network: the entire inter-connected ecosystem of scientific knowledge.

By not linking to scientific papers, traditional media is keeping itself outside of the entire ecosystem of empirical knowledge. By doing this, the traditional media is fast making itself irrelevant.

Reason Three: if an article in the media discusses a scientific study, that scientific paper is the source material for the article. If the link is missing, this is an automatic red flag for the readers. What is the journalist hiding? Why is the article making it difficult for readers to fact-check the journalist? Something does not smell good if the link is not provided (or worse, it is impossible to figure out even who are the authors and in which journal did they publish - yes, that is more common than you think).

The instant and automatic response of the readers is mistrust. Every time you fail to link to the paper, you further erode whatever trust and reputation you still may have with the audience. You soon cease to be a legitimate source of information. Sure, most readers will not go hunting for the paper to read it in order to fact-check you. But two or three will, and they will let everyone else know if your article is trustworthy or not, either in the comments under the article on your own site, or on their blogs which will be quickly picked up by Google (remember: Google loves blogs).

So please, media types, hurry up and catch up with the world. The 21st century is already a decade in - you really need to do some very fast learning. Right now. Or you'll go extinct in a nanosecond. And despite my reputation, I never said that I'd consider that result to be a Good Thing. We are in this together, you just need to do your part. To begin with, start linking.

No Easy Answers to Echinacea's Evolution

Every summer, gardens across the United States are visited by goldfinches feasting on seeds produced by the popular perennial Echinacea. But birds aren't the only ones that profit from these pretty coneflowers. According to estimates by Nutrition Business Journal, U.S. consumers looking for botanical remedies spent $126 million on Echinacea products in 2007. These products may modulate the human immune system, but they are also being studied for related effects on infections, inflammation, and pain receptors.

Only a few Echinacea species—E. purpurea, E. angustifolia, and E. pallida—are currently cultivated as remedies, and plant breeders would like to know whether other types also possess commercially useful traits. But first they need to know how many distinct Echinacea species there are. Previous studies have put the number between four and nine species, depending on classification criteria.

Mark Widrlechner, a horticulturist at the ARS North Central Regional Plant Introduction Station (NCRPIS) in Ames, Iowa, has joined an effort to solve this puzzle. Working with a team in Jonathan Wendel's lab at Iowa State University, Widrlechner selected 40 diverse Echinacea populations for DNA analysis from the many populations conserved at the NCRPIS.

Most of these Echinacea populations were found to have a remarkable range of genetic diversity. This complicated efforts to explain how so much diversity among different species could have evolved from a common ancestor.

"What we had was really, really hard to sort out," Widrlechner admits.

***An ARS scientist is studying the jumbled genetics of Echinacea, the coneflower known for its blossoms-and its potential for treating infections, inflammation, and other human ailments*. Photo courtesy of David Cappaert, Michigan State University, Bugwood.org.**

But the team has been able to make some sense out of the genetic jumble. For instance, DNA analysis suggested that when much of North America was covered with glaciers, Echinacea found southern refuges on both sides of the Mississippi River. But when the glaciers receded after thousands of years, the groups came together as they moved northward and began to hybridize, which might have blurred previous genetic distinctions.

Since DNA analysis did not provide conclusive results, Lankun Wu, from Eve Syrkin Wurtele's lab at Iowa State, focused on analyzing the same populations for chemical differences in root metabolites. These metabolites, which are often essential for survival and propagation, can vary widely among species and may play roles in human-health effects.

Using this approach, researchers were able to identify clear distinctions among all 40 populations. These distinctions were organized into three composite profiles that accounted for almost 95 percent of the metabolite variation among the populations.

Additional analysis indicated that the populations grouped together in ways that aligned well with earlier Echinacea species assignments that were based on plant morphology, supporting nine rather than only four distinct species. But Widrlechner says the research isn't close to a payoff for commercial producers—yet.

"Even though the metabolite study has given us some good species definitions, we still need to follow up with more genetic studies," Widrlechner says. "It's important to find the traits that may be medicinally beneficial."—By Ann Perry, Agricultural Research Service Information Staff.

It's who you kill that matters, according to new research

University of Denver sociology professor studied 504 cases in Harris County, Texas

A defendant is much more likely to be sentenced to death if he or she kills a "high-status" victim, according to new research by Scott Phillips, associate professor of sociology and criminology at the University of Denver (DU).

According to his research published in Law and Society Review, (43-4:807-837), the probability of being sentenced to death is much greater if a defendant kills a white or Hispanic victim who is married with a clean criminal record and a college degree, as opposed to a black or Asian victim who is single with a prior criminal record and no college degree.

Recent discussions of the death penalty tend to focus on innocence and cost. Phillips' research says that arbitrariness has long been a concern. Phillips research is based on 504 death penalty cases that occurred in Harris County, Texas between 1992 and 1999.

"The concept of arbitrariness suggests that the relevant legal facts of a capital case cannot fully explain the outcome: irrelevant social facts also shape the ultimate state sanction" Phillips says. "In the capital of capital punishment, death is more apt to be sought and imposed on behalf of high status victims. Some victims matter more than others."

Drawing on the same data, Phillips's previous research demonstrated that black defendants were more likely to be sentenced to death than white defendants in Houston. The racial disparities revealed in the prior paper become even more acute after accounting for victim social status – black defendants were more apt to be sentenced to death despite being less apt to kill high status victims.

The combined results of the two papers call into question the meaning of justice.

"Should justice be defined according to the punishment a particular defendant deserves?" Phillips asks, "Or should justice be defined according to whether the judicial system can hand out lethal punishment in an even-handed manner? The question strikes at the heart of the death penalty debate."

Major depression more than doubles risk of dementia among adults with diabetes

How diabetes and depression interact to lead to dementia is not yet clear

Adults who have both diabetes and major depression are more than twice as likely to develop dementia, compared to adults with diabetes only, according to a study published in the recent Journal of General Internal Medicine. Dementia is the progressive decline of thinking and reasoning abilities. These can include memory loss, difficulty with basic math, wandering, living in the past, personality changes, and not recognizing familiar people.

"Diabetes alone has shown to be a risk factor for dementia, as has major depression by itself," noted the lead author of the study, Dr. Wayne Katon, University of Washington (UW) professor of psychiatry and behavioral sciences. Also on the study team were researchers from the Group Health Research Institute in Seattle and the Veterans Affairs (VA) Puget Sound Health Care System, as well as UW researchers in medicine and in epidemiology.

Various other population studies, Katon and the other authors noted, have shown that the risk of Alzheimer's disease, vascular dementia, and other types of dementia is from 40 percent to 100 percent higher in people with diabetes, compared to people without diabetes. A history of depression more than doubles the subsequent risk of Alzheimer's disease and other forms of dementia in the general population. "We wanted to determine the effects of both conditions – diabetes and major depression--occurring together," Katon said. "Our analysis suggests that major depression more than doubles the risk of dementia in adults with diabetes."

The research team on this project, which is part of the Pathways Epidemiological Follow-Up Study, tracked the outcomes of adults from the Group Health Cooperative's diabetes registry who agreed to participate. They were patients from nine Puget Sound area primary-care clinics in western Washington state. The clinics were chosen for their socioeconomic and racial/ethnic diversity and were demographically similar to the area's population. Initial enrollment of patients took place between 2000 and 2002, and the patients were studied for five years. Patients already diagnosed with dementia were excluded from the study.

Over the five-year period, 36 of 455, or 7.9 percent, of the diabetes patients with major depression were diagnosed with dementia. Among the 3,382 patients with diabetes alone, 163 or 4.8 percent developed dementia.

The researchers calculated that major depression with diabetes was associated with a 2.7-fold increase of dementia, compared to diabetes alone. Because the onset of dementia can sometimes be marked by depression, the researchers also adjusted their hazard model to exclude patients who developed dementia in the first two years after their depression diagnosis. The team's previous findings from earlier studies showed that depression increases the mortality rate among people with diabetes, as well as the rate of complications such as heart, blood vessel, kidney and vision problems.

The exact manner in which diabetes and depression interact to result in poorer outcomes is not certain. Some studies suggest that a genetic marker for dementia is associated with a faster cognitive decline. Depression may also raise the risk of dementia, the authors noted, because of biological abnormalities linked to this affective illness, including high levels of the stress hormone cortisol, poor regulation in the hypothalamus-pituitary system, or autonomic nervous system problems that can affect heart rate, blood clotting, and inflammatory responses.

Depression, they added, might also raise the risk of dementia because of behaviors common in the condition, such as smoking, over-eating, lack of exercise, and difficulty in adhering to medication and treatment regimens. In the current study, patients with both diabetes and major depression were more likely to be female, single, smokers, physically inactive, and treated with insulin. They also had more diabetes complications and a higher body mass index, a ratio calculated from height and weight. However, these differences were controlled for in the analysis and depression remained an important risk factor.

Diabetes, the authors noted, is a risk factor for dementia because of blood vessel problems and also may accelerate the decline of Alzheimer's disease. Many factors linked to diabetes might also increase the odds of developing dementia, including tissue damage from high blood sugar levels, episodes of low blood sugar and insulin resistance.

Depression is common among people who have diabetes. Until more research is available on the exact mechanisms behind the links between depression, diabetes, and dementia, the researchers say, "It seems prudent for clinicians to add effective screening and treatment for depression to other preventive measures such

as exercise, weight control, and blood sugar control to protect against the development of cognitive deficits in patients with diabetes."

In addition to Katon, members of the research team were Elizabeth H.B. Lin, Evette Ludman, Carolyn Rutter, Malia Oliver and Michael Von Korff, all from the Group Health Research Institute; Lisa Williams from the UW Department of Medicine and the Epidemiologic Research and Information Center at the VA Puget Sound Health Care System; Paul Ciechanowski from the UW Department of Psychiatry and Behavioral Sciences; Susan R. Heckbert, from the Department of Epidemiology in the UW School of Public Health; and Paul K. Krane from the UW Department of Medicine.

Grants from the National Institute of Mental Health, National Institutes of Health, supported the study.

Most early-stage breast cancer patients may not need radiation after mastectomy

No significant increased risk of recurrence for women with spread to 1 lymph node, compared to others without metastasis

St. Louis, MO - Breast cancer patients with early stage disease that has spread to only one lymph node may not benefit from radiation after mastectomy, because of the low present-day risk of recurrence following modern surgery and systemic therapy, a finding that could one day change the course of treatment for thousands of women diagnosed each year, according to researchers at The University of Texas M. D. Anderson Cancer.

The research, presented today in the plenary session of the Society of Surgical Oncology Annual Cancer Symposium, showed that stage I and II patients without spread to axillary lymph nodes or with 1-3 lymph nodes with metastasis who received surgery and adjuvant chemotherapy without radiation to the chestwall post-mastectomy had a low overall risk of locoregional recurrences (LRR).

According to Henry Kuerer, M.D., Ph.D., professor and Training Program Director in M. D. Anderson's Department of Surgical Oncology, 90 percent of patients diagnosed with node-positive disease will present with three or fewer nodes. An estimated 47,000 women are diagnosed annually with breast cancer involving 1- 3 lymph nodes. Of those, 30,000 have only one lymph node involvement.

"There is currently no question that radiotherapy after mastectomy is effective at decreasing the chances of LRR and is indicated in breast cancer patients with lymph node spread in greater than four nodes and where the risk of LRR is higher than 10 to 15 percent. However, the need for post-mastectomy radiation in early stage breast cancer patients has been a topic of great debate within the cancer community for decades," explained Kuerer, the study's senior author.

In the 1990s, two landmark randomized trials demonstrated a survival benefit for early stage breast cancer patients with lymph node metastases who received the therapy post-mastectomy, explained Kuerer. Subsequently, in 2005, a meta-analysis of randomized clinical trials that were conducted in the 1960s to 1980s showed both a survival benefit, and a decreased risk of LRR for women with node positive breast cancer. These study findings shifted clinical practice: the National Comprehensive Cancer Network altered their medical guidelines in 2007 to suggest that stage I and II breast cancer patients with one to three lymph node metastases "strongly consider" radiation post-mastectomy.

"We have entered a new era of breast cancer diagnosis and treatment. Modern day advances in all modalities have been dramatic and, collaboratively, have had a significant impact on recurrence and survival. Given these advances, the goal of our study was to assess the present-day LRR risk in women who present with smaller breast tumors and metastases to fewer lymph nodes," said Kuerer.

Kuerer and his colleagues studied clinical and pathological factors from 1,022 stage I or II breast cancer patients who received a mastectomy at M. D. Anderson between 1997 and 2002. Of those women, 79 percent had no lymph node involvement, 26 percent had 1-3 positive lymph nodes, with the majority having just one positive node. None received post-mastectomy radiation and/or pre-operative chemotherapy; 77 percent received post-operative chemotherapy and/or hormonal therapy. The median age was 54 years and the median follow up time was 7.5 years.

The researchers found that there was no statistical difference in the 10-year risk of LRR in women without lymph node spread versus those with spread to one node - 2.1 percent to 3.3 percent, respectively.

The only independent risk factor for LRR was age; patients age 40 and younger, regardless of node involvement, were at significant increased risk for LRR.

"For these younger women, not less, but more treatment may be needed," said Rajna Sharma, M.D., a fellow in M. D. Anderson's Department of Surgical Oncology, who presented the findings.

"For the overwhelming majority of early-stage breast cancer patients treated with modern surgery and systemic therapies, LRR rates may be too low to justify routine use of post-mastectomy radiation," said Kuerer. "This research will provoke much discussion among those caring for women with early-stage breast disease. Replicating these findings should be a priority to ensure that patients only receive therapy that is medically necessary."

In addition to Kuerer and Sharma, other authors on the all-M.D. Anderson study include: Thomas A. Buchholz, M.D., professor, Department of Radiation Oncology; Funda Meric-Bernstam, M.D., professor, Kelly K. Hunt, M.D., professor, Isabelle Bedrosian, M.D., assistant professor, Gildy V. Babiera, M.D., associate professor, Anthony Lucci, M.D., associate professor, Rosa F. Hwang, M.D., assistant professor, Loren L. Rourke, MD., assistant professor, Elizabeth A. Mittendorf, M.D., assistant professor, all in the Department of Surgical Oncology; Steven J. Kronowitz, M.D., associate professor, Department of Plastic Surgery; 4 Savitri Krishnamurthy, M.D., professor, Department of Pathology; Ana M. Gonzalez-Angulo, M.D., associate professor, Department of Breast Medical Oncology; and Wei Qiao, Department of Biostatistics.

Gene site found for children's food allergy

Gene linked to eosinophilic esophagitis plays key role in inflammation

Pediatrics researchers have identified the first major gene location responsible for a severe, often painful type of food allergy called eosinophilic esophagitis (EoE). In this disease, which may cause weight loss, vomiting, heartburn and swallowing difficulties, a patient may be unable to eat a wide variety of foods.

After performing a genome-wide association study, the study team found EoE was linked to a region of chromosome 5 that includes two genes. The likely culprit is the gene TSLP, which has higher activity levels in children with EoE compared to healthy subjects. In addition, TSLP has been previously linked to allergic inflammatory diseases, such as asthma and the skin inflammation, atopic dermatitis.

"This gene is a plausible candidate because of its biological role in allergic inflammation," said study leader Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics at The Children's Hospital of Philadelphia. Hakonarson and colleagues collaborated with Marc E. Rothenberg, M.D., Ph.D., director of the Center for Eosinophilic Disorders at the Cincinnati Children's Hospital Medical Center.

The study appears online today in Nature Genetics.

Only recently recognized as a distinct condition, EoE, like other allergies, has been increasing over the past 20 years, and its reported incidence of one in 10,000 people may be an underestimate. The hallmark of EoE is swelling and inflammation in the esophagus, accompanied by high levels of immune cells called eosinophils. It can affect people of any age, but is more common among young men who have a history of other allergic diseases such as asthma and eczema. EoE is often first discovered in children with feeding difficulties and failure to thrive.

In the current study, the researchers performed a genome-wide analysis on 181 samples from the Cincinnati center, compared to nearly 2,000 healthy controls from The Children's Hospital of Philadelphia (CHOP). They then replicated the initial findings with additional DNA samples from EoE patients and controls at CHOP. The gene studies pointed to chromosome 5q22.1, which contains the TSLP gene. TLSP holds the genetic code to produce a cytokine, a specific signaling protein that regulates inflammatory responses occurring in allergic diseases.

Because children with EoE are often allergic to many foods, they may be limited to an elemental formula containing no large food proteins, to allow time for their symptoms to resolve. Physicians then perform tests to determine which foods a child can or cannot eat.

"Eosinophilic esophagitis is a highly allergic disease, and one that is rapidly expanding," said allergist Jonathan M. Spergel, M.D., a co-first author of the study, who sees large numbers of patients with EoE as director of the Center for Pediatric Eosinophilic Disorders at The Children's Hospital of Philadelphia. "This is the first genome-wide association study done on this disease, and now that we have elucidated a gene pathway, the hope is that physicians can eventually intervene in that pathway and discover a new treatment."

The National Institutes of Health provided funding support for this study, along with the Food Allergy Project, the Campaign Urging Research for Eosinophilic Disorders (CURED) Foundation, the American Partnership for Eosinophilic Disorders (APFED), The Children's Hospital of Philadelphia Chair's Institute, the Buckeye Foundation, and the Cotswold Foundation.
"Common variants at 5q22 associate with pediatric eosinophilic esophagitis," Nature Genetics, published online March 7, 2010. http://dx.doi.org/10.1038/ng.547

Ritalin boosts learning by increasing brain plasticity

Doctors treat millions of children with Ritalin every year to improve their ability to focus on tasks, but scientists now report that Ritalin also directly enhances the speed of learning.

In animal research, the scientists showed for the first time that Ritalin boosts both of these cognitive abilities by increasing the activity of the neurotransmitter dopamine deep inside the brain. Neurotransmitters are the chemical messengers neurons use to communicate with each other. They release the molecule, which then docks onto receptors of other neurons. The research demonstrated that one type of dopamine receptor aids the ability to focus, and another type improves the learning itself.

The scientists also established that Ritalin produces these effects by enhancing brain plasticity - strengthening communication between neurons where they meet at the synapse. Research in this field has accelerated as scientists have recognized that our brains can continue to form new connections - remain plastic - throughout life.

"Since we now know that Ritalin improves behavior through two specific types of neurotransmitter receptors, the finding could help in the development of better targeted drugs, with fewer side effects, to increase focus and learning," said Antonello Bonci, MD, principal investigator at the Ernest Gallo Clinic and Research Center and professor of neurology at UCSF. The Gallo Center is affiliated with the UCSF Department of Neurology.

Bonci is co-senior author of the paper, which will be published online in "Nature Neuroscience" on Sunday, March 7, 2010.

Bonci and his colleagues showed that Ritalin's therapeutic action takes place in a brain region called the amygdala, an almond-shaped cluster of neurons known to be critical for learning and emotional memory.

"We found that a dopamine receptor, known as the D2 receptor, controls the ability to stay focused on a task – the well-known benefit of Ritalin," said Patricia Janak, PhD, co-senior author on the paper. "But we also discovered that another dopamine receptor, D1, underlies learning efficiency."

Janak is a principal investigator at the Gallo Center and a UCSF associate professor of neurology. Lead author of the paper is Kay M. Tye, PhD, a postdoctoral scientist at the Gallo Center when the research was carried out.

The research assessed the ability of rats to learn that they could get a sugar water reward when they received a signal – a flash of light and a sound. The scientists compared the behavior of animals receiving Ritalin with those that did not receive it, and found those receiving Ritalin learned much better.

However, they also found that if they blocked the dopamine D1 receptors with drugs, Ritalin was unable to enhance learning. And if they blocked D2 receptors, Ritalin failed to improve focus. The experiments established the distinct role of each of the dopamine receptors in enabling Ritalin to enhance cognitive performance.

In addition, animals that performed better after Ritalin treatment showed enhanced synaptic plasticity in the amygdala. Enhanced plasticity is essentially increased efficiency of neural transmission. The researchers confirmed this by measuring electrical activity in neurons in the amygdala after Ritalin treatment.

The research confirmed that learning and focus were enhanced when Ritalin was administered to animals in doses comparable to those used therapeutically in children.

"Although Ritalin is so frequently prescribed, it induces many brain changes, making it difficult to identify which of those changes improve learning." said Kay Tye. "By identifying the brain mechanisms underlying Ritalin's behavioral enhancements, we can better understand the action of Ritalin as well as the properties governing brain plasticity."

Other co-authors on the paper and collaborators in the research were Jackson Cone and Lynne Tye, who were undergraduate assistants at the time of the study, and Evelien Hekkelman, a medical student working with Kay Tye at the Gallo Center.