Cocoa could be a healthy treat for diabetic patients

Flavanols in cocoa improve artery function, help relieve stress on heart

For people with diabetes, sipping a mug of steaming, flavorful cocoa may seem a guilty pleasure. But new research suggests that indulging a craving for cocoa can actually help blood vessels to function better and might soon be considered part of a healthy diet for the prevention of cardiovascular disease.

Flavanols, natural plant compounds also found in tea, red wine, and certain fruits and vegetables, are responsible for cocoa's healthful benefits. In fact, according to new research published in the June 3 issue of the Journal of the American College of Cardiology (JACC), after diabetic patients drank specially formulated high-flavanol cocoa for one month, blood vessel function went from severely impaired to normal.

The improvement was as large as has been observed with exercise and many common diabetic medications, the researchers noted. These findings suggest that it may be time to think not just outside the box, but inside the cup, for innovative ways to ward off cardiovascular disease—the number one cause of death in diabetic patients.

"Medical treatments alone often do not prevent complications of diabetes that are associated with atherosclerosis and cardiovascular disease," said Malte Kelm, M.D., a professor and chairman of cardiology, pulmonology and vascular medicine at the University Hospital Aachen and the Technical University Aachen, in Aachen, Germany. "Physicians should be increasingly looking to lifestyle changes and new approaches to help in addressing the cardiovascular risks associated with diabetes."

For the study, Dr. Kelm and his colleagues first tested the feasibility of using high-flavanol cocoa to improve cardiovascular health by observing, on three separate days, the effects of cocoa with varying amounts of flavanols on blood vessel function in 10 patients with stable type 2 diabetes.

The second, larger part of the study tested the effectiveness of long-term, routine consumption of high-flavanol cocoa in comparison with low-flavanol cocoa in 41 patients with stable type 2 diabetes. Patients were randomly assigned to drink cocoa with either 321 mg of flavanols per serving or only 25 mg of flavanols per serving three times daily for 30 days. The two types of cocoa tasted and looked the same, despite differences in flavanol content. In addition, neither patients nor investigators were aware of which type of cocoa each patient had been assigned to drink.

Blood vessel function was tested on the first day before the patients consumed any cocoa and again two hours after drinking the beverage. The test was repeated before and after cocoa consumption on day 8 and day 30.

To gauge the effect of high-flavanol cocoa on blood vessel function, the researchers used a test called "flow-mediated dilation" (FMD), which evaluates the ability of the arteries to expand (dilate) in response to an increase in the demand for blood, oxygen and nutrients. The FMD test involves measuring the diameter of the brachial artery in the upper arm using ultrasound, then inflating a blood pressure cuff on the forearm for several minutes. The squeezing of the blood pressure cuff temporarily starves the forearm muscles of blood and oxygen, causing the body to increase blood flow to those muscles. In healthy people, the inner lining of the arteries, or endothelium, senses the increased blood flow and sends a chemical signal telling the arteries to expand. In Dr. Kelm's laboratory, a normal FMD response among healthy people the same age as those participating in the study is a 5.2 percent expansion in arterial diameter, on average.

The researchers found that patients with type 2 diabetes had a severely impaired FMD response at the beginning of the study. Before patients consumed any cocoa, the brachial artery expanded by only 3.3 percent, on average. Two hours after drinking high-flavanol cocoa, the FMD response was 4.8 percent.

Over time, those findings improved, however. After patients drank high-flavanol cocoa three times daily for eight days, the average FMD response improved to 4.1 percent at baseline and to 5.7 percent two hours after cocoa ingestion. By day 30, the FMD response had improved to 4.3 percent at baseline and 5.8 percent after cocoa ingestion. All of the improvements were highly statistically significant.

Among patients who consumed low-flavanol cocoa, there were no significant differences in baseline FMD response over time, or in FMD response after cocoa ingestion on days 8 and 30.

FMD measurements can provide valuable information about a person's cardiovascular health. Previous studies have shown that people with an impaired FMD response have an increased risk of heart attack, need for bypass surgery or catheter procedure to open clogged coronary arteries, and even death from heart disease.

Dr. Kelm speculated that cocoa flavanols improve FMD response by increasing the production of nitric oxide, the chemical signal that tells arteries to relax and widen in response to increased blood flow. Relaxation of the arteries takes stress off of the heart and blood vessels.

The high-flavanol cocoa used in this study—which provided many times more flavanols than the typical U.S. dietary intake of 20 to 100 mg daily—is not sold in the supermarket. Dr. Kelm cautioned that the take-home message of the study is not that people with diabetes should guzzle cocoa, but rather, that dietary flavanols hold promise as a way to prevent heart disease.

"Patients with type 2 diabetes can certainly find ways to fit chocolate into a healthy lifestyle, but this study is not about chocolate, and it's not about urging those with diabetes to eat more chocolate. This research focuses on what's at the true heart of the discussion on "healthy chocolate"—it's about cocoa flavanols, the naturally occurring compounds in cocoa," he said. "While more research is needed, our results demonstrate that dietary flavanols might have an important impact as part of a healthy diet in the prevention of cardiovascular complications in diabetic patients."

Umberto Campia, M.D., who co-wrote an editorial about the new study in the same issue of JACC, noted that diabetics are an ideal population in which to study the effects of flavanols on arterial function, because high blood sugar damages the endothelium and because these patients have a high risk of cardiovascular disease.

Any therapy that helps the lining of the arteries to function better is potentially important, said Dr. Campia, a research associate with MedStar Research Institute in Washington, D.C.. "The endothelium is one of the largest organs in the body," he said. "It maintains the health of the arteries and prevents blockages that can cause heart attacks, strokes and limb loss."

"This study is important and thought-provoking," he noted. "We now have sizeable evidence that cocoa flavanols have a positive effect on the health of the arteries. This is the foundation we need for doing a much larger prospective study that looks at the effect of cocoa flavanols not just on endothelial function, but also on the risk of heart attack, stroke, and other serious forms of cardiovascular disease."

This study was supported by an unrestricted grant from Mars Inc., McLean, VA. The company also provided the instant cocoa beverage powders used in the study but had no role in the design, conduct, or analysis of the study. One of the authors, Hagen Schroeter, Ph.D., is employed by Symbioscience, a newly established scientific division of Mars, Inc.

Short-term use of antipsychotics in older adults with dementia linked to serious adverse events

Older adults with dementia who receive short-term courses of antipsychotic medications are more likely to be hospitalized or die than those who do not take the drugs, according to a report in the May 26 issue of Archives of Internal Medicine, one of the JAMA/Archives journals.

"Newer antipsychotic drugs (olanzapine, quetiapine fumarate and risperidone) have been on the market for more than a decade and are commonly used to treat the behavioral and psychological symptoms of dementia," the authors write as background information in the article. "Antipsychotic drugs are often used for short periods to treat agitation in clinical practice. They are frequently prescribed around the time of nursing home admission." About 17 percent of individuals admitted to nursing homes are starting on antipsychotic medication within 100 days, and 10 percent receive only a single prescription. Given the widespread use of short-term prescriptions, it is important to evaluate their safety, the authors note.

Paula A. Rochon, M.D., M.P.H., F.R.C.P.C., of the Institute for Clinical Evaluative Sciences (ICES), Ontario, and colleagues studied older adults with dementia living in the community or in nursing homes between 1997 and 2004. In each setting, the researchers identified three groups of equal size who were identical except for their exposure to antipsychotic medications. Among 20,682 older adults with dementia living in the community, 6,894 did not receive antipsychotics, 6,894 were prescribed atypical or newer antipsychotics and 6,894 were prescribed conventional antipsychotics, such as haloperidol or loxaprine. Among 20,559 older adults with dementia living in nursing homes, 6,853 received no antipsychotics, 6,853 received atypical antipsychotics and 6,853 received conventional antipsychotics.

Participants' medical records were examined for serious adverse events, defined as hospital admissions and death within 30 days of beginning therapy. "Relative to community-dwelling older adults with dementia who did not receive a prescription for antipsychotic drugs, similar older adults who did receive atypical antipsychotic drugs were three times more likely and those who received a conventional antipsychotic drug were almost four times more likely to experience a serious adverse event within 30 days of starting therapy," the authors write. "Relative to nursing home residents in the control group, individuals in the conventional antipsychotic therapy group were 2.4 times more likely to experience a serious adverse event leading to an acute care hospital admission or death. Those in the atypical antipsychotic group were 1.9 times more likely to experience a serious adverse event during 30 days of follow-up."

The analysis may underestimate the number of adverse events because of the short length of follow-up, the authors note. In addition, physicians who notice early signs of a problem may take patients off antipsychotics, avoiding more serious consequences, and many serious events experienced by nursing home residents are dealt with in the facility without hospital admission. "Our results exploring serious adverse events likely identify only the 'tip of the iceberg'," they write. "Antipsychotic drugs should be prescribed with caution even for short-term therapy."

(Arch Intern Med. 2008;168[10]:1090-1096. Available pre-embargo to the media at www.jamamedia.org.)

To fight the Cancer before the Tumour grows

Immunization against "false" proteins could sensitize the immune system against tumour cells / Heidelberg scientists publish in "Gastroenterology"

Researchers in Heidelberg have discovered a new strategy for an immunization against certain forms of cancer. They have determined that immune cells react strongly to the modified proteins in tumor cells in which a DNA repair defect has occurred. It is estimated that this repair defect is present in some 15 percent of all tumours.

The researchers, led by Professor Dr. Magnus von Knebel Doeberitz, Medical Director of the Department of Applied Tumor Biology at the Heidelberg University Hospital, studied the most frequent form of hereditary colon cancer, the HNPCC syndrome (Hereditary Non-Polyposis Colorectal Cancer Syndrome). The results of their research, which was conducted in co-operation with the German Cancer Research Center and the European Molecular Biology Laboratory (EMBL) and was funded with € 380,000 by the Deutsche Krebshilfe (German Cancer Aid) have been published in the April edition of the renowned American professional journal "Gastroenterology".

In Germany, colon cancer, with about 65,000 new cases per year, is the third most common form of cancer. In about 15 percent of these tumors, there is a defect in certain repair mechanisms of the DNA that leads mainly to changes in the so-called microsatellites. As the researchers in Heidelberg have now discovered, these changes in microsatellites cause the tumour cells to begin forming foreign proteins, which can be recognized and attacked by the immune system. But why are tumours formed despite the immune reaction? "There are two reasons for this," says Professor von Knebel Doeberitz. "The immune system often reacts too slowly – and some tumor cells are able to hide because they lose the ability to express the foreign proteins on their surface."

The results of the Heidelberg research team suggest that the growth of tumous with microsatellite changes can be prevented if the immune system can be activated against the foreign proteins in time. The researchers' next goal is thus to develop a vaccine against these types of cancer from the new foreign proteins that are created from mutations. If the immune system is sensitized against the "enemy" by immunization, it could react rapidly and strongly when cancer cells or their early stages appear.

The new immunization strategy could be effective against 10 to 15 percent of all cancers. The new results are especially significant for patients who suffer from the most frequent form of hereditary colon cancer, the HNPCC syndrome (Hereditary Non-Polyposis Colorectal Cancer Syndrome). Almost all tumours of this form are affected by the changes in microsatellites.

References:*Yvette Schwitalle, Matthias Kloor, Susanne Eiermann, Michael Linnebacher, Peter Kienle, Hanns Peter Knaebel, Mirjam Tariverdian, Axel Benner, Magnus von Knebel Doeberitz, Immune Response Against Frameshift-Induced Neopeptides in HNPCC Patients and Healthy HNPCC Mutation Carriers, Gastroenterology 2008, 134, 988-997.*

(The original article can be requested from the press office of the Heidelberg University Hospital at contact@med.uni-heidelberg.de .)

Childhood lead exposure associated with criminal behavior in adulthood

CINCINNATI—New research from the University of Cincinnati (UC) reports the first evidence of a direct link between prenatal and early-childhood lead exposure an increased risk for criminal behavior later in life.

Based on long-term data from a childhood lead study in Cincinnati, Ohio, Kim Dietrich, PhD, and his team have determined that elevated prenatal and postnatal blood-lead concentrations are associated with higher rates of criminal arrest in adulthood.

"Previous studies either relied on indirect measures of exposure or failed to follow subjects into adulthood to examine the relationship between lead exposure and criminal activity in young adults," explains Dietrich, principal investigator of the study and professor of environmental health at UC.

"We have monitored this specific sub-segment of children who were exposed to lead both in the womb and as young children for nearly 30 years," he adds. "We have a complete record of the neurological, behavioral and developmental patterns to draw a clear association between early-life exposure to lead and adult criminal activity."

Dietrich says few studies have attempted to evaluate the consequences of childhood lead exposure as a risk of criminal behavior. The UC-led study is the first of its kind to demonstrate an association between developmental exposure to lead and adult criminal behavior.

Dietrich and his colleagues report their findings in the May 27, 2008, issue of the journal PLoS Medicine.

This new study is part of a long-term lead exposure study conducted through the Cincinnati Children's Environmental Health Center, a collaborative research group funded by the National Institute of Environmental Health Sciences (NIEHS) and U.S. Environmental Protection Agency (EPA) that involved scientists from the UC College of Medicine and Cincinnati Children's Hospital Medical Center.

Led by Dietrich, researchers recruited pregnant women living in Cincinnati neighborhoods with a higher concentration of older, lead-contaminated housing. Recruitment took place at four prenatal clinics between 1979 and 1984. Dietrich's team has monitored this population group since birth to assess the long-term health effects of early-life lead exposure.

Of the original 376 newborns recruited, 250 were identified for the current study. Researchers measured blood-lead levels during pregnancy and then at regular intervals until the children were 6 ½ years old to calculate cumulative lead exposure.

Blood-lead level data was then correlated with public criminal arrest records from a search of Hamilton County, Ohio, criminal justice records. These records provided information about the nature and extent of arrests and were coded by category: violent, property, drugs, fraud, obstruction of justice, serious motor vehicle, disorderly conduct and other offenses.

Researchers found that individuals with increased blood-lead levels before birth and during early childhood had higher rates of arrest—for both violent and total crimes—than the rest of the study population after age 18.

Approximately 55 percent of the subjects had at least one arrest—the majority of which involved drugs (28 percent) or serious motor vehicle violations (27 percent). The strongest association between childhood blood-lead level and criminal behavior was for arrests involving acts of violence.

Dietrich says that although both environmental lead levels and crime rates in the United States have dropped in the past 30 years, they have not done so in a uniform way.

"Lower income, inner-city children remain particularly vulnerable to lead exposure," he explains. "Although we've made great strides in reducing lead exposure, our findings send a clear message that further reduction of childhood lead exposure may be an important and achievable way to reduce violent crime.

"Aggressive or violent behavioral patterns often emerge early and continue throughout life," adds Dietrich. "Identifying the risk factors that may place youth on an early trajectory toward a life of crime and violence should be a public health priority."

Study coauthor John Wright, PhD, a member of UC's criminal justice faculty who studies the impact of factors like genetics, psychology and biology on criminality, says he had limited expectations for how strong a correlation between lead exposure and criminality could be established.

"I did not expect we would see an effect, much less a substantive effect and even less likely a highly resilient effect," says Wright. "The fact that we are able to detect the effects from childhood exposures now into adulthood stands as a testament of lead's power to influence behavior over a long period of time."

UC coauthors include M. Douglas Ris, PhD, Richard Hornung, PhD, Stephanie Wessel, Bruce Lanphear, MD, Mona Ho, and Mary Rae, PhD. Funding for the study came from grants from the NIEHS and U.S. EPA.

US reporters often do a poor job of reporting about new medical treatments

Most medical news stories about health interventions fail to adequately address costs, harms, benefits, the quality of evidence, and the existence of other treatment options, finds a new analysis in this week's PLoS Medicine. The analysis was conducted by Gary Schwitzer from the University of Minnesota School of Journalism and Mass Communication.

Schwitzer publishes an online project called HealthNewsReview.org (www.HealthNewsReview.org) that evaluates and grades media stories about new health interventions, notifying journalists of their grades. The project monitors news coverage by the top 50 most widely circulated newspapers in the US; the most widely used wire service (Associated Press); the three leading newsweekly magazines—TIME, Newsweek, and U.S. News & World Report; and the ABC, CBS and NBC television network morning and evening newscasts. Each news story is given a grade from 1 to 10, according to a set of criteria that include whether a story adequately quantifies the benefits of an intervention, appraises the supporting evidence, and gives information on the sources of a story and the sources' competing interests.

For his analysis in PLoS Medicine, Schwitzer reviewed the ratings for 500 US health news stories that were published or aired over a period of almost two years, and found that 62%–77% of stories had major failings in the quality of reporting. Schwitzer gives examples of particularly poor reporting. ABC World News, for example, was graded only 2 out of 10 for a TV report about a new test for prostate cancer, a test that the show claimed was "more accurate" than existing tests. This poor grade reflected the fact that ABC World News failed to discuss the enormous controversies surrounding the risks and benefits of prostate cancer screening, failed to discuss any evidence that the new test was superior, and failed to mention that the principal investigator of the new test receives a share of the royalties received on sales of the test.

The high rate of inadequate reporting found in this study, says Schwitzer, "raises important questions about the quality of the information US consumers receive from the news media on these health news topics."

In an editorial discussing the analysis, the PLoS Medicine editors explore some of the reasons why the quality of health news reporting is often poor, including reporters' inadequate training in understanding health research, the tendency of the 24-hour news cycle towards sensationalism, and the "complicit collaboration" between scientists, reporters, and medical journals in hyping a new study.

"Schwitzer's alarming report card of the trouble with medical news stories is a wake-up call," say the editors "for all of us involved in disseminating health research—researchers, academic institutions, journal editors, reporters, and media organizations—to work collaboratively to improve the standards of health reporting."

***CITATION**: Schwitzer G (2008) How do US journalists cover treatments, tests, products, and procedures" An evaluation of 500 stories. PLoS Med 5(5): e95.*
http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050095

Disease mongering is now part of the global health debate

Two years ago, Ray Moynihan and David Henry at the University of Newcastle in Australia helped organize the world's first international conference on disease mongering, the process of widening the boundaries of illness in order to grow markets for those who sell and deliver treatments. The conference coincided with a special theme issue of PLoS Medicine on the same subject (http://collections.plos.org/plosmedicine/diseasemongering-2006.php). Now, in an Essay in this week's PLoS Medicine, Moynihan and colleagues look back over the last two years to ask what kind of impact the conference and theme issue have had.

There are reliable signs, they say, that disease mongering is now part of the global health debate: "Within the media, consumer movements, and the professional and research communities, increasing numbers of people are formulating ways to confront the problem, in some cases forcing the pharmaceutical industry to respond."

For example, high-profile articles on disease mongering have emerged in the mainstream media recently. In covering a new drug called Requip—for "restless legs syndrome"—The Wall Street Journal headlined the story "How Glaxo Marketed a Malady to Sell a Drug." Similarly, The New York Times recently ran a story about a new medicine called Lyrica—for "fibromyalgia"—under the headline "Drug Approved. Is Disease Real""

In November 2007, disease mongering was a key subject of debate at the annual congress of Consumers International, an organization involving 220 member groups in over 100 countries. Responding to the issue at that conference, the head of the International Federation of Pharmaceutical Manufacturers and Associations, Harvey Bale, conceded that there were examples of "egregious over-promotion", though he defended the industry's capacity to ethically market medicines.

"While we have noted some signs of media, consumer, and academic debate and action about the problem of disease mongering," say Moynihan and colleagues, "we are not aware of a similar increase in policy interest or action. In fact, to the contrary, there is some evidence of complacency about disease mongering on the part of regulators." The US Food and Drug Administration's recent proposal to relax restrictions on off-label marketing of drugs, they argue, risks setting the conditions for disease mongering to flourish.

"Unnecessary medicalisation and medication may be wasting many precious health resources, with obvious opportunity costs for private and public health insurers alike. Producing credible estimates of the magnitude of those costs is a future direction that should be urgently pursued."

***CITATION**: Moynihan R, Doran E, Henry D (2008) Disease mongering is now part of the global health debate. PLoS Med 5(5): e106.*
PUBLISHED PAPER: http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050106

No association found between vitamin D concentration in blood and risk of prostate cancer

High vitamin D concentration in the blood is not associated with a reduced risk of prostate cancer, researchers report in an article published online May 27 in the Journal of the National Cancer Institute.

Laboratory studies suggested that high doses of vitamin D may reduce the risk of prostate cancer, but epidemiological studies that have examined the relationship have reported inconsistent results.

In a nested case-control study, Jiyoung Ahn, Ph.D., and Richard Hayes D.D.S., Ph.D., of the National Cancer Institute in Bethesda, Md., and colleagues compared the vitamin D concentrations in the blood of 749 men diagnosed with prostate cancer with that of 781 men without prostate cancer. All of the men were participants in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial and were included in the regular screening arm. Vitamin D concentration was measured in a blood sample taken when the men enrolled in the study, and all prostate cancer cases included in the current analysis were diagnosed 1 to 8 years after the blood samples were taken.

The researchers found that there was no statistically significant difference in the risk of prostate cancer with increasing vitamin D concentration. The researchers did see some evidence of an increased risk of aggressive

disease associated with higher concentration of vitamin D, but the trend was not statistically significant and the association did not show a linear dose-dependence.

"Results from this large prospective study of men who underwent standardized prostate cancer screening in the context of a screening trial do not support the hypothesis that higher serum vitamin D status is associated with decreased risk of prostate cancer," the authors write. "The study showed no association of vitamin D with nonaggressive disease; however, it raises the possibility that higher vitamin D level may be associated with increased risks for aggressive disease, although a clear monotonic dose–response relationship was lacking."

In an accompanying editorial, Lorelei Mucci, Sc.D., and Donna Spiegelman, Sc.D., of the Harvard School of Public Health in Boston reviewed previous studies that have looked for a possible association between vitamin D and prostate cancer risk. The evidence to date does not strongly support an association between vitamin D status in adulthood and prostate cancer risk. They note that because prostate cancer is often diagnosed at an early stage and as low-grade disease, Ahn and colleagues' effort to study the vitamin's association with aggressive prostate cancer, which is the most important clinically, is valuable. The editorialists comment, however, that other groups have not seen a similar association, and Ahn's data should be viewed in that context.

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***Citation**: * Article: Ahn J, Peters U, Albanes D, Purdue MP, Abnet CC, Chatterjee N, et al. Serum Vitamin D Concentration and Prostate Cancer Risk: A Nested Case – Control Study. J Natl Cancer Inst 2008; 100:796-804*

** Editorial: Mucci LA, Spiegelman D. Vitamin D and Prostate Cancer Risk — A Less Sunny Outlook" J Natl Cancer Inst 2008; 100:759-761*

Antioxidant supplements may lessen benefit of radiation and chemotherapy

Cancer patients should avoid the routine use of antioxidant supplements during radiation and chemotherapy because the supplements may reduce the anticancer benefits of therapy, researchers concluded in a commentary published online May 27 in the Journal of the National Cancer Institute.

Radiation and many chemotherapy agents work to kill cells by inducing free radicals that damage DNA and proteins. Therefore, there is a possibility that taking antioxidant supplements, such as vitamin E or ß-carotene, may interfere with the therapies and reduce their anticancer activity. On the other hand, some investigators hypothesize that antioxidant supplementation may protect healthy tissues and reduce the side effects of treatment. Despite two decades of research into this question, no clear answer has appeared.

To evaluate the potential harms or benefits of antioxidant supplementation, Brian D. Lawenda, M.D., of the Naval Medical Center San Diego and colleagues reviewed all of the randomized trials they could identify that tested the effect of antioxidant supplements on radiation therapy or chemotherapy.

In the case of radiotherapy, they identified nine studies that addressed the question, including two meta-analyses. However, only three studies were randomized controlled trials designed to look at the clinical effect of antioxidant therapy on radiation. In the largest of the randomized trials, antioxidant supplementation was associated with a reduction in overall survival. One antioxidant agent, amifostine, which is already approved by the U.S. Food and Drug Administration to increase radioresistance in healthy salivary gland tissues, may protect normal tissues without increasing tumor radioresistance. Lawenda and colleagues caution that the question needs to be studied further before a solid conclusion can be made.

The authors identified 16 randomized controlled trials that examined the impact of antioxidant supplementation on chemotherapy. Six of the trials were placebo-controlled.

Of the studies that included information on response rates, none reported a decrease in response in the antioxidant arm of the trial compared with the control arm. However, Lawenda and colleagues caution that none of the trials was large enough to reliably detect such differences.

"Despite some intriguing studies that have suggested the benefit of adjunctive antioxidant treatments in cancer patients, the totality of the available evidence is equivocal at best and leaves us with serious concerns about the potential for harm," the authors write.

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Citation: Lawenda BD, Kelly KM, Ladas EJ, Sagar SM, Vickers A, Blumberg JB. Should Supplemental Antioxidant Administration Be Avoided During Chemotherapy and Radiation Therapy" J Natl Cancer Inst 2008;100:773-783

Heart doctors don't follow guidelines for treating patients; pre-operative statins reduce deaths

2 separate studies reveal new findings on: Adherence to guidelines, and the best evidence so far that pre-operative statins reduce the risk of death and other complications after surgery

A Europe-wide survey has revealed significant differences between doctors in the way they treat patients with heart failure, with many physicians failing to give the best care to their patients despite the existence of

recommended guidelines. The elderly are particularly at risk, with only about half of primary care physicians correctly referring those aged 65-80 with suspected heart failure to a specialist for diagnosis.

Professor Willem Remme, the first author of the study, which is published online in Europe's leading cardiology journal, the European Heart Journal [1] today (Wednesday 28 May), said the findings were "very worrying".

Another study, also published online in the EHJ today [2], has found that if doctors gave the cholesterol-lowering drugs, statins, to patients before surgery for heart disease, the patients were significantly less likely to die or suffer other serious complications post-surgery. The first author of this study, Dr Oliver Liakopoulos, said that the meta-analysis of over 30,000 patients provided the best evidence so far of the need for intensive statin therapy before cardiac surgery, but, as less than half of cardiac surgery patients currently received the optimum pre-surgery treatment even under existing guidelines, there was an urgent need to change clinical practice.

Prof Remme, Professor of Medicine at Sticares Cardiovascular Research Foundation (Rhoon, The Netherlands), and his colleagues from the Study group on HF Awareness and Perception in Europe (SHAPE), randomly selected cardiologists, internists, geriatricians and primary care physicians from nine European countries [3] to answer questions on the diagnosis and treatment of heart failure. They received 2041 replies from cardiologists (C), 1881 from internists and geriatricians (I/G) and 2965 from primary care physicians (PCP).

"We found that despite the widespread availability of evidence-based guidelines on the management of heart failure, there were significant differences between physicians and countries," said Prof Remme. "This was particularly apparent in the use (or lack of it) of echocardiography as a routine diagnostic tool, the prescription of ACE inhibitors and beta-blockers, the use of doses that were too low of these agents, the unsafe reliance on diuretics as a single treatment for heart failure, the use of inappropriate drugs and timings of medications."

The researchers found that while 92% cardiologists and 71% I/Gs would use echocardiography to diagnose heart failure, 75% of PCPs would use only signs and symptoms to diagnose it. "This is concerning because if heart failure is not diagnosed correctly using echocardiography and echo-Doppler, patients may be treated wrongly, based on signs and symptoms alone, and given heart failure medication that they might not need, which could lead to untoward effects," said Prof Remme.

Only 55% of PCPs said they would refer a patient in the typical age range for heart failure (65-80) to a specialist and only 32% would do this in those older than 80. "This is very worrying as, according to our survey, PCPs are less inclined to diagnose properly and treat heart failure correctly," he said. "A correct diagnosis of heart failure requires objective evaluation of cardiac function. This is particularly important in the elderly, in whom the preponderance of women and high prevalence of other illnesses make a correct diagnosis based on symptoms and signs alone even more hazardous."

PCPs, but also I/Gs, were far less likely to prescribe ACE inhibitors and beta-blockers, and if they did, they were often at the incorrect doses. Similarly, fewer PCPs and I/Gs would prescribe spironolactone rather than digoxin for worsening symptoms, even though spironolactone has been recommended as the better treatment for some time now.

"Our finding that I/Gs report practices that frequently deviate from those recommended in guidelines is also of concern, as many patients admitted to hospital with heart failure are cared for by these specialists," report the authors.

They said their survey made it apparent that many PCPs and I/Gs do not read the guidelines, although most are aware of their existence. Even though more cardiologists had read the guidelines, only 32% chose them as their main source of information on treatment. "I find these figures very worrying as guidelines are the only source of information which gives management advice in a complete and unbiased way, based on data from controlled studies or real expert opinion," said Prof Remme.

He said that, while some progress has been made since guidelines were first issued in 1995, with more patients receiving appropriate treatments in the hospital setting, the SHAPE survey showed several areas for concern. "What is worrying is that, even in cardiology care, beta-blocker dosage remains on average too low. With regards to PCPs, there does not seem to have been much progress over the years in terms of how they diagnose and prescribe essential medication. Education programmes are clearly needed for both PCPs and I/Gs as these non-cardiology physicians care for many heart failure patients."

In the second study – the largest and most complete meta-analysis to date of the effect of pre-operative statins – Dr Liakopoulos, a senior resident doctor in the Department of Cardiothoracic Surgery, University of Cologne, Germany, together with Professor Thorsten Wahlers and other colleagues, analysed 19 studies

containing a total of 31,725 patients undergoing cardiac surgery. Of these, 17,201 (54.2%) were receiving statins before surgery and the rest were not.

They found that pre-operative statins reduced the absolute risk of early death from any cause by 1.5% during the early post-operative period (up to 30 days), meaning that for every 67 patients treated, one death after cardiac surgery would be avoided. Patients treated with pre-operative statins had odds of dying after surgery that were 43% lower than those who did not receive statins.

When they looked at particular events – atrial fibrillation (AF), myocardial infarction (MI), stroke and renal failure – they found a reduction of 4.3% in absolute risk of AF, meaning that patients receiving statins were 33% less likely to develop AF after surgery. Similarly, a 0.8% reduction in absolute risk of stroke was observed in the statin group, meaning that patients had odds of suffering a stroke after surgery that were 26% lower if they had received a statin before surgery than if they had not. However, statin use had no impact on postoperative MI or renal failure.

Dr Liakopoulos said that the effect on AF was probably underestimated, and recalculations that excluded two problematic trials showed that, in fact, pre-operative statins resulted in an absolute risk reduction for AF of 17%, meaning that only six patients would need to receive pre-operative statins to avoid one case of post-operative AF.

He said: "Our study is the largest meta-analysis to date to have evaluated the impact of pre-operative statin use on early adverse outcomes in patients undergoing cardiac surgery and suggests significant benefits on early post-operative outcomes in statin pre-treated patients (i.e. reduction of early all-cause mortality, stroke and atrial fibrillation).

"We strongly believe that in the absence of large randomised controlled trials (and currently none are planned) our meta-analysis gives the best clinical evidence to date for an intensive pre-operative statin treatment for all coronary artery disease patients scheduled for cardiac surgery, and it advocates the urgency for a more aggressive interdisciplinary approach between cardiologists and cardiac surgeons to provide the best pre-operative preparation for all cardiac patients scheduled for operative myocardial revascularisation.

"When you consider that only about 40-50% of heart patients admitted for cardiac surgery receive statins, and even fewer patients achieve sufficient lipid-levels prior to surgery and in compliance with existing European and American guidelines, our report underlines the need to change current clinical practice for both the cardiologist and cardiac surgeon, who are primarily responsible for providing optimal peri-operative care for our cardiac patients."

Dr Liakopoulos concluded that well-designed, multi-centre randomised controlled trials were urgently needed to answer questions that still remain about whether all patients would benefit from statin therapy (patients with or without high cholesterol levels or both), which statins were best, and what were the best doses to give and for how long.

Notes:

[1] Awareness and perception of heart failure among European cardiologists internists, geriatricians, and primary care physicians. European Heart Journal, doi:10.1093/eurheartj/ehn196

[2] Impact of preoperative statin therapy on adverse postoperative outcomes in patients undergoing cardiac surgery: a meta-analysis of over 30,000 patients. European Heart Journal, doi:10.1093/eurheartj/ehn198

[3] The nine countries were: France, Germany, Italy, The Netherlands, Poland, Romania, Spain, Sweden, the UK.

Giant flying reptiles preferred to walk

New research into gigantic flying reptiles has found that they weren't all gull-like predators grabbing fish from the water but that some were strongly adapted for life on the ground.

Pterosaurs lived during the age of dinosaurs 230 to 65 million years ago. A new study, published in PLoS ONE this week, by researchers at the University of Portsmouth on one particular type of pterosaur, the azhdarchids, claims they were more likely to stalk animals on foot than to fly.

A picture of Mark Wiitton next to the biggest known flying animal in the world, ever, the azhdarchid Hatzegopteryx. It stands about 3m tall at the shoulder and has a jaw well over 2m long. **Credit: Mark Witton**

Until now virtually all pterosaurs have been imagined by palaeontologists to have lived like modern seabirds: as gull- or pelican-like predators that flew over lakes and oceans, grabbing fish from the water. But a study of azhdarchid anatomy, footprints and the distribution of their fossils by Mark Witton and Dr Darren Naish shows that this stereotype does not apply to all flying reptiles and some were strongly adapted for terrestrial life.

Azhdarchids were probably better than any other ptersosaurs at walking because they had long limbs and skulls well suited for picking up small animals and other food from the ground.

Azhdarchids, named after the Uzbek word for 'dragon', were gigantic toothless pterosaurs. Azhdarchids include the largest of all pterosaurs: some had wingspans exceeding 10 metres and the biggest ones were as tall as a giraffe.

Dr Naish said: “Azhdarchids first became reasonably well known in the 1970s but how they lived has been the subject of much debate. Originally described as vulture-like scavengers, they were later suggested to be mud-probers (sticking their long bills into the ground in search of prey), and later still suggested to make a living by flying over the water’s surface, grabbing fish.

“Other lifestyles have been suggested too. These lifestyles all seem radically divergent so Mark and I sat down and carefully examined the evidence and we argue that azhdarchids were specialised terrestrial stalkers. All the details of their anatomy, and the environment their fossils are found in, show that they made their living by walking around, reaching down to grab and pick up animals and other prey.”

Animals like azhdarchids no longer exist but the closest analogues in the modern world are large ground-feeding birds like ground-hornbills and storks.

The researchers studied fossils in London, Portsmouth and Germany and compared the anatomy of azhdarchid with those of modern animals. This showed that azhdarchids were strikingly different from mud-probers and animals that grab prey from the water’s surface while in flight.

A

group of Quetzalcoatlus, another type of giant azhdarchid, strolling around a fern prairie eating baby dinosaurs for lunch.
Credit: Mark Witton

Dr Naish said: “We also worked out the range of motion possible in the azhdarchid neck: this bizarrely stiff neck has previously been a problem for other ideas about azhdarchid lifestyle, but it fits with our model as all a terrestrial stalker needs to do its raise and lower its bill tip to the ground.”

Other aspects of azhdarchid anatomy, such as their relatively small padded feet and long but weak jaws often pose problems in other proposed lifestyles but fit perfectly with the terrestrial stalker hypothesis. Mr. Witton said: “The small feet of azhdarchids were no good for wading around lake margins or swimming should they land on water but are excellent for strutting around on land. As for what azhdarchids would eat, they’d have snapped up bite-size animals or even bits of fruit. But if your skull is over two metres in length then bite-size includes everything up to a dinosaur the size of a fox.”

The researchers found that over 50 percent of azhdarchid fossils come from sediments that were laid down inland. Significantly, the only articulated azhdarchid fossils we have come from these inland sediments.

Hormone may hold key to helping elderly men live longer

Elderly men with higher activity of the hormone IGF-1—or insulin-growth factor 1—appear to have greater life expectancy and reduced cardiovascular risk, according to a new study accepted for publication in the Journal of Clinical Endocrinology & Metabolism (JCEM).

IGF-1 is a hormone similar in molecular structure to insulin. It is released from the liver and plays an important role in childhood growth and continues to have anabolic effects in adults.

In this study, researchers evaluated 376 healthy elderly men between the ages of 73 and 94 years. A serum sample was taken from each subject at the beginning of the study and researchers were contacted about the status of the participants over a period of eight years.

Subjects with the lowest IGF-1 function had a significantly higher mortality rate than subjects with the highest IGF-1 bioactivity. These results were especially significant in individuals who have a high risk to die from cardiovascular complications.

These new findings come as a result of a new form of testing for IGF-bioactivity. Researchers in this study used a new method, a bioassay, to measure the function of IGF-1 in the blood. Compared to commonly used methods to measure IGF-1, the IGF-1 bioassay gives more information about the actual function (bioactivity) of circulating IGF-1 in the body.

“The bioassay allowed us to more clearly see the association between high circulating IGF-1 bioactivity and extended survival,” said Michael Brugts, MD, of the Erasmus Medical Center in Rotterdam, The Netherlands and lead author of the study. “Interestingly, we could not find such a relationship when IGF-1 in blood was measured with the more commonly used methods.”

Immunoassays, commonly used previously to determine IGF-1 circulation levels, remove certain proteins that interfere with accurate measurements. Recent studies however have found that these proteins are important modulators of IGF-1 bioactivity. The bioassay used in this study does not disregard or remove this protein, thus enabling researchers to have a more accurate understanding of IGF-1 function.

Determination of IGF-1 function using the bioassay opens the possibility to gather new insights about the functions of IGF-1 in the body, said Brugts.

Other researchers working on the study include A.W. Van den Beld, L.J. Hofland, K. van der Wansem, P.M. van Koetsveld, S.W.J. Lamberts, and J.A.M.J.L. Janssen of Erasmus Medical Center in Rotterdam, The Netherlands and J. Frystyk of Aarhus University Hospital in Aarhus, Denmark.

The article “Low Circulating IGF-1 Bioactivity in Elderly Men is Associated with Increased Mortality,” will appear in the June issue of JCEM, a publication of The Endocrine Society.

Weizmann Institute Scientists Produce The First Smell Map

Is the smell of almonds closer to that of roses or bananas? Weizmann Institute scientists have now answered that question (roses) by showing for the first time that smells can be mapped and the relative distance between various odors determined. Their findings, which appeared recently in Nature Methods, may help scientists to unravel the basic laws underlying our sense of smell, as well as potentially enabling odors to be digitized and transferred via computer in the future.

We know the musical note do is farther from la than from re on a scale – not only because our ears tell us the distance is greater, but because their frequencies are farther apart. No such physical relationship had been discovered for smells, in part because odor molecules are much more difficult to pin down than sound frequencies. To create their map, the scientists began with 250 odorants and generated, for each, a list of around 1,600 chemical characteristics. From this dataset, the researchers, led by Rafi Haddad, a graduate student with Prof. Noam Sobel in the Neurobiology Department, and Prof. David Harel of the Computer Science and Applied Mathematics Department, together with their colleague Rehan Khan, created a multidimensional map of smells that revealed the distance between one odor molecule and another.

Eventually, they pared the list of traits needed to situate an odor on the map down to around 40. They then checked to see whether the brain recognizes this map, similar to the way it recognizes musical scales. They reexamined numerous previously published studies that measured the neural response patterns to smells in a variety of lab animals – from fruit flies to rats – and found that across all the species, the closer any two smells were on the map, the more similar the neural patterns. The scientists also tested 70 new odors by predicting the neural patterns they would arouse and running comparisons with the unpublished results of olfaction experiments done at the University of Tokyo. They found that their predictions closely matched the experimental results.

These findings lend support to the scientist's theory that, contrary to the commonly held view that smell is a subjective experience, there are universal laws governing the organization of smells, and these laws determine how our brains perceive them.

Prof. Noam Sobel's research is supported by the Nella and Leon Benoziyo Center for Neurosciences; the J&R Foundation; and the Eisenberg Keefer Fund for New Scientists.

Prof. David Harel's research is supported by the Arthur and Rochelle Belfer Institute of Mathematics and Computer Science; and the Henri Gutwirth Fund for Research. Prof. Harel is the incumbent of the William Sussman Professorial Chair.

When Plants "Think" Alike

New genetic evidence shows that the same trait developed independently on separate branches of the evolutionary tree

Frond of the lycophyte Selaginella moellendorffii. **Jing-Ke Weng, Department of Biochemistry, Purdue University**

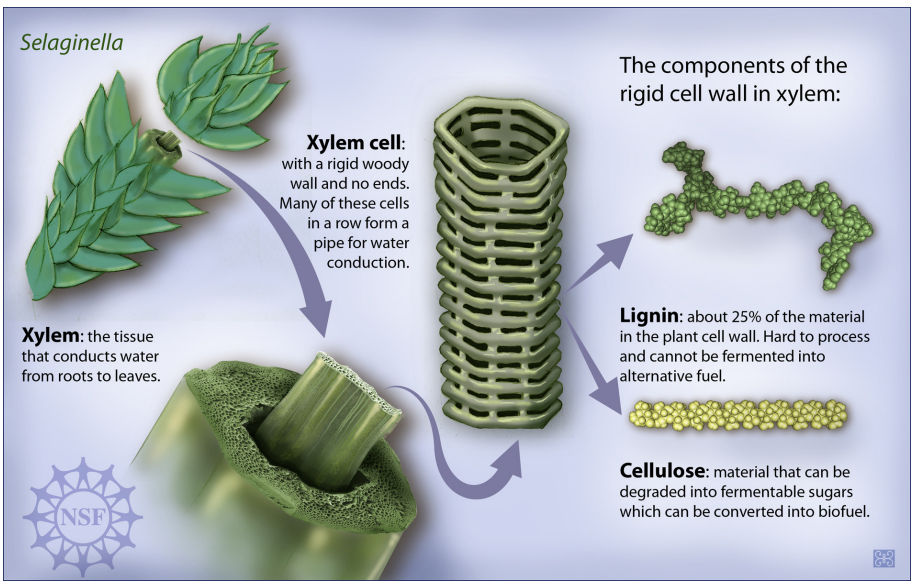
Biologists have discovered that a fundamental building block in the cells of flowering plants evolved independently, yet almost identically, on a separate branch of the evolutionary tree--in an ancient plant group called lycophytes that originated at least 420 million years ago.

Researchers believe that flowering plants evolved from gymnosperms, the group that includes conifers, ginkgos and related plants. This group split from lycophytes hundreds of millions of years before flowering plants appeared.

The building block, called syringyl lignin, is a critical part of the plants' scaffolding and water-transport systems. It apparently emerged separately in the two plant groups, much like flight arose separately in both bats and birds.

Purdue University researcher Clint Chapple and graduate students Jing-Ke Weng and Jake Stout, along with post-doctoral research associate Xu Li, conducted the study with the support of the National Science Foundation, publishing their findings in the May 20, 2008, Proceedings of the National Academy of Sciences.

"We're excited about this work not only because it may provide another tool with which we can manipulate lignin deposition in plants used for biofuel production, but because it demonstrates that basic research on plants not used in agriculture can provide important fundamental findings that are of practical benefit," said Chapple.



The plant studied--Selaginella moellendorffii, an ornamental plant sold at nurseries as spike moss--came from Purdue colleague Jody Banks. While not a co-author on the paper, Banks helped kick-start the study of the Selaginella genome with NSF support in 2002, and is now scientific coordinator for the plant's genome-sequencing effort conducted by the Department of Energy Joint Genome Institute in Walnut Creek, Calif.

Both lignin and cellulose are found in the rigid cell walls of the xylem cells (those that conduct water) in the primitive plant, Selaginella. **Zina Deretsky, National Science Foundation; Selaginella cross section SEM by Jing-Ke Weng, Clint Chapple, Purdue University; Lignin structure from Wout Bergjan, John Ralph, Marie Baucher (Annual Review of Plant Biology, Vol. 54:519-546, June 2003); Cellulose structure from http://www.chusa.jussieu.fr/disc/bio_cell/**

"Because Selaginella is a relict of an ancient vascular plant lineage, its genome sequence will provide the plant community with a resource unlike any other, as it will allow them to discover the genetic underpinnings of the evolutionary innovations that allowed plants to thrive on land, including lignin," said Banks.

Chapple and his colleagues conducted the recent study as part of a broader effort to understand the genetics behind lignin specifically, as the material is an impediment to some biofuel production methods because of its durability and tight integration into plant structures.

"Findings from studies such as this really have implications regarding the potential for designing plants to better make use of cellulose in cell walls," said Gerald Berkowitz, a program director for the Physiological and Structural Systems Cluster at the National Science Foundation and the program officer overseeing Chapple's grant. "Different forms of lignin are present in crop plant cell walls; engineering plants to express specifically syringyl lignin could allow for easier break down of cellulose. Overcoming this obstacle is an important next step for advancing second generation biofuel production." **-NSF-**

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Religion is a product of evolution, software suggests

* 11:56 27 May 2008
* NewScientist.com news service
*** Ewen Callaway**

God may work in mysterious ways, but a simple computer program may explain how religion evolved

By distilling religious belief into a genetic predisposition to pass along unverifiable information, the program predicts that religion will flourish. However, religion only takes hold if non-believers help believers out – perhaps because they are impressed by their devotion.

"If a person is willing to sacrifice for an abstract god then people feel like they are willing to sacrifice for the community," says James Dow, an evolutionary anthropologist at Oakland University in Rochester, Michigan, US, who wrote the program – called Evogod (download the code here).

Dow is by no means the first scientist to take a stab at explaining how religion emerged. Theories on the evolution of religion tend toward two camps. One argues that religion is a mental artefact, co-opted from brain functions that evolved for other tasks.

Aiding the people

Another contends that religion benefited our ancestors. Rather than being a by-product of other brain functions, it is an adaptation in its own right. In this explanation, natural selection slowly purged human populations of the non-religious.

"Sometime between 100,000 years ago to the point where writing was invented, maybe about 7000 BC, we begin to have records of people's supernatural beliefs," Dow says.

To determine if it was possible for religion to emerge as an adaptation, Dow wrote a simple computer program that focuses on the evolutionary benefits people receive from their interactions with one another.

"What people are adapting to is other people," he says.

Religious attraction

To simplify matters, Dow picked a defining trait of religion: the desire to proclaim religious information to others, such as a belief in the afterlife. He assumed that this trait was genetic.

The model assumes, in other words, that a small number of people have a genetic predisposition to communicate unverifiable information to others. They passed on that trait to their children, but they also interacted with people who didn't spread unreal information.

The model looks at the reproductive success of the two sorts of people – those who pass on real information, and those who pass on unreal information.

Under most scenarios, "believers in the unreal" went extinct. But when Dow included the assumption that non-believers would be attracted to religious people because of some clear, but arbitrary, signal, religion flourished.

"Somehow the communicators of unreal information are attracting others to communicate real information to them," Dow says, speculating that perhaps the non-believers are touched by the faith of the religious.

Ancient needs

Richard Sosis, an evolutionary anthropologist at the University of Connecticut in Storrs, US, says the model adds a new dimension to the debate over how religion could have evolved, which has previously relied on verbal arguments and speculation. But "these are baby steps", he cautions.

Sosis previously found that in some populations – kibbutzim in Israel, for instance – more religious people receive more assistance from others than the less faithful. But he notes that the forces that maintain religion in modern humans could be very different from those that promoted its emergence, thousands of years ago.

Palaeolithic humans were probably far more reliant than modern humans on the community they were born into, Sosis says. "[Now] you can be a Lutheran one week and decide the following week you are going to become a Buddhist." *Journal reference: Journal of Artificial Societies and Social Stimulation, vol 11, p 2*

Personal Health

Red Flags for Hereditary Cancers

By JANE E. BRODY

Published: May 27, 2008

Correction Appended

Andy Martin

All cancers are genetic in origin. When genes are working properly, cell growth is tightly regulated, as if a stoplight told cells to divide only so many times and no more. A cancer occurs when something causes a mutation in the genes that limit cell growth or that repair DNA damage.

This is true even if the carcinogen is environmental, like tobacco smoke or radon, or if the cause is viral, like Helicobacter pylori or human papillomavirus.

Carcinogenic agents induce cancer by causing genetic mutations that allow cells to escape normal biological controls. Most cancers arise in this way, sporadically in an individual, and may involve several mutations that permit a tumor to grow.

But sometimes, a single potent cancer-causing mutation is inherited and can be passed from one generation to the next. An estimated 5 to 10 percent of cancers are strongly hereditary, and 20 to 30 percent are more weakly hereditary, said Dr. Kenneth Offit, chief of clinical genetics at Memorial Sloan-Kettering Cancer Center in New York.

Genetic Chances

In hereditary cancer, the mutated gene can be transmitted through the egg or sperm to children, with each child facing a 50 percent chance of inheriting the defective gene if one parent carries it and a 75 percent chance if both parents carry the same defect.

You might be familiar with the BRCA1 and BRCA2 mutations that are strongly linked to breast and ovarian cancer in women and somewhat less strongly to breast and prostate cancer in men. A woman with a BRCA mutation faces a 56 to 87 percent chance of contracting breast cancer and a 10 to 40 percent chance of ovarian cancer.

For some hereditary cancer genes, the risks are even greater. A child who inherits a so-called RET mutation faces a 100 percent chance of developing an especially lethal form of thyroid cancer. Likewise, the risk of stomach cancer approaches 100 percent in those with a CDH mutation, Dr. Daniel G. Coit, a surgeon at Memorial Sloan-Kettering, said at a recent meeting there.

Megan Harlan, senior genetic counselor at Sloan-Kettering, said these were red flags that suggest a cancer might be hereditary:

* Diagnosis of cancer at a significantly younger age than it ordinarily occurs.
* Occurrence of the same cancer in more than one generation of a family.
* Occurrence of two or more cancers in the same patient or blood relatives.

For example, a woman with a BRCA mutation is at high risk for both breast and ovarian cancer. A mismatch repair mutation, known as MMR, significantly raises the risk for colon cancer and somewhat for uterine and ovarian cancer. Thus, the occurrence of colon, uterine and ovarian cancers among blood relatives suggests that the family may carry the MMR mutation.

Preventive Actions

Knowing that you have a high-risk cancer gene mutation offers the chance to take preventive actions like scheduling frequent screenings starting at a young age or removing the organ at risk. While surgery is clearly a

drastic form of cancer prevention, in the future drugs may be able to thwart cancers in people at high risk, Dr. Offit said.

A third possibility, when a cancer gene runs in a family, is in vitro fertilization and genetic analysis to identify affected embryos and implant those lacking the defective gene.

Ms. Harlan suggested that a woman with a BRCA mutation should start at an early age to conduct monthly breast self-exams and have a doctor examine the breasts two to four times a year. She also advised alternating mammograms and breast M.R.I.'s every 6 to 12 months, starting at age 25.

Likewise, someone who carries an inherited colon cancer gene should start yearly colonoscopies at 20 or 25. A woman with a uterine cancer gene mutation should be screened with sonography and endometrial biopsies yearly and, Dr. Offit added, consider having her uterus removed when she has finished having children.

A growing number of women with BRCA mutations are choosing prophylactic mastectomies and, in some cases, oophorectomies, or removal of the ovaries. That reduces their risk of breast or ovarian cancer 75 percent.

Dr. Coit described a family in which the father and his father both developed thyroid cancer linked to the RET mutation. The younger man's 6-year-old son was tested and found to carry the same damaged gene. Because the boy was certain to develop thyroid cancer, most likely at a young age, his thyroid was removed. Although the boy will need to take thyroid hormone for the rest of his life, the surgery reduced to zero his chance of developing this often fatal cancer.

Dr. Coit also told of a 33-year-old woman who carried the CDH mutation associated with highly lethal stomach cancer. Her stomach was removed and found to contain three microscopic cancer sites, making her preventive surgery also curative. She is one of 131 patients with the mutation who have had their stomachs removed and a stomachlike pouch created from the small intestine.

The doctor acknowledged that the surgery was a drastic measure, with an operative mortality of 1.5 percent and a complication rate of 53 percent. Most patients cannot eat as much as they used to after the surgery. They develop food intolerances and lose weight, but they do eventually adapt to their new digestive system, Dr. Coit said.

Practical Considerations

Before choosing surgery to reduce risk in an otherwise healthy person, Dr. Coit said these factors should be carefully considered:

* Possible nonsurgical alternatives.
* Actual cancer risk from the inherited gene and how much surgery can reduce it.
* Timing of any operation.
* Effects of surgery on quality of life.

Another question is how and whether to disclose hereditary cancer risk. Though many people fear limits on their job and ability to obtain affordable health insurance, a federal law was passed this month to prevent such genetic discrimination.

What if someone with a hereditary cancer gene refuses to warn family members of the possible risk and need for tests? These types of questions have begun to arise, in a handful of lawsuits against doctors. In a 1995 case in Florida, for example, the state Supreme Court ruled that a doctor has to inform patients of the risk to family members, but left it to patients to tell them about tests and the potential for prevention.

The deciphering of the human genome has prompted a number of entrepreneurs to cash in on people's genetic concerns. They offer DNA testing to look for aberrant genes associated with the risk of developing various diseases, especially cancer.

Such testing, when done reliably, might encourage some people to take charge of their health and make better plans for the future. But some professional genetics counselors say this approach to determining cancer risk is fraught with hazards, not the least of which is a false warning of a serious risk that does not exist.

"This kind of testing is premature," said Dr. Kenneth Offit, chief of clinical genetics at Memorial Sloan-Kettering Cancer Center. "Some companies are selling research tests for mutations that carry a low risk of causing cancer, leading people to worry needlessly or be falsely reassured."

Another problem, he said, is the prescription offered after the tests.

"Other companies are telling people what kind of foods to eat and what to put on their skin based on their genes," Dr. Offit said. "Testing for known cancer genes is legitimate, but often the prescription given for a 'gene makeover' is not. Regulation of these labs is sorely needed. And people facing real hereditary cancer risks require intensive professional counseling.

This article has been revised to reflect the following correction:

Correction: May 29, 2008 The Personal Health column on Tuesday, about inherited cancers, misstated a viral cause of certain cancers. It is human papillomavirus, not herpes papilloma virus.

Experts Question Placebo Pill for Children

By CHRISTIE ASCHWANDEN

iStockphoto

Jennifer Buettner was taking care of her young niece when the idea struck her. The child had a nagging case of hypochondria, and Ms. Buettner's mother-in-law, a nurse, instructed her to give the girl a Motrin tablet.

"She told me it was the most benign thing I could give," Ms. Buettner said. "I thought, why give her any drug? Why not give her a placebo?"

Studies have repeatedly shown that placebos can produce improvements for many problems like depression, pain and high blood pressure, and Ms. Buettner reasoned that she could harness the placebo effect to help her niece. She sent her husband to the drugstore to buy placebo pills. When he came back empty handed, she said, "It was one of those 'aha!' moments when everything just clicks."

Ms. Buettner, 40, who lives in Severna Park, Md., with her husband, 7-month-old son and 22-month-old twins, envisioned a children's placebo tablet that would empower parents to do something tangible for minor ills and reduce the unnecessary use of antibiotics and other medicines.

With the help of her husband, Dennis, she founded a placebo company, and, without a hint of irony, named it Efficacy Brands. Its chewable, cherry-flavored dextrose tablets, Obecalp, for placebo spelled backward, goes on sale on June 1 at the Efficacy Brands Web site. Bottles of 50 tablets will sell for $5.95. The Buettners have plans for a liquid version, too.

Because they contain no active drug, the pills will not be sold as a drug under Food and Drug Administration rules. They will be marketed as dietary supplements, meaning they can be sold at groceries, drugstores and discount stores without a prescription.

"This is designed to have the texture and taste of actual medicine so it will trick kids into thinking that they're taking something," Ms. Buettner said. "Then their brain takes over, and they say, 'Oh, I feel better.' "

But some experts question the premise behind the tablets. "Placebos are unpredictable," said Dr. Howard Brody, a medical ethicist and family physician at the University of Texas Medical Branch at Galveston. "Each and every time you give a placebo you see a dramatic response among some people and no response in others."

He added that there was no way to predict who would respond.

"The idea that we can use a placebo as a general treatment method," Dr. Brody said, "strikes me as inappropriate."

Ms. Buettner does not spell out the conditions that her pills could treat. As a parent, she said, "you'll know when Obecalp is necessary."

Franklin G. Miller, a bioethicist at the National Institutes of Health, is skeptical. "As a parent of three now grown children," he said, "I can't think of a single instance where I'd want to give a placebo."

Much of the power of the placebo effect seems to lie in the belief that it will work, and some experts question whether this expectation can be sustained if the person giving it knows it is a sham.

Most clinical trials that have shown benefits from placebos are double blinded. Neither the recipient nor the giver knows that the pills are fake.

"For this to work really well as placebo, you cannot let the parents know that it's a sugar pill," Dr. Brody said. "You have to lie to the parents, too, if you expect them to fool their kids."

At least one study has shown that placebos can be effective even when the patients know that they are inert. In a study in 2007, 70 children with attention deficit hyperactivity disorder were asked to reduce their medications gradually by replacing some of their drugs with placebo pills. The children and their parents were explicitly told that these "dose extender" pills contained no drug.

After three months, 80 percent of the children reported that the placebo had helped them. Although that study used a placebo in a different context from Obecalp, it did suggest that deception might not be necessary for a placebo to work, said the senior author, Gail Geller, a bioethicist at the Berman Institute of Bioethics at Johns Hopkins.

Even if Obecalp proved helpful, some doctors worry that giving children "medicine" for every ache and pain teaches that every ailment has a cure in a bottle.

"Kids could grow up thinking that the only way to get better is by taking a pill," Dr. Brody said. If they do that, he added, they will not learn that a minor complaint like a scraped knee or a cold can improve on its own.

Dr. David Spiegel, a psychiatrist who studies placebos at the Stanford School of Medicine, said conditioning children to reach for relief in a pill could also make them easy targets for quacks and pharmaceutical pitches

later. “They used to sell candied cigarettes to kids to get them used to the idea of playing with cigarettes,” he said.

Ms. Buettner acknowledged that “we expect controversy with this,” but she added, “We are not promoting drug use.”

Despite his misgivings, Dr. Brody predicted that Obecalp would entice many parents. “Anybody who has ever been up in the middle of the night with a crying child would be tempted to try something like this,” he said. “You’re so desperate for anything that could quiet down your poor, miserable kid.”

Doctors themselves have been known to dole out placebos to overwhelmed parents, said Dr. Brian Olshansky, a physician at the University of Iowa Hospitals. A screaming child with an earache may leave the emergency room with a prescription for antibiotics, even though the drug will not speed recovery and could potentially cause harm.

Ms. Buettner said her pill could satisfy that need while reducing potential harms from unnecessary medications. “The overprescription of drugs is a serious problem, and I think there needs to be an alternative,” she said.

Some experts question whether an alternative should involve deception. “I don’t like the idea of parents lying to their kids,” said Dr. Steven Joffe, a pediatrician and bioethicist at the Dana-Farber Cancer Institute in Boston. “It makes me squeamish.”

Dr. Geller, the bioethicist, agrees that parents should not deceive their children. But she added that a parent who truly believed in the power of the placebo was not really being deceptive. “In principle,” she said, “I don’t have a problem with the thoughtful use of placebo. The starting premise and your own belief about what you’re doing matters a lot.”

Dr. Brody said parents did not need a pill to induce the placebo effect. Mothers have long promised to “kiss it and make it better” and it is that type of placebo children really yearn for, he said.

“Does a sick child really want X-rays or M.R.I.’s or the latest antibiotic?” he asked. “No. All the sick child wants is comforting.”

Monkeys Think, Moving Artificial Arm as Own

By BENEDICT CAREY

Two monkeys with tiny sensors in their brains have learned to control a mechanical arm with just their thoughts, using it to reach for and grab food and even to adjust for the size and stickiness of morsels when necessary, scientists reported on Wednesday.

The report, released online by the journal Nature, is the most striking demonstration to date of brain-machine interface technology. Scientists expect that technology will eventually allow people with spinal cord injuries and other paralyzing conditions to gain more control over their lives.

The findings suggest that brain-controlled prosthetics, while not practical, are at least technically within reach.

In previous studies, researchers showed that humans who had been paralyzed for years could learn to control a cursor on a computer screen with their brain waves and that nonhuman primates could use their thoughts to move a mechanical arm, a robotic hand or a robot on a treadmill.

The new experiment goes a step further. In it, the monkeys’ brains seem to have adopted the mechanical appendage as their own, refining its movement as it interacted with real objects in real time. The monkeys had their own arms gently restrained while they learned to use the added one.

Experts not involved with the study said the findings were likely to accelerate interest in human testing, especially given the need to treat head and spinal injuries in veterans returning from Iraq and Afghanistan.

“This study really pulls together all the pieces from earlier work and provides a clear demonstration of what’s possible,” said Dr. William Heetderks , director of the extramural science program at the National Institute of Biomedical Imaging and Bioengineering. Dr. John P. Donoghue, director of the Institute of Brain Science at Brown University, said the new report was “important because it’s the most comprehensive study showing how an animal interacts with complex objects, using only brain activity.”

The researchers, from the University of Pittsburgh and Carnegie Mellon University, used monkeys partly because of their anatomical similarities to humans and partly because they are quick learners.

In the experiment, two macaques first used a joystick to gain a feel for the arm, which had shoulder joints, an elbow and a grasping claw with two mechanical fingers.

Then, just beneath the monkeys’ skulls, the scientists implanted a grid about the size of a large freckle. It sat on the motor cortex, over a patch of cells known to signal arm and hand movements. The grid held 100 tiny electrodes, each connecting to a single neuron, its wires running out of the brain and to a computer.

The computer was programmed to analyze the collective firing of these 100 motor neurons, translate that sum into an electronic command and send it instantaneously to the arm, which was mounted flush with the left shoulder.

The scientists used the computer to help the monkeys move the arm at first, essentially teaching them with biofeedback.

After several days, the monkeys needed no help. They sat stationary in a chair, repeatedly manipulating the arm with their brain to reach out and grab grapes, marshmallows and other nuggets dangled in front of them. The snacks reached the mouths about two-thirds of the time — an impressive rate, compared with earlier work.

The monkeys learned to hold the grip open on approaching the food, close it just enough to hold the food and gradually loosen the grip when feeding.

On several occasions, a monkey kept its claw open on the way back, with the food stuck to one finger. At other times, a monkey moved the arm to lick the fingers clean or to push a bit of food into its mouth while ignoring a newly presented morsel.

The animals were apparently freelancing, discovering new uses for the arm, showing "displays of embodiment that would never be seen in a virtual environment," the researchers wrote.

"In the real world, things don't work as expected," said the senior author of the paper, Dr. Andrew Schwartz, a professor of neurobiology at the University of Pittsburgh. "The marshmallow sticks to your hand or the food slips, and you can't program a computer to anticipate all of that.

"But the monkeys' brains adjusted. They were licking the marshmallow off the prosthetic gripper, pushing food into their mouth, as if it were their own hand."

The co-authors were Meel Velliste, Sagi Perel, M. Chance Spalding and Andrew Whitford.

Scientists have to clear several hurdles before this technology becomes practical, experts said. Implantable electrode grids do not generally last more than a period of months, for reasons that remain unclear.

The equipment to read and transmit the signal can be cumbersome and in need of continual monitoring and recalibrating. And no one has yet demonstrated a workable wireless system that would eliminate the need for connections through the scalp.

Yet Dr. Schwartz's team, Dr. Donoghue's group and others are working on all of the problems, and the two macaques' rapid learning curve in taking ownership of a foreign limb gives scientists confidence that the main obstacles are technical and, thus, negotiable.

In an editorial accompanying the Nature study, Dr. John F. Kalaska, a neuroscientist at the University of Montreal, argued that after such bugs had been worked out, scientists might even discover areas of the cortex that allow more intimate, subtle control of prosthetic devices.

Such systems, Dr. Kalaska wrote, "would allow patients with severe motor deficits to interact and communicate with the world not only by the moment-to-moment control of the motion of robotic devices, but also in a more natural and intuitive manner that reflects their overall goals, needs and preferences."

Lotus Therapy

By BENEDICT CAREY

The patient sat with his eyes closed, submerged in the rhythm of his own breathing, and after a while noticed that he was thinking about his troubled relationship with his father.

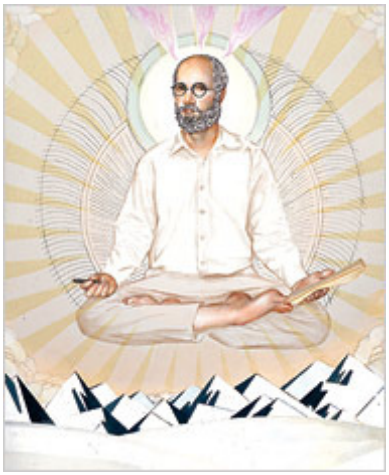
"I was able to be there, present for the pain," he said, when the meditation session ended. "To just let it be what it was, without thinking it through."

The therapist nodded.

"Acceptance is what it was," he continued. "Just letting it be. Not trying to change anything."

"That's it," the therapist said. "That's it, and that's big."

This exercise in focused awareness and mental catch-and-release of emotions has become perhaps the most popular new psychotherapy technique of the past decade. Mindfulness meditation, as it is called, is rooted in the teachings of a fifth-century B.C. Indian prince, Siddhartha Gautama, later known as the Buddha. It is catching the attention of talk therapists of all stripes, including academic researchers, Freudian analysts in private practice and skeptics who see all the hallmarks of another fad.



Steven Tabbutt

For years, psychotherapists have worked to relieve suffering by reframing the content of patients' thoughts, directly altering behavior or helping people gain insight into the subconscious sources of their despair and anxiety. The promise of mindfulness meditation is that it can help patients endure flash floods of emotion

during the therapeutic process — and ultimately alter reactions to daily experience at a level that words cannot reach. “The interest in this has just taken off,” said Zindel Segal, a psychologist at the Center of Addiction and Mental Health in Toronto, where the above group therapy session was taped. “And I think a big part of it is that more and more therapists are practicing some form of contemplation themselves and want to bring that into therapy.”

At workshops and conferences across the country, students, counselors and psychologists in private practice throng lectures on mindfulness. The National Institutes of Health is financing more than 50 studies testing mindfulness techniques, up from 3 in 2000, to help relieve stress, soothe addictive cravings, improve attention, lift despair and reduce hot flashes.

Some proponents say Buddha’s arrival in psychotherapy signals a broader opening in the culture at large — a way to access deeper healing, a hidden path revealed.

Yet so far, the evidence that mindfulness meditation helps relieve psychiatric symptoms is thin, and in some cases, it may make people worse, some studies suggest. Many researchers now worry that the enthusiasm for Buddhist practice will run so far ahead of the science that this promising psychological tool could turn into another fad.

“I’m very open to the possibility that this approach could be effective, and it certainly should be studied,” said Scott Lilienfeld, a psychology professor at Emory. “What concerns me is the hype, the talk about changing the world, this allure of the guru that the field of psychotherapy has a tendency to cultivate.”

Buddhist meditation came to psychotherapy from mainstream academic medicine. In the 1970s, a graduate student in molecular biology, Jon Kabat-Zinn, intrigued by Buddhist ideas, adapted a version of its meditative practice that could be easily learned and studied. It was by design a secular version, extracted like a gemstone from the many-layered foundation of Buddhist teaching, which has sprouted a wide variety of sects and spiritual practices and attracted 350 million adherents worldwide.

In transcendental meditation and other types of meditation, practitioners seek to transcend or “lose” themselves. The goal of mindfulness meditation was different, to foster an awareness of every sensation as it unfolds in the moment.

Dr. Kabat-Zinn taught the practice to people suffering from chronic pain at the University of Massachusetts medical school. In the 1980s he published a series of studies demonstrating that two-hour courses, given once a week for eight weeks, reduced chronic pain more effectively than treatment as usual.

Word spread, discreetly at first. “I think that back then, other researchers had to be very careful when they talked about this, because they didn’t want to be seen as New Age weirdos,” Dr. Kabat-Zinn, now a professor emeritus of medicine at the University of Massachusetts, said in an interview. “So they didn’t call it mindfulness or meditation. “After a while, we put enough studies out there that people became more comfortable with it.”

One person who noticed early on was Marsha Linehan, a psychologist at the University of Washington who was trying to treat deeply troubled patients with histories of suicidal behavior. “Trying to treat these patients with some change-based behavior therapy just made them worse, not better,” Dr. Linehan said in an interview. “With the really hard stuff, you need something else, something that allows people to tolerate these very strong emotions.”

In the 1990s, Dr. Linehan published a series of studies finding that a therapy that incorporated Zen Buddhist mindfulness, “radical acceptance,” practiced by therapist and patient significantly cut the risk of hospitalization and suicide attempts in the high-risk patients.

Finally, in 2000, a group of researchers including Dr. Segal in Toronto, J. Mark G. Williams at the University of Wales and John D. Teasdale at the Medical Research Council in England published a study that found that eight weekly sessions of mindfulness halved the rate of relapse in people with three or more episodes of depression.

With Dr. Kabat-Zinn, they wrote a popular book, “The Mindful Way Through Depression.” Psychotherapists’ curiosity about mindfulness, once tentative, turned into “this feeding frenzy, of sorts, that we have going on now,” Dr. Kabat-Zinn said.

Mindfulness meditation is easy to describe. Sit in a comfortable position, eyes closed, preferably with the back upright and unsupported. Relax and take note of body sensations, sounds and moods. Notice them without judgment. Let the mind settle into the rhythm of breathing. If it wanders (and it will), gently redirect attention to the breath. Stay with it for at least 10 minutes.

After mastering control of attention, some therapists say, a person can turn, mentally, to face a threatening or troubling thought — about, say, a strained relationship with a parent — and learn simply to endure the anger or

sadness and let it pass, without lapsing into rumination or trying to change the feeling, a move that often backfires.

One woman, a doctor who had been in therapy for years to manage bouts of disabling anxiety, recently began seeing Gaea Logan, a therapist in Austin, Tex., who incorporates mindfulness meditation into her practice. This patient had plenty to worry about, including a mentally ill child, a divorce and what she described as a "harsh internal voice," Ms. Logan said.

After practicing mindfulness meditation, she continued to feel anxious at times but told Ms. Logan, "I can stop and observe my feelings and thoughts and have compassion for myself."

Steven Hayes, a psychologist at the University of Nevada at Reno, has developed a talk therapy called Acceptance Commitment Therapy, or ACT, based on a similar, Buddha-like effort to move beyond language to change fundamental psychological processes.

"It's a shift from having our mental health defined by the content of our thoughts," Dr. Hayes said, "to having it defined by our relationship to that content — and changing that relationship by sitting with, noticing and becoming disentangled from our definition of ourselves."

For all these hopeful signs, the science behind mindfulness is in its infancy. The Agency for Healthcare Research and Quality, which researches health practices, last year published a comprehensive review of meditation studies, including T.M., Zen and mindfulness practice, for a wide variety of physical and mental problems. The study found that over all, the research was too sketchy to draw conclusions.

A recent review by Canadian researchers, focusing specifically on mindfulness meditation, concluded that it did "not have a reliable effect on depression and anxiety."

Therapists who incorporate mindfulness practices do not agree when the meditation is most useful, either. Some say Buddhist meditation is most useful for patients with moderate emotional problems. Others, like Dr. Linehan, insist that patients in severe mental distress are the best candidates for mindfulness.

A case in point is mindfulness-based therapy to prevent a relapse into depression. The treatment significantly reduced the risk of relapse in people who have had three or more episodes of depression. But it may have had the opposite effect on people who had one or two previous episodes, two studies suggest.

The mindfulness treatment "may be contraindicated for this group of patients," S. Helen Ma and Dr. Teasdale of the Medical Research Council concluded in a 2004 study of the therapy.

Since mindfulness meditation may have different effects on different mental struggles, the challenge for its proponents will be to specify where it is most effective — and soon, given how popular the practice is becoming.

The question, said Linda Barnes, an associate professor of family medicine and pediatrics at the Boston University School of Medicine, is not whether mindfulness meditation will become a sophisticated therapeutic technique or lapse into self-help cliché.

"The answer to that question is yes to both," Dr. Barnes said.

The real issue, most researchers agree, is whether the science will keep pace and help people distinguish the mindful variety from the mindless.

A variety of meditative practices have been studied by Western researchers for their effects on mental and physical health.

Tai Chi An active exercise, sometimes called moving meditation, involving extremely slow, continuous movement and extreme concentration. The movements are to balance the vital energy of the body but have no religious significance.

Studies are mixed, some finding it can reduce blood pressure in patients, and others finding no effect. There is some evidence that it can help elderly people improve balance.

Transcendental Meditation Meditators sit comfortably, eyes closed, and breathe naturally. They repeat and concentrate on the mantra, a word or sound chosen by the instructor to achieve state of deep, transcendent absorption. Practitioners "lose" themselves, untouched by day-to-day concerns. Studies suggest it can reduce blood pressure in some patients.

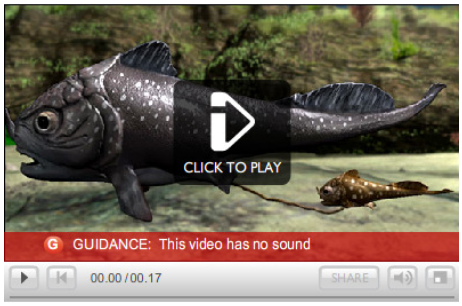
Mindfulness Meditation Practitioners find a comfortable position, close the eyes and focus first on breathing, passively observing it. If a stray thought or emotion enters the mind, they allow it to pass and return attention to the breath. The aim is to achieve focused awareness on what is happening moment to moment.

Studies find that it can help manage chronic pain. The findings are mixed on substance abuse. Two trials suggest that it can cut the rate of relapse in people who have had three or more bouts of depression.

Yoga Enhanced awareness through breathing techniques and specific postures. Schools vary widely, aiming to achieve total absorption in the present and a release from ordinary thoughts. Studies are mixed, but evidence shows it can reduce stress.

Fossil reveals oldest live birth

Rebecca Morelle
Science reporter, BBC News



What the live birth of prehistoric fish might have looked like **(Museum Victoria)**

A fossil fish uncovered in Australia is the oldest-known example of a mother giving birth to live young, scientists have reported in the journal Nature.

The 380 million-year-old specimen has been preserved with an embryo still attached by its umbilical cord.

The find, reported in Nature, pushes back the emergence of this reproductive strategy by some 200 million years.

Until now, scientists thought creatures from these times were only able to develop their young inside eggs.

Before this find, the earliest evidence for this form of reproduction came from reptile fossils dating to the Mesozoic Era (248 to 65 million years ago)

The team said the latest discovery had a remarkably advanced reproductive biology, similar to modern sharks and rays.

The extremely well-preserved fossil represents a new species of "placoderm" fish.

The placoderms were an incredibly diverse group and are thought to be the most primitive known vertebrates with jaws.

These armoured fish dominated seas, rivers and lakes throughout the Devonian Period (420-360 million years ago).

This latest placoderm specimen, which measures about 25cm (10in) in length, was found in the Gogo area of Western Australia in 2005 by a team led by John Long from Museum Victoria.

Close examination revealed that the team had unearthed something unusual.

Professor Lane said: "When I looked at it, my jaw dropped. I said: 'we are onto something big here'."

The team found an embryo and an umbilical cord, which had been exquisitely preserved along with the female fish.

The scientists have named it Materpiscis attenboroughi , in honour of the naturalist Sir David Attenborough, who first drew attention to the Gogo fish fossil sites in the 1970s.

Sir David told the team that he was "very very flattered" to have had his name given to such an "astonishing creature".

The discovery prompted the researchers to return to another fossil that they had unearthed in 1986.

Close investigation revealed that this too contained evidence of live births - it contained three embryos.

Professor Lane said: "After we saw this, we realised we had totally nailed it, everyone was convinced that this creature bore live young."

Until the latest fossil find, scientists thought life forms that existed during these times had only evolved to reproduce using externally fertilised eggs - a primitive version of the way fish spawn today.

Now, however, the team believes this ancient species bore live young through internal fertilisation (viviparity).

Dr Long commented: "This is not only the first time ever that a fossil embryo has been found with an umbilical cord, but it is also the oldest known example of any creature giving birth to live young.

"The existence of the embryo and umbilical cord within the specimen provides scientists with the first ever example of internal fertilisation - or sex - confirming that some placoderms had remarkably advanced reproductive biology.

He added: "This is a world first fossil find, and it opens up a window into the developmental biology of an entire extinct class of organisms."

Commenting on the paper, Zerina Johanson, a palaeontologist at London's Natural History Museum, said: "It is extremely rare to find preservation like this in the fossil record. This new discovery extends the record of viviparity back almost 200 million years in the fossil record.

"Placoderms represent the most primitive group of jawed vertebrates, so this work shows that the capacity for internal fertilisation and giving birth to live young evolved very early during vertebrate history."

Story from BBC NEWS: *http://news.bbc.co.uk/go/pr/fr/-/2/hi/science/nature/7424281.stm*

Regulatory B cells exist -- and pack a punch

DURHAM, N.C. – Researchers at Duke University Medical Center have uncovered definitive evidence that a small but potent subset of immune system B cells is able to regulate inflammation.

Using a new set of scientific tools to identify and count these cells, the team showed that these B cells can block contact hypersensitivity, the type of skin reactions that many people have when they brush against poison ivy.

The findings may have large implications for scientists and physicians who develop vaccines and study immune-linked diseases, including cancer. Once the cells that regulate inflammatory responses are identified, scientists may have a better way to develop treatments for many diseases, particularly autoimmune diseases such as arthritis, type 1 diabetes and multiple sclerosis.

"While the study of regulatory T cells is a hot area with obvious clinical applications, everyone has been pretty skeptical about whether regulatory B cells exist," said Thomas F. Tedder, Ph.D., chairman of the Immunology Department and lead author of the study published in the May issue of Immunity. "I am converted. They do exist."

Koichi Yanaba and Jean-David Bouaziz identified this unique subset of small white blood cells, which they call B10 cells, in the Tedder laboratory.

The researchers found that B10 cells produce a potent cytokine, called IL-10 (interleukin-10), a protein that can inhibit immune responses. The B10 cells also can affect the function of T cells, which are immune system cells that generally boost immune responses by producing cytokines. T cells also attack tumors and virus-infected cells.

The study was supported by grants from the NIH, the Association pour la Recherche contre le Cancer (ARC), Foundation Rene Touraine, and the Philippe Foundation.

Depleting B10 cells may enhance some immune responses, Tedder said. Enhancing B10 cell function may inhibit inflammation and immune responses in other diseases, like contact hypersensitivity.

"Now that we have been able to identify this regulatory B cell subset, we have already developed treatments that deplete these cells in mice. We are moving to translate these findings to benefit people," he said.

"The discovery of the ability to identify this potent regulatory cell type should provide important clues to how the immune system regulates itself in response to vaccines as well as infectious agents," says Barton F. Haynes, M.D., leader of the international Center for HIV/AIDS Vaccine Immunology (CHAVI), a consortium of universities and academic medical centers, and director of the Duke Human Vaccine Institute. "This information should enable researchers to design ways to help the immune system control infections more effectively, and could be a useful advance as we refine approaches to preventing HIV infection."

There's a huge initiative underway to look at regulatory T cells in autoimmune disease, HIV infection, and cancer therapy," Tedder said. "What we have also shown is that it is not only regulatory T cells, but also regulatory B cells that could prevent a person from making effective immune responses in HIV and many other diseases, particularly cancer."

The Duke researchers developed a way to mark the B10 cells so that they could see that just these cells were producing IL-10. Previously, scientists could only purify a population of B cells and see whether IL-10 could be produced by some of these cells in the population.

In this study, they found that the B10 cells represented only 1-2 percent of all of the B cells in the spleen of a normal mouse. Before this, no one had definitively identified this B cell subset or such regulatory B cells in normal mice, although B cell regulatory function had been described in some genetically altered mice with chronic inflammation.

"In this study, we could directly look at the B cells that were producing IL-10, and figure out what their cell surface molecules looked like, so that we could isolate them. This allowed us to show that this rare subset of B cells controlled immune responses by producing IL-10, which inhibits T cell inflammatory responses," Tedder said.

The scientists studied a special mouse (CD19-deficient) with altered genes that give them an increased contact hypersensitivity reaction. As it turned out, these mice lacked B10 cells, which resulted in exaggerated inflammation reaction. "This allowed us to show that giving CD19-deficient mice a few B10 cells had a big effect on reducing inflammation," Tedder said.

They found that depleting all B cells in the mice also resulted in worse inflammation. Since total B cell depletion therapies are now being used to treat people with B cell cancers and autoimmune disease, these findings help to further explain how these therapies treat disease. They also open the door to creating new therapies that take advantage of the power of B10 cells.

This is the first of several papers that will describe cases in which regulatory B10 cells help control immune responses, Tedder said.

Karen Haas and Jonathan Poe of the Duke Department of Immunology, and Manabu Fujimoto of the Department of Dermatology at Kanazawa University Graduate School of Medical Science in Ishikawa, Japan, were the paper's other authors.

Estrogen Helps Drive Distinct, Aggressive Form of Prostate Cancer

Innovative Technology Reveals a New Hormonal Target for Drug Treatment, Scientists Say

NEW YORK (May 27, 2008) — Using a breakthrough technology, researchers led by a Weill Cornell Medical College scientist have pinpointed the hormone estrogen as a key player in about half of all prostate cancers.

Estrogen-linked signaling helps drive a discrete and aggressive form of the disease caused by a chromosomal translocation, which in turn results in the fusion of two genes.

"Fifty percent of prostate cancers harbor a common recurrent gene fusion, and we believe that this confers a more aggressive nature to these tumors," explains study senior author Dr. Mark A. Rubin, professor of pathology and laboratory medicine, and vice chair for experimental pathology at Weill Cornell Medical College. Dr. Rubin is also attending pathologist at New York-Presbyterian Hospital/Weill Cornell Medical Center.

"Interfering with this gene fusion — or its downstream molecular pathways — will be crucial in the search for drugs that fight the disease. Based on our new data, we now believe that inhibiting estrogen may be one way of doing so," he says.

The findings are published in the May 27 online edition of the Journal of the National Cancer Institute. Dr. Rubin conducted the study while at the Brigham and Women's Hospital and in collaboration with Dr. Todd Golub and other members of the Broad Institute of MIT and Harvard, in Cambridge, Mass. His team is now continuing this line of research at Weill Cornell.

Dr. Rubin, along with researchers at the University of Michigan, first discovered and described the common fusions between the TMPRSS2 and ETS family member genes subset of prostate cancer in the journal Science in 2005. "The discovery showed that these malignancies occur after an androgen (male hormone)-dependent gene fuses with an oncogene — a type of gene that causes cancer," he explains.

Experts have long understood that male hormones help spur prostate cancer — in fact, androgen-deprivation therapy is a first-line treatment against the disease. And yet the disease can progress despite androgen reduction, suggesting that other pathways might be at work.

"So, we wanted to learn more — what is the genetic and molecular 'fingerprint' of this aggressive subset of prostate tumor?" Dr. Rubin says.

Answering that question required the analysis of 455 prostate cancer samples from trials in Sweden and the United States that were conducted as far back as the mid-1970s.

"These samples were placed in fixative and not frozen, so we needed new methods of retrieving the genetic information," Dr. Rubin says. To do so, his team led by co-lead authors Dr. Sunita Setlur and Dr. Kirsten Mertz developed an innovative technology for effectively "reading" the gene transcription profiles hidden in the samples.

"That led us to perform the largest gene-expression microarray analysis yet conducted in prostate cancer research, amassing information on more than 6,000 genes," Dr. Rubin says. "This allowed us to obtain a robust, 87-gene expression 'signature' that distinguishes fusion-positive TMPRSS2-ERG cancers from other prostate malignancies."

A close analysis of the signature yielded a surprise: that estrogen-dependent molecular pathways appear to play a crucial role in regulating (and encouraging) this aggressive subset of prostate cancer.

While estrogen is typically thought of as a "female" hormone, men produce it as well.

"Now, we show for the first time that this natural estrogen can stimulate the production of the cancer-linked TMPRSS2-ERG transcript, via the estrogen receptor (ER)-alpha and ER-beta. These receptors are found on the surface of some prostate cancer cells," Dr. Rubin explains.

The finding could have implications for prostate cancer research, including drug development. According to Dr. Rubin, "We now believe that agents that dampen estrogen activity (ER-alpha antagonists) could inhibit fusion-positive prostate cancers. Alternatively, any intervention that boosts estrogen activity (ER-alpha) might also give a boost to these aggressive malignancies."

Research into just why fusion-positive prostate cancers are so aggressive — and potential molecular drug targets to help curb that aggression — will continue under Dr. Rubin's direction at Weill Cornell, in collaboration with members of his group and with computational biologist Dr. Francesca Demichelis.

"The technological achievement of using fixed samples that were up to 30 years old is significant," Dr. Rubin says. "In the future, we hope to explore banked tissues from clinical trials to help understand why they failed. This should lead to insight for designing the next trial."

This work was funded by the U.S. National Institutes of Health, a Prostate SPORE grant at the Dana-Farber/Harvard Cancer Center, Swiss Foundation for Medical-Biological Grants SSMBS, U.S. Department of Defense and the Prostate Cancer Foundation.
Co-researchers include study co-lead authors Dr. Sunita Setlur and Dr. Kirsten Mertz of Brigham and Women's Hospital and Harvard Medical School, Boston; Dr. Yujin Hoshida and Dr. Todd Golub of the Broad Institute and the Dana-Farber Cancer Institute, Boston; Dr. Francesca Demichelis of Weill Cornell Medical College and Harvard Medical School, Boston; Dr. Mathieu Lupien of the Dana-Farber Cancer Institute; Dr. Sven Perner and Jeff Tang of Weill Cornell Medical College; Andrea Sboner of Yale University, New Haven; Dr. Yudi Pawitan and Dr. Katja Fall of the Karolinska Institutet, Stockholm, Sweden; Dr. Ove Andren, Dr. Jan-Erik Johansson and Dr. Swen-Olof Andersson, of Orebro University Hospital, Orebro, Sweden; Laura A. Johnson of Brigham and Women's Hospital, Boston; Dr. Hans-Olov Adami, of Karolinska Institutet, Sweden, and Harvard School of Public Health, Boston; Dr. Stefano Calza, of the Karolinska Institutet, Sweden, and the University of Brescia, Italy; Dr. Arul M. Chinnaiyan, Dr. Daniel Rhodes and Scott Tomlins, of the University of Michigan Medical School, Ann Arbor; Dr. Lorelei Mucci and Dr. Meir Stampfer of Harvard Medical School, Harvard School of Public Health and Brigham and Women's Hospital, Boston; Dr. Philip Kantoff of Dana-Farber Cancer Institute and Harvard Medical School; Dr. Eberhard Varenhorst, of University Hospital Linkoping, Sweden; and Dr. Myles Brown of the Dana-Farber Cancer Institute. Dr. Mark A. Rubin, Dr. Francesca Demichelis, Dr. Sven Perner, Dr. Arul M. Chinnaiyan and Scott Tomlins are co-inventors on a patent filed by the University of Michigan and the Brigham and Women's Hospital, covering the diagnostic and therapeutic fields for ETS fusions in prostate cancer.

New breathing exercises help manage asthma

A presentation that demonstrates breathing exercises designed to help reduce the use of asthma inhalers is today available to the general public for free from the Cooperative Research Centre (CRC) for Asthma and Airways website.

The 40 minute production is in response to a research paper on the management of asthma through the use of breathing exercises, conducted by researchers and doctors at Sydney's Woolcock Institute of Medical Research and Melbourne's Alfred Hospital, which was published in the August 20061 edition of Thorax.

The results of this study showed that asthmatics who undertook regular breathing exercises reduced their preventer medication levels by up to half and reliever use by up to 86%.

The presentation demonstrates the breathing exercise techniques used in the study and features Professor Christine Jenkins, Head of Asthma Research at the Woolcock Institute and Project Leader of the research study.

In the presentation, she outlines our current understanding of asthma, and the potential role of breathing techniques in helping to control asthma symptoms. She puts this into the context of good asthma management and review. Two different groups of breathing techniques are demonstrated. One set is for practicing daily and one set is for relief of asthma symptoms.

Professor Christine Jenkins, Head of Asthma Research at the Woolcock Institute said, "The research study was designed to measure the effect of two very different exercise regimes on a person's asthma symptoms, lung function, use of medication and quality of life".

"However it found no evidence to favour one breathing technique over the other. Instead, both groups of exercises were associated with a dramatic reduction in reliever use. Using either type of exercise was effective in markedly reducing the use of reliever medication. A reduction in inhaled corticosteroid (ICS) dose was also achieved, probably resulting from trial participation and clinical care in the study."

According to Professor Jenkins the results of regularly undertaking the exercises could be particularly beneficial to the management of patients with mild asthma symptoms, who use a reliever frequently,

"Our study suggests that breathing exercises as a first-line symptom treatment can help to reinforce the message of relaxation and self-efficacy and provide a deferral strategy for beta-agonist use.

"The presentation advises a person to do the exercises twice a day and also whenever they experience asthma symptoms," she said.

"We hope that people with asthma will avail themselves of the information, presented in this easily understood format, and see it as a complementary approach to their asthma management."

The presentation can be viewed at the Asthma CRC's website www.asthmacrc.org.au.
For further information the general public can call (02) 9036 3125.

Ibuprofen, aspirin, naproxen may be equally effective at reducing risk of Alzheimer's disease

ST. PAUL, Minn. – Different types of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen, and aspirin, appear to be equally effective in lowering the risk of Alzheimer's disease, according to the largest study of its kind published in the May 28, 2008, online issue of Neurology®, the medical journal of the American Academy of Neurology. Experts have debated whether a certain group of NSAIDs that includes ibuprofen may be more beneficial than another group that includes naproxen and aspirin.

Using information from six different studies, researchers examined data on NSAID use in 13,499 people without dementia. Over the course of these six studies, 820 participants developed Alzheimer's disease.

Researchers found that people who used NSAIDs had 23 percent lower risk of developing Alzheimer's disease compared to those who never used NSAIDs. The risk reduction did not appear to depend upon the type of NSAID taken.

"This is an interesting finding because it seems to challenge a current theory that the NSAID group which includes ibuprofen may work better in reducing a person's risk of Alzheimer's," said study author Peter P. Zandi, PhD, with Johns Hopkins Bloomberg School of Public Health in Baltimore, MD. "The NSAID group that includes ibuprofen was thought to target a certain type of plaque in the brain found in Alzheimer's patients. But our results suggest there may be other reasons why these drugs may reduce the risk of Alzheimer's."

The study's lead author Chris Szekely, PhD, with Cedars Sinai Medical Center in Los Angeles, says the discrepancy between studies such as this one and the negative clinical trials of NSAIDs in treatment or prevention of Alzheimer's need to be further explored.

Data used in the study were collected with support from the National Institutes of Health and the Canadian Institutes of Health Research.

Large methane release could cause abrupt climate change as happened 635 million years ago

UCR-led research team says methane-triggered global warming ended last 'snowball' ice age; dramatically reorganized Earth system

RIVERSIDE, Calif. – An abrupt release of methane, a powerful greenhouse gas, about 635 million years ago from ice sheets that then extended to Earth's low latitudes caused a dramatic shift in climate, triggering a series of events that resulted in global warming and effectively ended the last "snowball" ice age, a UC Riverside-led study reports.

The researchers posit that the methane was released gradually at first and then in abundance from clathrates – methane ice that forms and stabilizes beneath ice sheets under specific temperatures and pressures. When the ice sheets became unstable, they collapsed, releasing pressure on the clathrates which began to degas.

"Our findings document an abrupt and catastrophic means of global warming that abruptly led from a very cold, seemingly stable climate state to a very warm also stable climate state with no pause in between," said Martin Kennedy, a professor of geology in the Department of Earth Sciences, who led the research team.

"This tells us about the mechanism, which exists, but is dormant today, as well as the rate of change," he added. "What we now need to know is the sensitivity of the trigger: how much forcing does it take to move from one stable state to the other, and are we approaching something like that today with current carbon dioxide warming." Study results appear in the May 29 issue of Nature.

According to the study, methane clathrate destabilization acted as a runaway feedback to increased warming, and was the tipping point that ended the last snowball Earth. (The snowball Earth hypothesis posits that the Earth was covered from pole to pole in a thick sheet of ice for millions of years at a time.)

"Once methane was released at low latitudes from destabilization in front of ice sheets, warming caused other clathrates to destabilize because clathrates are held in a temperature-pressure balance of a few degrees," Kennedy said. "But not all the Earth's methane has been released as yet. These same methane clathrates are present today in the Arctic permafrost as well as below sea level at the continental margins of the ocean, and remain dormant until triggered by warming.

"This is a major concern because it's possible that only a little warming can unleash this trapped methane. Unzippering the methane reservoir could potentially warm the Earth tens of degrees, and the mechanism could be geologically very rapid. Such a violent, zipper-like opening of the clathrates could have triggered a catastrophic climate and biogeochemical reorganization of the ocean and atmosphere around 635 million years ago."

Today, the Earth's permafrost extends from the poles to approximately 60 degrees latitude. But during the last snowball Earth, which lasted from 790 to 635 million years ago, conditions were cold enough to allow clathrates to extend all the way to the equator.

According to Kennedy, the abruptness of the glacial termination, changes in ancient ocean-chemistry, and unusual chemical deposits in the oceans that occurred during the snowball Earth ice age have been a curiosity and a challenge to climate scientists for many decades.

"The geologic deposits of this period are quite different from what we find in subsequent deglaciation," he said. "Moreover, they immediately precede the first appearance of animals on earth, suggesting some kind of

environmental link. Our methane hypothesis is capable also of accounting for this odd geological, geochemical and paleooceanographic record."

Also called marsh gas, methane is a colorless, odorless gas. As a greenhouse gas, it is about 30 times more potent than carbon dioxide, and has largely been held responsible for a warming event that occurred about 55 million years ago, when average global temperatures rose by 4-8 degrees Celsius.

When released into the ocean-atmosphere system, methane reacts with oxygen to form carbon dioxide and can cause marine dysoxia, which kills oxygen-using animals, and has been proposed as an explanation for major oceanic extinctions.

"One way to look at the present human influence on global warming is that we are conducting a global-scale experiment with Earth's climate system," Kennedy said. "We are witnessing an unprecedented rate of warming, with little or no knowledge of what instabilities lurk in the climate system and how they can influence life on Earth. But much the same experiment has already been conducted 635 million years ago, and the outcome is preserved in the geologic record. We see that strong forcing on the climate, not unlike the current carbon dioxide forcing, results in the activation of latent controls in the climate system that, once initiated, change the climate to a wholly different state."

As part of their research, Kennedy and his colleagues collected hundreds of marine sediment samples in South Australia for stable isotope analysis, an important tool used in climate reconstruction. At UCR, the researchers analyzed the samples and found the broadest range of oxygen isotopic variation ever reported from marine sediments that they attribute to melting waters in ice sheets as well as destabilization of clathrates by glacial meltwater.

Next in their research, Kennedy and his colleagues will work on estimating how much of the temperature change that occurred 635 million years ago was due solely to methane.

Kennedy, who directs the Global Climate and Environmental Change Graduate Program in UCR's Department of Earth Sciences, was joined in the study by UCR's David Mrofka; and Chris von der Borch of Flinders University, Australia. The study was supported by grants from the National Science Foundation and NASA Exobiology.

Medication shows promise for patients with severe chronic constipation

ROCHESTER, Minn. -- A new medication appears to offer significant relief to patients with severe chronic constipation while minimizing the likelihood of cardiac-related side effects, according to results of a study published this week in the New England Journal of Medicine.

The trial involved 38 medical centers and was led by Michael Camilleri, M.D., a Mayo Clinic gastroenterologist. Patients who met the study criteria were randomly assigned to receive either of two dosage levels of prucalopride, a medication that stimulates protein receptors involved in contraction of the colon, or a placebo.

"Many more of the patients taking prucalopride were able to have spontaneous bowel movements without having enemas or taking laxatives, as compared to those who were given placebo," says Dr. Camilleri. "The time it took to have a first bowel movement was much shorter, and quality of life and other abdominal symptoms also were improved for those taking the study drug."

Constipation is a common medical problem, affecting about 15 percent of Americans who spend several billion dollars each year on laxatives and other treatments. Prevalence is higher among women and African-Americans and is particularly increased in the elderly. This study involved patients with an extreme but common version of constipation called severe chronic constipation. To participate, patients had to have at least six months of constipation, defined as an average of fewer than three bowel movements a week. Those who had more than four bowel movements during the two-week "run-in" period before treatment began were not eligible.

"The normal range of bowel movements is anywhere from three per day to three per week," explains Dr. Camilleri. "The 620 patients studied in this trial were severely constipated, averaging only one bowel movement during the two weeks before entering treatment, and most had struggled with the problem for several years, not merely months."

The 2 milligram (mg) and 4 mg doses of prucalopride appeared roughly equal in benefit, with about 30 percent of patients averaging three bowel movements per week during the 12-week study. Only 12 percent of patients on placebo averaged three bowel movements per week. Nearly half (47.3 and 46.6 percent, respectively) of the patients taking prucalopride increased their bowel movements by at least one per week, while about a quarter (25.8 percent) of those on placebo had a similar improvement.

The most common adverse effect from the drug was diarrhea, which tended to occur in the early stages of treatment, but most patients later settled into a more normal routine of bowel movements. Increased bowel movements and diarrhea are expected effects of the drug. Only 1.5 percent and 4.4 percent of patients treated with 2 mg and 4 mg of prucalopride, respectively, stopped the drug due to diarrhea. "This suggests that the

diarrhea was less bothersome than the constipation had been," Dr. Camilleri says. Headaches were a less frequent side effect.

Dr. Camilleri says the cardiac risk issues that have been raised about related drugs for constipation including tegaserod, appear to be less of a concern for prucalopride. "Prucalopride is highly selective in its effect, and doesn't interact significantly with other protein receptors, such as those involved in regulating heart rhythm," he explains. "We conducted electrocardiogram testing during the study and did not find heart rhythm issues, although two of the three patients who withdrew from the study did have symptoms, palpitations and dizziness that may have been attributable to an effect on the cardiovascular system."

Prucalopride is not yet approved for use in the United States or in any other country.

Dr. Camilleri says results from other studies will need to be compiled and published, and safety and efficacy data submitted to the Food and Drug Administration for review, before it can be approved in the United States as a treatment for chronic constipation.

Where man boldly goes, bacteria follow

Are we contaminating space?

Life in outer space is an absolute certainty, and it is likely to be more familiar than we might think, according to an article in the May issue of Microbiology Today. Ever since the start of the space race we have sent more than just satellites and astronauts into space: spacecraft are not routinely decontaminated and are teeming with microbial life.

"Wherever man boldly goes his microbial fauna is sure to follow," said Lewis Dartnell, an astrobiologist at University College London. The Russian space station Mir was launched in 1986 and microbial studies investigated the diversity of bacteria living alongside the astronauts. In 1998, free-floating blobs of water found during a NASA mission to the station were analyzed and discovered to contain microbes including faecal bacteria like E. coli, plague bacterium-related species of Yersinia, and even what was suspected to be Legionella, as well as fungi, amoebae and protozoa.

"Preventing the spread of microbial life between worlds of the solar system has been a top priority for decades now," said Lewis. "This effort is known as planetary protection." Today's International Space Station (ISS) is much cleaner than Mir was 20 years ago, thanks to HEPA filters, weekly cleaning and biweekly disinfecting regimes. But inevitably, the ISS is still far from being bug-free; recent sampling revealed the bacterium Staphylococcus epidermidis surviving in different areas.

But it's not just planets we need to protect – astronauts are at increased risk of infection in space. Respiratory infections are common among astronauts and diseases occur in a quarter of space shuttle flights. "Prolonged exposure to cosmic radiation and microgravity is believed to have a negative effect on the immune system, and disease transmission is enhanced within the closed environment of recycled air and water," said Lewis Dartnell. Microbes also pose an increased risk of allergies, toxic air and water supply and even biodegradation of critical spacecraft components.

This week, the Phoenix lander touched down on Mars, hoping to take the first ever direct measurements of Martian water and organic molecules. "To guarantee the cleanliness of the robotic arm, it was enclosed in a biobarrier bag – effectively an interplanetary condom," said Lewis. But this will not be a feasible control measure for humans. "Humans and spaceships are inherently dirty and once we arrive to plant flags in the rusty soil our microbial entourage will begin leaking out onto Mars." What's more, microbes have an uncanny ability to survive as spores, resistant to heat, cold and radiation. "Once humans have visited Mars, we may never be certain that any biological discoveries weren't simply signs of our own dirty sleeves," said Lewis Dartnell.

In fact, we might actually need to take microbes on a manned mission to Mars. "For longer missions, it will not be possible to take sufficient supplies from Earth," said Lewis. "Scientists are developing ingenious life support systems relying on plants and micro-organisms to provide food, waste recycling and water purification." Of course, in this case, an outbreak of harmful microbes could crash life support systems as well as affecting the health of the crew, endangering the whole mission. "For better or worse, space bugs are here to stay."

Scripps Research scientists find seizure drug reverses cellular effects

Study supports promise of gabapentin as potential therapy for alcoholism

In the new research, published in the May 28, 2008 edition of The Journal of Neuroscience, the scientists found that gabapentin normalizes the action of certain brain cells altered by chronic alcohol abuse in an area of the brain known as the central amygdala, which plays an important role in fear- and stress-related behaviors, as well as in regulating alcohol drinking. In the study, alcohol-dependent rodents receiving gabapentin drank less alcohol.

“The results are exciting,” said Scripps Research Assistant Professor Marisa Roberto, Ph.D., who was first author of the study. “Our research shows that gabapentin not only changes the alcohol-consumption patterns of addicted rats (and not of the control group), but also may reverse some of the effects of addiction on a specific neurotransmitter in the brain.”

"This is an example of the strength of the translational approach of the Pearson Center, where the clinical uses of gabapentin led us to hypothesize that gabapentin may act to restore homeostatic dysregulation of the GABAergic system," said George Koob, Ph.D., chair of the Scripps Research Committee on the Neurobiology of Addictive Disorders and co-director of the Pearson Center for Alcoholism and Addiction Research at Scripps Research. "Cellular and behavioral studies converged to suggest that indeed gabapentin could normalize GABAergic tone in a specific brain region known to be dysregulated in dependent animals. Such results provide a strong rationale for translating these observations back to the clinical setting for the treatment of alcoholism."

In previous studies, gabapentin has been shown to effectively treat alcohol withdrawal and reduce alcohol consumption and cravings following detoxification in alcoholics. However, how gabapentin could act to combat alcohol dependence in the brain has been unclear. The new study sheds light on this question by detailing the action of gabapentin (known commercially as Neurontin)—a structural analogue of the inhibitory synaptic transmitter gamma aminobutyric acid (GABA)—on neural signaling in the brain.

In the new study, the scientists first tested the effects of gabapentin on the behavior of alcohol-dependent and non-dependent rats. The researchers found that alcohol-dependent rats that received gabapentin drank significantly less alcohol and demonstrated fewer anxiety-like behaviors in the face of alcohol abstinence than those who did not receive the drug. The behavior of non-dependent rats receiving gabapentin remained unaffected. These results were observed both when the rats received gabapentin systemically and when the medication was infused directly into the central amygdala region of the brain.

At the cellular level, dependence on alcohol has been associated with increased strength of inhibitory synapses (junctions between two nerve cells) in the central amygdala. In the new study, the scientists found gabapentin, like alcohol, increased the strength of these central amygdala inhibitory synapse cells from non-dependent rats, but decreased their strength in cells from alcohol-dependent rats.

Interestingly, these effects of gabapentin disappeared in the presence of a specific inhibitor of so-called GABAB receptors, indicating that gabapentin’s cellular mechanisms likely involve changes in release of the transmitter GABA at the inhibitory synapses. The scientists also found that the sensitivity of GABAB receptors decreased with alcohol dependence, suggesting a biological mechanism for the development of alcohol dependence in general and for gabapentin’s contrasting effects before and after long-term alcohol exposure in particular.

The scientists plan to further explore the mechanism of action of gabapentin in the brain. In addition, clinical trials on the effectiveness of gabapentin as a treatment for alcohol dependence are currently under way at The Scripps Research Institute.

In addition to Roberto and Koob, the study “Cellular and Behavioral Interactions of Gabapentin with Alcohol Dependence” was authored by Nicholas W. Gilpin, Maureen T. Cruz, and George R. Siggins of Scripps Research; Laura E. O’Dell of the University of Texas at El Paso; and Andrew C. Morse of Brain Cells.

The work was supported by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health, the Harold L. Dorris Neurological Research Institute at Scripps Research, and The Scripps Research Institute.

How fairness is wired in the brain

PASADENA, Calif.--In the biblical story in which two women bring a baby to King Solomon, both claiming to be the mother, he suggests dividing the child so that each woman can have half. Solomon's proposed solution, meant to reveal the real mother, also illustrates an issue central to economics and moral philosophy: how to distribute goods fairly.

Now, researchers at the California Institute of Technology have discovered that reason struggles with emotion to find equitable solutions, and have pinpointed the region of the brain where this takes place. The concept of fairness, they found, is processed in the insular cortex, or insula, which is also the seat of emotional reactions.

"The fact that the brain has such a robust response to unfairness suggests that sensing unfairness is a basic evolved capacity," notes Steven Quartz, an associate professor of philosophy at Caltech and author of the study, voicing a sentiment that anyone who has seen children fight over a treat can relate to.

"The movement to look into the neural basis for ethical decision making is only about seven years old," Quartz says. "This is the first study where people made real decisions with real consequences."

The subjects in the study, 26 men and women between 28 and 55 years old, faced a real-world moral dilemma. They started their participation in the experiment by reading a short biography of each of the 60 orphans at the Canaan Children's Home in Uganda. The orphanage would receive a sum of money that would depend on decisions the subjects made. In the end, $2,279 was donated.

While a functional magnetic resonance imaging (fMRI) machine scanned their brains for peak activity regions, the participants each had about eight seconds to decide how to distribute meals among groups of children in different scenarios. In one, their choice would grant either four extra meals to each of two children or six extra meals to one child. The children they didn't choose would get nothing. In another scenario, the kids had been given extra meals and the subjects had to decide whether it was better to take six meals away from each of two kids, or ten meals away from one.

Ultimately the subjects' brains made a choice, and Quartz and his collaborators got to peek into where that calculation was made. "You wonder what is happening at different levels--is your brain's decision right or not""

When they got to give food to the children, the study participants' orbital frontal cortex, the reward region of the brain, lit up. When instead they had to take food away, the insula region--the emotional processor--was activated.

Quartz suggests that the insula was triggered by the inequity of the choices. The activity varied considerably across subjects, indicating that individual differences in moral sensitivity may be rooted in the strength of the biological responses, he adds.

"The emotional response to unfairness pushes people from extreme inequity and drives them to be fair," Quartz says. This observation, he adds, suggests that "our basic impulse to be fair isn't a complicated thing that we learn."

This study, which appears in the May 8 early online edition of the journal Science, is the first to examine "neuroethics"--the neural underpinnings of moral decision making--with real-world consequences. It may also help guide how to make policy decisions about distributing resources. And, adds Jonathan Katz, chair of Caltech's Division of the Humanities and Social Sciences, "It's one of the first studies to bridge humanities research with social science and biology," a central effort at Caltech.

'Horror frog' breaks own bones to produce claws

* 00:01 28 May 2008
* NewScientist.com news service
*** Catherine Brahic**

"Amphibian horror" isn't a movie genre, but on this evidence perhaps it should be. Harvard biologists have described a bizarre, hairy frog with cat-like extendable claws.

Trichobatrachus robustus actively breaks its own bones to produce claws that puncture their way out of the frog's toe pads, probably when it is threatened.

David Blackburn and colleagues at Harvard University's Museum of Comparative Zoology, think the gruesome behaviour is a defence mechanism.

The researchers say there are salamanders that force their ribs through their skin to produce protective barbs on demand, but nothing quite like this mechanism has been seen before.

The feature is also found in nine of the 11 frogs belonging to the Astylosternus genus, most of which live in Cameroon.

Male Hairy Frogs grow threads of vascularised skin during mating season **(Image: Gustavocarra / Creative Commons License)**

Instant weapon

"Some other frogs have bony spines that project from their wrist, but in those species it appears that the bones grow through the skin rather than pierce it when needed for defence," says Blackburn.

At rest, the claws of T. robustus, found on the hind feet only, are nestled inside a mass of connective tissue. A chunk of collagen forms a bond between the claw's sharp point and a small piece of bone at the tip of the frog's toe.

The other end of the claw is connected to a muscle. Blackburn and his colleagues believe that when the animal is attacked, it contracts this muscle, which pulls the claw downwards. The sharp point then breaks away from the bony tip and cuts through the toe pad, emerging on the underside.

Hirsute horror

The end result may look like a cat's claw, but the breaking and cutting mechanism is very different and unique among vertebrates. Also unique is the fact that the claw is just bone and does not have an outer coating of keratin like other claws do.

Because Blackburn has only studied dead specimens, he says he does not know what happens when the claw retracts – or even how it retracts. It does not appear to have a muscle to pull it back inside so the team think it may passively slide back into the toe pad when its muscle relaxes.

"Being amphibians, it would not be surprising if some parts of the wound heal and the tissue is regenerated," says Blackburn.

Males of the species, which grows to about 11 centimetres, also produce long hair-like strands of skin and arteries when they breed (see image). It is thought that the "hairs" allow them to take in more oxygen through their skin while they take care of their brood.

The sharp bony claws look like small barbs **(Image: Blackburn)**

Spiky snack

In Cameroon, they are roasted and eaten. Hunters use long spears and machetes to kill the frogs, apparently to avoid being hurt by their claws.

"This is an incredible story," says Ian Stephen, curator of herpetology at the Zoological Society of London, UK. "Some frogs grow spines on their thumbs during breeding season, but this is entirely different."

"For me, it highlights the need for a lot more research on amphibians especially in light of the threat of mass extinctions," he adds.

The existence of frogs with erectile claws like cats was first described by Belgian zoologist George Boulenger in 1900 in frogs found in the French Congo, now the Republic of Congo.

Journal reference: Biology Letters (DOI: 10.1098/rsbl.2008.0219)

Nothing beats a home-cooked meal – even for apes

* 12:30 28 May 2008
* NewScientist.com news service
*** Ewen Callaway**

Chimps, bonobos, gorillas and orang-utans all seem to prefer cooked food to raw forms of meat, sweet potatoes and carrots, a team of anthropologists has found.

This suggests that our ancestors had an innate preference for cooked meals, and probably started cooking as soon as they wielded fire, says Richard Wrangham, an anthropologist at Harvard University, Cambridge, Massachusetts, US, who led the new study.

"It would not be long before bits of food would get accidentally cooked and if they liked it they would do it again," he told New Scientist.

Wrangham is using the finding that apes liked cooked food to support his argument that cooking was pivotal in human evolution.

Cooked food is easier to digest, he says, and eating it helped propel anatomical changes in Homo erectus around 1.8 million years ago, including bigger brains, smaller guts and weaker teeth. But other anthropologists say data supporting the claim is scant.

First fires

After about 250,000 years ago there is good evidence, in the form of the charred remains of hearths, that our ancestors controlled fire. Further back in time, though, the evidence isn't so strong.

Wrangham, however, argues that darkened patches of dirt near fossil bones are evidence that pre-humans harnessed fire more than 1.6 million years ago.

To determine whether prehistoric hominids might have quickly used fire to cook their food because it improved taste or texture, Wrangham and colleague Victoria Wobber, of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, tested whether several species of great apes chose cooked foods over raw items.

"We wanted to see if we could regard the ancestors of humans, the australopithecine ancestors, as pre-adapted to enjoy cooked food," he says.

When presented with carrots and sweet potatoes, either raw or cooked, captive chimps showed preferences for the cooked food. The chimps had tasted cooked food before, which may have influenced the outcome, and Wrangham says the novelty of cooked food could also have influenced the results.

Physical proof

Another experiment with captive chimps, bonobos, gorillas and orang-utans also found the apes had an affinity for cooked meats, even though they had probably never tasted cooked meat before.

Experiments to determine why apes liked cooked foods – because they were sweeter or softer, for instance – were inconclusive.

If apes take to cooked foods quickly, then our ancestors probably did too, Wrangham reasons. "I can't imagine that it would have taken more than a generation for these apes to discover that their food tasted better when it was warmed," he says.

However, Henry Bunn, a paleoanthropologist at the University of Wisconsin in Madison, US, says Wrangham's early cooking theory is based on too little physical proof.

"Chimps are not australopithecines or early Homo, and their food preferences don't constitute evidence of what happened," he says. Journal reference: *Journal of Human Evolution, DOI: 10.1016/j.hevol.2008.03.003*

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To 0/30/2008

Fastest spinning asteroid spied by amateur stargazer

* 17:48 28 May 2008
* NewScientist.com news service
*** Hazel Muir**

An amateur astronomer has discovered the fastest rotating natural object known in our Solar System. It's a house-sized space rock that zoomed past the Earth in April 2008, spinning once every minute.

The asteroid's record-breaking spin rate is not scientifically surprising. But the finding, which comes from an educational observatory project, shows that providing the public and schools with professional grade telescopes can lead to record-breaking astronomical discoveries.

"It's nice to have this record at the moment, but we're really hoping to get some schools on board to break that record in future, working with amateurs," says Paul Roche of Cardiff University, director of the Faulkes Telescope Project, an educational charity founded in 2000.

The project offers schools and both amateur and professional astronomers access to two cutting-edge telescopes at observatories in Hawaii and Australia.

The newly discovered asteroid, known as 2008 HJ, was first discovered on 24 April by a robotic telescope in Socorro, New Mexico. It was then flagged up as a potential observing target by the Faulkes project's website.

Cutting-edge telescopes

Richard Miles, a Dorset-based retired petrochemical researcher and a vice-president of the British Astronomical Association, measured the spin rate of 2008 HJ on 29 April by remotely controlling the 2-metre Faulkes telescope at Siding Spring in Australia. The asteroid was only visible for a few days as it came within 2.8 lunar distances of Earth.

The asteroid was travelling at a speed of about 45 kilometres per second relative to the Earth. Short exposures of a few seconds showed telltale changes in brightness as the oblong-shaped asteroid turned, each face reflecting sunlight differently.

Superfast rotator

The pattern revealed that the asteroid revolves once every 42.7 seconds, making it a "superfast rotator". The International Astronomical Union has since confirmed the discovery.

The rotation rate of 2008 HJ smashes the record set by the previous holder, 2000 DO8, discovered eight years ago. That asteroid rotates around half as fast, once every 78 seconds.

Miles's observations suggest that 2008 HJ is a compact stony object some 12 metres by 24 metres wide, but probably with a mass exceeding 5000 tonnes.

The spin rate of the rock fits with the theory that the smaller the asteroid, the faster it can revolve. "People have suspected that these asteroids with very high rotation speeds exist," Roche told New Scientist. "This now pushes us into a new area and hopefully we'll find something even faster in the future."

Roche encourages schools to take up the challenge. "This discovery is a great incentive for schools – we're trying to encourage them to do real science," he says. "I think they can jump on this bandwagon now that the amateurs have opened it up."

Mars' water appears to have been too salty to support life

Salt deposits suggest salinity was commonly above what terrestrial life can tolerate

CAMBRIDGE, Mass. -- A new analysis of the Martian rock that gave hints of water on the Red Planet -- and, therefore, optimism about the prospect of life -- now suggests the water was more likely a thick brine, far too salty to support life as we know it.

The finding, by scientists at Harvard University and Stony Brook University, is detailed this week in the journal Science.

"Liquid water is required by all species on Earth and we've assumed that water is the very least that would be necessary for life on Mars," says Nicholas J. Tosca, a postdoctoral researcher in Harvard's Department of Organismic and Evolutionary Biology. "However, to really assess Mars' habitability we need to consider the properties of its water. Not all of Earth's waters are able to support life, and the limits of terrestrial life are sharply defined by water's temperature, acidity, and salinity."

Together with co-authors Andrew H. Knoll and Scott M. McLennan, Tosca analyzed salt deposits in four-billion-year-old Martian rock explored by NASA's Mars Exploration Rover, Opportunity, and by orbiting spacecraft. It was the Mars Rover whose reports back to Earth stoked excitement over water on the ancient surface of the Red Planet.

The new analysis suggests that even billions of years ago, when there was unquestionably some water on Mars, its salinity commonly exceeded the levels in which terrestrial life can arise, survive, or thrive.

"Our sense has been that while Mars is a lousy environment for supporting life today, long ago it might have more closely resembled Earth," says Knoll, Fisher Professor of Natural Sciences and professor of Earth and planetary sciences at Harvard. "But this result suggests quite strongly that even as long as four billion years ago, the surface of Mars would have been challenging for life. No matter how far back we peer into Mars' history, we may never see a point at which the planet really looked like Earth."

Tosca, Knoll, and McLennan studied mineral deposits in Martian rock to calculate the "water activity" of the water that once existed on Mars. Water activity is a quantity affected by how much solute is dissolved in water; since water molecules continuously adhere to and surround solute molecules, water activity reflects the amount of water that remains available for biological processes.

The water activity of pure water is 1.0, where all of its molecules are unaffected by dissolved solute and free to mediate biological processes. Terrestrial seawater has a water activity of 0.98. Decades of research, largely from the food industry, have shown that few known organisms can grow when water activity falls below 0.9, and very few can survive below 0.85.

Based on the chemical composition of salts that precipitated out of ancient Martian waters, Tosca and his colleagues project that the water activity of Martian water was at most 0.78 to 0.86, and quite possibly reaching below 0.5 as evaporation continued to concentrate the brines, making it an environment uninhabitable by terrestrial species.

"This doesn't rule out life forms of a type we've never encountered," Knoll says, "but life that could originate and persist in such a salty setting would require biochemistry distinct from any known among even the most robust halophiles on Earth."

The scientists say that the handful of terrestrial halophiles -- species that can tolerate high salinity -- descended from ancestors that first evolved in purer waters. Based on what we know about Earth, they say that it's difficult to imagine life arising in acidic, oxidizing brines like those inferred for ancient Mars.

"People have known for hundreds of years that salt prevents microbial growth," Tosca says. "It's why meat was salted in the days before refrigeration."

Tosca and Knoll say it's possible there may have been more dilute waters earlier in Mars' history, or elsewhere on the planet. However, the area whose rocks they studied -- called Meridiani Planum -- is believed, based on Mars Rover data, to have been one of the wetter, more hospitable areas of ancient Mars.

Tosca, Knoll, and McLennan's work was supported by NASA and the Harvard Origins of Life Project.

A common aquatic animal's genome can capture foreign DNA

Apparent ease of DNA incorporation may reveal a bizarre new form of sexual reproduction

CAMBRIDGE, Mass. -- Long viewed as straitlaced spinsters, sexless freshwater invertebrate animals known as bdelloid rotifers may actually be far more promiscuous than anyone had imagined: Scientists at Harvard University have found that the genomes of these common creatures are chock-full of DNA from plants, fungi, bacteria, and animals.

The finding, described this week in the journal Science, could take the sex out of sexual reproduction, showing that bdelloid rotifers, all of which are female, can exchange genetic material via other means.

"Our result shows that genes can enter the genomes of bdelloid rotifers in a manner fundamentally different from that which, in other animals, results from the mating of males and females," says Matthew S. Meselson, Thomas Dudley Cabot Professor of the Natural Sciences in Harvard's Faculty of Arts and Sciences.

In essence, Meselson and colleagues say, bdelloids may acquire DNA by habitually disintegrating their genomes -- something these unusual animals do regularly during periods of desiccation, which fractures their genetic material and ruptures cellular membranes. Miraculously, bdelloids can then spring back to life upon rehydration of their habitats, readily reconstituting their genomes and their membranes.

In the process of rebuilding their shattered DNA, though, they may adopt shreds of genetic material from other bdelloids in the same puddle, as well as from unrelated species.

Meselson and co-authors Eugene A. Gladyshev and Irina R. Arkhipova believe the findings may solve the longstanding mystery of bdelloids' sexless ways, and may shed light on their ability to adapt to new environments.

"These fascinating animals not only have relaxed the barriers to incorporation of foreign genetic material, but, more surprisingly, they even managed to keep some of these alien genes functional," says Arkhipova, a staff scientist in Harvard's Department of Molecular and Cellular Biology.

"In principle, this gives them an opportunity to take advantage of the entire environmental metagenome," adds Gladyshev, a graduate student in molecular and cellular biology at Harvard.

While the scientists have yet to pinpoint the exact sources of the invasive DNA, they have ascertained that the foreign genes are concentrated in bdelloid telomeres, the regions at the ends of DNA thought to prevent its strands from unraveling -- much like the plastic cap on the end of a shoelace.

A next step, Meselson says, is to determine whether bdelloid genomes also contain homologous genes imported from other bdelloids. He and his colleagues also hope to examine whether the animals actually use any of the hundreds of snippets of foreign DNA they appear to vacuum up.

Nearly all other multicellular animals have strong safeguards against foreign DNA, but bdelloids' seeming embrace of genetic detritus is in keeping with their general quirkiness: Shunning sex and entirely lacking males, the ubiquitous creatures are also extraordinarily resistant to radiation, as Meselson and Gladyshev demonstrated earlier this year in a paper published in the Proceedings of the National Academy of Sciences.

With nearly 500 recognized species worldwide, bdelloid rotifers were discovered in 1702, when the renowned Dutch scientist and microscopy pioneer Antony van Leeuwenhoek added water to dust retrieved from a rain gutter on his house and observed the organisms in the resulting fluid. He subsequently described the creatures in a letter to Britain's Royal Society, which still counts an envelope of van Leeuwenhoek's rain-gutter dust among its holdings.

In addition to Harvard, Meselson and Arkhipova are also affiliated with the Marine Biological Laboratories in Woods Hole, Mass. Their work with Gladyshev is funded by the National Institutes of Health and the National Science Foundation.

Carnegie Mellon computer model reveals how brain represents meaning

Predicts brain activation patterns for thousands of concrete nouns

PITTSBURGH—Scientists at Carnegie Mellon University have taken an important step toward understanding how the human brain codes the meanings of words by creating the first computational model that can predict the unique brain activation patterns associated with names for things that you can see, hear, feel, taste or smell.

Researchers previously have shown that they can use functional magnetic resonance imaging (fMRI) to detect which areas of the brain are activated when a person thinks about a specific word. A Carnegie Mellon team has taken the next step by predicting these activation patterns for concrete nouns — things that are experienced through the senses — for which fMRI data does not yet exist.

The work could eventually lead to the use of brain scans to identify thoughts and could have applications in the study of autism, disorders of thought such as paranoid schizophrenia, and semantic dementias such as Pick's disease.

The team, led by computer scientist Tom M. Mitchell and cognitive neuroscientist Marcel Just, constructed the computational model by using fMRI activation patterns for 60 concrete nouns and by statistically analyzing a set of texts totaling more than a trillion words, called a text corpus. The computer model combines this information about how words are used in text to predict the activation patterns for thousands of concrete nouns contained in the text corpus with accuracies significantly greater than chance.

The findings are being published in the May 30 issue of the journal Science.

"We believe we have identified a number of the basic building blocks that the brain uses to represent meaning," said Mitchell, who heads the School of Computer Science's Machine Learning Department. "Coupled with computational methods that capture the meaning of a word by how it is used in text files, these

building blocks can be assembled to predict neural activation patterns for any concrete noun. And we have found that these predictions are quite accurate for words where fMRI data is available to test them."

Just, a professor of psychology who directs the Center for Cognitive Brain Imaging, said the computational model provides insight into the nature of human thought. "We are fundamentally perceivers and actors," he said. "So the brain represents the meaning of a concrete noun in areas of the brain associated with how people sense it or manipulate it. The meaning of an apple, for instance, is represented in brain areas responsible for tasting, for smelling, for chewing. An apple is what you do with it. Our work is a small but important step in breaking the brain's code."

In addition to representations in these sensory-motor areas of the brain, the Carnegie Mellon researchers found significant activation in other areas, including frontal areas associated with planning functions and long-term memory. When someone thinks of an apple, for instance, this might trigger memories of the last time the person ate an apple, or initiate thoughts about how to obtain an apple.

"This suggests a theory of meaning based on brain function," Just added.

In the study, nine subjects underwent fMRI scans while concentrating on 60 stimulus nouns — five words in each of 12 semantic categories including animals, body parts, buildings, clothing, insects, vehicles and vegetables.

To construct their computational model, the researchers used machine learning techniques to analyze the nouns in a trillion-word text corpus that reflects typical English word usage. For each noun, they calculated how frequently it co-occurs in the text with each of 25 verbs associated with sensory-motor functions, including see, hear, listen, taste, smell, eat, push, drive and lift. Computational linguists routinely do this statistical analysis as a means of characterizing the use of words.

These 25 verbs appear to be basic building blocks the brain uses for representing meaning, Mitchell said.

By using this statistical information to analyze the fMRI activation patterns gathered for each of the 60 stimulus nouns, they were able to determine how each co-occurrence with one of the 25 verbs affected the activation of each voxel, or 3-D volume element, within the fMRI brain scans.

To predict the fMRI activation pattern for any concrete noun within the text corpus, the computational model determines the noun's co-occurrences within the text with the 25 verbs and builds an activation map based on how those co-occurrences affect each voxel.

In tests, a separate computational model was trained for each of the nine research subjects using 58 of the 60 stimulus nouns and their associated activation patterns. The model was then used to predict the activation patterns for the remaining two nouns. For the nine participants, the model had a mean accuracy of 77 percent in matching the predicted activation patterns to the ones observed in the participants' brains.

The model proved capable of predicting activation patterns even in semantic areas for which it was untrained. In tests, the model was retrained with words from all but two of the 12 semantic categories from which the 60 words were drawn, and then tested with stimulus nouns from the omitted categories. If the categories of vehicles and vegetables were omitted, for instance, the model would be tested with words such as airplane and celery. In these cases, the mean accuracy of the model's prediction dropped to 70 percent, but was still well above chance (50 percent).

Plans for future work include studying the activation patterns for adjective-noun combinations, prepositional phrases and simple sentences. The team also plans to study how the brain represents abstract nouns and concepts.

The Carnegie Mellon team included Andrew Carlson, a Ph.D. student in the Machine Learning Department; Kai-Min Chang, a Ph.D. student in the Language Technologies Institute; and Robert A. Mason, a post-doctoral fellow in the Department of Psychology. Others are Svetlana V. Shinkareva, now a faculty member at the University of South Carolina, and Vicente L. Malave, now a graduate student at the University of California, San Diego. The research was funded by grants from the W.M. Keck Foundation and the National Science Foundation.

Dehydrated tomatoes show promise for preventing prostate cancer

PHILADELPHIA – New research suggests that the form of tomato product one eats could be the key to unlocking its prostate cancer-fighting potential, according to a report in the June 1 issue of Cancer Research, a journal of the American Association for Cancer Research.

"Processing of many edible plants through heating, grinding, mixing or drying dramatically increases their nutrition value, including their cancer prevention potential. It appears that the greatest protective effect from tomatoes comes by rehydrating tomato powder into tomato paste," said Valeri V. Mossine, Ph.D., research assistant professor of biochemistry at the University of Missouri.

The protective effect of tomato products against prostate cancer has been suggested in many studies, but researchers remain uncertain about the exact mechanisms. Mossine and colleagues demonstrated that FruHis, an organic carbohydrate present in dehydrated tomato products, exerts a strong protective effect.

Researchers divided rats into groups of 20 and fed them a control diet or a diet that included tomato paste, tomato powder or tomato paste plus additional FruHis. All animals were then injected with prostate cancer-causing chemicals.

Animals fed the tomato paste plus FruHis diet had the longest survival from cancer at 51 weeks compared with 50 weeks in the tomato powder group, 45 weeks in the tomato paste alone group and 40 weeks in the control group.

On post-mortem exam, prostate tumors were found in 10 percent of the rats that had been given a combination of tomato paste and FruHis, compared with 30 percent of animals in the tomato powder group, 25 percent in the tomato paste alone group and 60 percent in the control group.

Mossine said the protective effect of tomato-based products was restricted to prostate tumors, which is consistent with other research on tomatoes and cancer. Incidence of other tumors was too small to examine.

In vitro, Mossine and colleagues evaluated the anti-cancer properties of FruHis and 14 other D-fructose amino acids and found that FruHis in a concentrated form protected against DNA damage known to lead to prostate cancer. When combined with lycopene, FruHis stopped cancerous cell growth more than 98 percent of the time.

"Before this study, researchers attributed the protective effect of tomatoes to ascorbic acid, carotenoids, or phenolic compounds," Mossine said. "FruHis may represent a novel type of potential dietary antioxidant. Experiments like these suggest that a combination of FruHis and lycopene should be investigated as a potential therapeutic anti-tumor agent, not just a prevention strategy."

Although Mossine cautioned against drawing broad conclusions from this animal study, he said, "the result may introduce an additional intrigue into an ongoing dispute over the beneficial effects of dietary lycopene and tomato products in lowering the risk of prostate cancer. Human trials are certainly warranted."

Ancient hair suggests multiple migrations into Americas

* 19:00 29 May 2008
* NewScientist.com news service

*** Ewen Callaway**

An ancient tuft of dark-brown human hair suggests that a tribe of humans trekked from north Asia to settle in what is now Greenland more than 4000 years ago – and then vanished.

A team of Danish scientists has found that DNA collected from the hair traces back to Asians, not Native Americans or the Eskimos that currently populate the region. This suggests that the first humans to colonise the American Arctic were distinct from the first people who arrived in America more than 14,000 years ago.

An ancient tuft of hair suggests that the first Greenlanders weren't related to Native Americans or modern Eskimos
(Image: Bjarne Grønnow)

The hair – found in northern Greenland – may even be a relic of a steady trickle of human migrations across a harsh Arctic landscape, says evolutionary anthropologist Tom Gilbert of Copenhagen University in Denmark, who led the study. "It's bloody hard work to colonise the Arctic. It is not an easy venture," he adds.

Lucky break

The origins of the first Greenlanders – known as the Saqqaq – still puzzle archaeologists who have unearthed settlements, ornately sculpted tools made of animal bones, yet few human remains.

"One of the biggest mysteries is why the hell there are no bones," Gilbert says. Based on archaeological evidence, the Saqqaq lived in Greenland between around 2500 and 800 BC.

In an effort to hunt for human remains, Gilbert's colleague Eske Willerslev spent a summer in Greenland meticulously sampling animal bones for traces of human DNA, donning a forensic suit and mask to prevent contamination.

The search came up empty, but an archaeologist studying the Saqqaq mentioned he had collected a few clumps of hair in the 1980s. "It was chock full of human DNA," Gilbert says, despite thousands of years in a deposit in Greenland and 25 years in a Copenhagen basement.

The DNA extracted from the hair is thought to be contaminant free because its sequences don't match those of the European excavators.

Siberian link

To determine where the DNA came from, Gilbert's team sequenced the genome of the owner's mitochondria.

Humans inherit mitochondria – the cell's "power houses" – only from their mothers, allowing geneticists to chart a person's maternal lineage, from mother to grandmother to great grandmother, and so on.

Due to mutation and geographic isolation, differences that develop in mitochondrial DNA sequences can be used to trace the ancestry of humans, whether ancient or modern.

The Saqqaq hair belonged to a man descended from ancient Siberians, Gilbert's team discovered. The DNA also matched people living on the Commander Islands, 175 kilometres east of Russia's Kamchatka peninsula, whose descendents were exiled from Russia in the 19th century.

However, the Saqqaq man's DNA bore little resemblance to the mitochondrial DNA characteristic of Native Americans, who first arrived in America at least 14,000 years ago, or to modern Eskimos, whose ancestors arrived in the area about 1000 years ago.

Tribal trickle?

Because the sample is distinct from modern Eskimo populations, Gilbert's team speculates that the Saqqaq originated from a distinct migration via Beringia – the landmass that connected Asia and America intermittently until about 7000 thousand years ago.

"If this is for real, then the suggestion is that the first migrants into Greenland must have come from the Bering region," agrees Michael Crawford, a genetic anthropologist at the University of Kansas in Lawrence, US. However, he cautions that more sequences will be needed to confirm that conclusion.

Yet the Saqqaq migration may be the tip of the iceberg. Gilbert speculates that other tribes may have made it out of Beringia and into the American Arctic, some flourishing, others fizzling.

"On the grandest scale, it shows there were people coming in continually," he says.

Journal reference: Science, DOI: 10.1126/science.1159750

DNA Offers Clues to Greenland's First Inhabitants

By NICHOLAS WADE

A swatch of hair, so thick and tangled it could have belonged to man or bear, has provided answers about a mysterious culture and its origins half a world away.

The culture is that of the first people to have occupied Greenland some 4,500 years ago. Known to archaeologists as the first Paleo-Eskimo culture, it gave way to a second Paleo-Eskimo culture some 2,500 years ago and then 700 years ago to the Thule culture of the present-day Inuit peoples. Some archaeologists suggested that each culture might have descended from its predecessor, but proof required obtaining DNA from the earlier cultures and comparing it with that of the Inuit.

Eske Willerslev, an expert on ancient DNA at the University of Copenhagen, recently spent two months in the frozen wastes of northern Greenland. Dr. Willerslev wore a full body suit while digging so as not to contaminate samples with his own DNA. But human remains from the early culture are hard to find, and archaeologists have speculated that the dead were laid on the sea ice.

Despite working in freezing weather for two months, Dr. Willerslev could find no human DNA from the period.

It was only on expressing his frustration to a friend that he learned of the swatch of hair in a museum collection, excavated by the friend's archaeologist father from a Paleo-Eskimo site on Disko Bay in western Greenland. The hair had been kept cold and yielded plentiful DNA. It turned out to be human, not from bears, and contained a baleen comb, from which whale DNA was extracted.

The human DNA differed from that of the Thule people and of American Indians. Its closest match was to people who live in the Commander Islands, the two westernmost islands of the Aleutian chain that arcs from southern Alaska to the Kamchatka Peninsula in Russia, Dr. Willerslev and colleagues reported in an article published online Thursday by the journal Science.

Because the Commander Islands are at the Siberian end of the Aleutian chain, the new finding indicates a heretofore unknown migration from Siberia to the New World, Dr. Willerslev said. Earlier migrations brought the ancestors of American Indians and of the Neo-Eskimos who developed the Thule culture. Michael Crawford, an expert on circumpolar populations at the University of Kansas, said that it was not yet known if there had been a single migration or many, but that "this finding may turn things around." But Dr. Crawford noted that the hair had provided DNA just on the maternal side and from a single individual, making it hard to generalize about populations.

The Thule culture, which originated in Alaska, developed the technology for hunting bowhead whales. This enabled it to expand across the northern coast of Canada, eventually reaching Greenland. Dr. Crawford said the Aleutian people probably took the same route but depended on fish and seals.

Early peoples had no maps and were not traveling to known destinations; rather, as their population expanded, they followed the natural resources on which they depended. This strategy evidently led the Aleutians some 5,000 years ago to embark on a circumpolar journey that took them all the way to Greenland.

The three Eskimo cultures in Greenland now seem to have been generated by at least two separate arrivals. Archaeologists do not know if each culture perished from natural causes or was obliterated by its successor.

Why rebel groups attack civilians

In civil war, rebel groups often target civilians despite the fact that their actual target is the government and that they are often dependent on the support of the civilian groups they attack. This may seem illogical, but there are rational reasons for this type of violence. Swedish peace and conflict researcher Lisa Hultman describes these reasons.

"Rebels are almost always considerably weaker than the government and are often lacking the means for defeating government forces by military action. Therefore, they seek alternative means to pressure the government into making concessions. Violence towards civilians is one such strategy," explains Lisa Hultman of the Department of Peace and Conflict Research, Uppsala University.

In her dissertation "Targeting the Unarmed: Strategic Rebel Violence in Civil War", she shows that rebel groups primarily target civilians when they believe it will help them debilitate the government.

"A strong parallel can be drawn between these types of attacks and terrorist attacks, namely that groups that rebel against a democratic state are more inclined to attack civilians," she states.

Rebel groups take advantage of the fact that such attacks put democratic states in a more vulnerable position than dictatorships since the people living in democracies can hold the government accountable for upholding national security. By attacking the population that the government is dependent on, rebels cause the government indirect harm.

This conflict strategy is most often employed when rebel groups are at a military disadvantage. Hultman's research shows that rebel groups that lose battles, and thus fail to exert force on the government by military means, are more likely to kill civilians. The purpose of the extreme violence employed by the rebels is to demonstrate that they are prepared to take whatever means necessary to attain their political goals. With this strategy, rebels hope to convince the government that continued conflict would prove costly, thus influencing them to make immediate political concessions.

"Violence towards civilians should be viewed as an intentional group strategy rather than individual action taken by undisciplined rebels. If the international community had a better understanding of why and when rebel groups target civilians, we would be in a better position to prevent such violence," says Hultman.

She will present her dissertation on 31 May. Read the dissertation on Uppsala University's website: http://publications.uu.se/theses/abstract.xsql?dbid=8852

Rapid wound healing

A new type of wound dressing made of silica gel fibers will soon help to heal difficult wounds caused by burns or diabetes. The dressing forms a supporting matrix for newly growing skin cells and is fully absorbed by the body during the healing process.

In Germany alone, about three million – mostly elderly – patients suffer from poorly healing large-area wounds caused by complaints such as diabetes, burns or bedsores. The wounds can be treated with conventional collagen dressings or polylactic acid dressings, but the success rate is not as good as it should be. A new type of dressing made of silica gel fibers, developed by scientists at the Fraunhofer Institute for Silicate Research ISC in Würzburg, shall solve the problem. This novel dressing has many advantages: it is shape-stable, pH-neutral and 100 percent bioresorbable. Once applied it remains in the body, where it gradually degrades without leaving any residues. What's more, the fibre fleece provides the healthy cells around the edges of the wound with the structure they additionally need for a proper supply of growth-supporting nutrients. To prevent any infection, treatment of the wound must be absolutely sterile. "As only the outer bandage needs to be changed, the risk of contaminating the wound is low," explains Dr. Jörn Probst of the ISC. And thanks to the supporting matrix for the cells, the chances of a scar-free natural closure of the wound are very good.

The fibers are produced by means of wet-chemical material synthesis, a sol-gel process in which a transparent, honey-like gel is produced from tetraethoxysilane (TEOS), ethanol and water in a multi-stage, acidically catalyzed synthesis process. The gel is processed in a spinning tower: "We press it through fine nozzles at constant temperatures and humidity levels," explains Walther Glaubitt, the inventor of the silica gel fibers. "This produces fine endless threads which are collected on a traversing table and spun in a specific pattern to produce a roughly A4-sized multi-layer textile web." The dressings are then cut, packed and sterilized.

Dr. Jörn Probst and Dipl.-Ing. Walther Glaubitt will receive the Joseph von Fraunhofer Prize 2008 for developing the biocompatible dressing.

A partner to support the development and market the dressing has already been found: Bayer Innovation GmbH BIG, a wholly owned subsidiary of Bayer AG. "We anticipate that hospitals will start to use the silica gel wound dressing in 2011," states Iwer Baecker, project manager at Bayer Innovation GmbH. And that is by no means the end of the story. The scientists plan to integrate active substances such as antibiotics or painkillers in the dressing to improve and accelerate the healing process.

Did walking on 2 feet begin with a shuffle?

Somewhere in the murky past, between four and seven million years ago, a hungry common ancestor of today's primates, including humans, did something novel. While temporarily standing on its rear feet to reach a piece of fruit, this protohominid spotted another juicy morsel in a nearby shrub and began shuffling toward it instead of dropping on all fours, crawling to the shrub and standing again.

A number of reasons have been proposed for the development of bipedal behavior, or walking on two feet, and now researchers from the University of Washington and Johns Hopkins University have developed a mathematical model that suggests shuffling emerged as a precursor to walking as a way of saving metabolic energy.

"Metabolic energy is produced by what an animal eats, enabling it to move. But it is a limited resource, particularly for young-bearing females which have to take care of and feed their offspring. Finding food is vitally important, and an animal needs to save energy and use it efficiently," said Patricia Kramer, a UW research assistant professor of anthropology and co-author of a recent study.

She believes it was an empty belly, along with a need to conserve energy, that prompted that early ancestor to shuffle.

"Hunger. It is always hunger," said Kramer. "There is nothing that will get you to do something you don't want to do other than food. That's why we bribe animals with food to train them."

Because of a huge gap in the fossil record that hides when humans split off from other primates, Kramer and co-author Adam Sylvester, now a postdoctoral fellow at Johns Hopkins University, used the chimpanzee as a way of looking into the past and testing other researchers' ideas about the origins of bipedalism.

Chimpanzees are humans' closest relatives. They basically walk on all fours, partially resting their weight on the knuckles of their hands.

"A chimp's body plan is very much like that of a primitive ape, and our last common ancestor probably had a body like that of a chimp. Modern humans are different with long legs and a big head. So chimps are a good place to start," Kramer said.

Using the model they devised, Kramer and Sylvester calculated it would not be metabolically efficient for a chimp to use bipedalism for distances greater than about 50 feet. But it would be efficient and that most shuffling would occur for distances less than 30 feet. In addition, walking on two feet would be used most frequently for distances less than three feet.

"These are predictions other people can test. You should rarely, if ever, see a chimp walking upright at longer distances. The flipside of this is if a chimp is going a short distance returning to all fours is not going to happen. You can see this in human babies learning to walk. If they are going between a couch and a coffee table they are up on their feet. But if they are going a longer distance, they go down and crawl," she said.

"We think metabolic energy is extremely important and we have only touched the surface of the information we can get with this work. The model allows people to plug in the body characteristics of any primate so a researcher can change the parameters for a specific species."

The study was published in the American Journal of Physical Anthropology.

Human remains explain Stonehenge mystery

* 17:19 29 May 2008
* NewScientist.com news service
*** Linda Geddes**

Alternative theories about Stonehenge

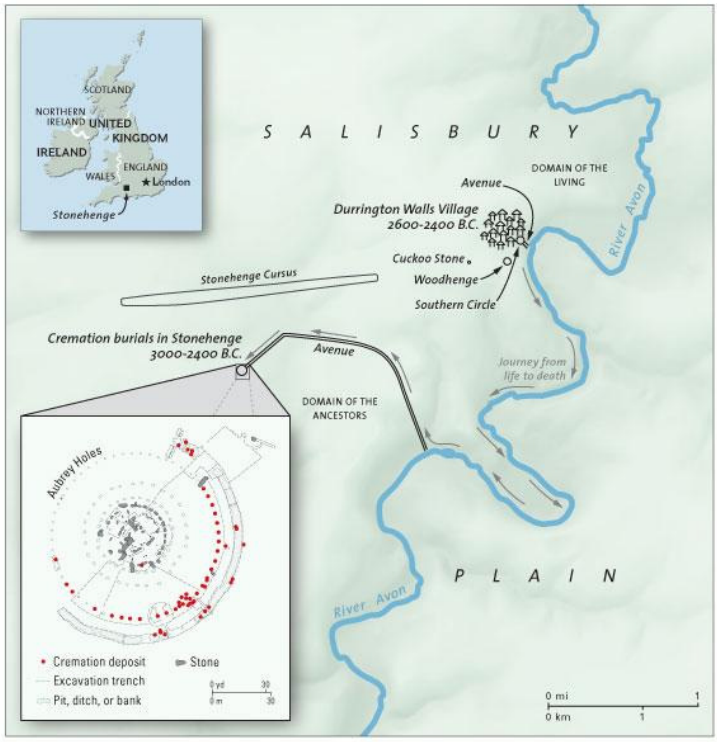
Theories have ranged from moon temple, to observatory, and even a UFO landing site. Stonehenge is one of the enduring landmarks of prehistoric times, but the mystery of why it was built has eluded people for centuries.

Now one group of archaeologists believe that they are a step closer to an answer. For the first time, human cremation remains excavated from the site have been radiocarbon dated and suggest that, for 500 years from its earliest beginnings around 3000 BC, Stonehenge was used as a cemetery.

"It is clear that the burials were a major component of Stonehenge in all its main stages," says Mike Parker-Pearson of the University of Sheffield, UK, who led the work. "This was a cemetery which grew over many centuries."

Archaeologists had previously assumed that the site was mainly used as a burial ground only between 2800 and 2700BC.

The carbon-dated remains are three of 52 cremation burials originally excavated during the 1920s. They were stored in a local museum, while the remaining 49 were reburied because they were thought to be of no scientific value.



(Image: National Geographic)

Earliest phase

The oldest remains were found in one of the 56 pits circling Stonehenge, called the Aubrey Holes, which date to the earliest phases of Stonehenge, around 3000 BC. The remains also date to around this period – between 3030 and 2880 BC, the study suggests.

The second and third burials were recovered from within and near the ditch that surrounds Stonehenge, and date from between 2930 to 2870 BC, and 2570 to 2340 BC respectively. The latter was therefore buried at around the time the sarsen stones – the large upright stones – were first erected at Stonehenge.

At the same time, Parker-Pearson's team has been conducting excavations at Durrington Walls – a massive circular earthwork located 2 miles north of Stonehenge.

Within Durrington Walls are the remains of a giant wooden henge – a circular area enclosed by a bank and ditch – called the Southern Circle, close to a smaller wooden henge called Woodhenge.

Paired henges

In 2005, Parker-Pearson's team discovered the remains of several houses close to the Southern Circle, but they have since uncovered more houses along a broad avenue linking Durrington Walls with the nearby River Avon.

Parker-Pearson now believes that Durrington Walls housed up to 300 dwellings – making it the largest village in Northern Europe at the time.

"This was part of an enormous settlement, at least 17 hectares in extent, and its central focus appears to have been this great timber circle – a comparison in wood to the great circle at Stonehenge."

(Image: stock.xchng)

Not only do the two henges look very similar, but radiocarbon dating has also revealed that Durrington Walls was in use from 2600 to 2500 BC – around the same time the sarsen stones were erected at Stonehenge.

Parker-Pearson says this supports his theory that the two were linked. "Stonehenge wasn't set in isolation, but was actually one half of this monument complex," he says. "We are looking at a pairing – one in timber to represent the transience of life, the other in stone marking the eternity of the ancestral dead."

Burial place

Connecting the two is the River Avon: "a prehistoric version of the River Styx, a river that takes people from the world of life into death itself," Parker-Pearson says.

The dating of the remains at Stonehenge, "strengthens the idea that Stonehenge was a place for the dead, while Durrington Walls was a place for the living," says Christopher Chippindale, curator at the Cambridge University Museum of Archaeology and Anthropology, and author of Stonehenge Complete.

However, the fact that Stonehenge was a burial site is not necessarily proof that its primary purpose was as a cemetery.

"Ceremonial places have all sorts of meanings," he says. For example, churches are full of burials because they are sacred places, but that's not their primary purpose.

"It is another part of the puzzle, but it's not the final answer," Chippindale says.

'Prehistoric Lourdes'

Meanwhile, Tim Darvill at Bournemouth University, UK, has a different explanation as to why Stonehenge was built.

He and Geoff Wainwright, former head of archaeology at English Heritage, believe that the arrival of the stones marked a transition in the site's use to a centre of healing – a kind of prehistoric Lourdes.

"I don't think the new dates change one iota what we already knew, which was that pretty much all the burials were before 2500 BC," Darvill says.

"It's a good step forward to have these fully dated examples," he says, "but they simply reinforce our model that after about 2500 BC, when the stones start being put up, the burials decline in number and the stones become the focus of the monument."

Dual purpose?

In its earliest phase, he says, Stonehenge was a monument like many others scattered across the British Isles. What makes Stonehenge unique is the stones – in particular the bluestones, which were transported around 250 miles, from the Preseli hills in Wales.

Last month, Darvill and Wainwright conducted a dig at Stonehenge – the first in 44 years – which they hope will precisely date the arrival of the bluestones, and provide evidence for their use in healing. The results are expected in June.

Until arrival of the bluestones is dated, it is difficult to put Parker-Pearson's findings in context, Wainwright says. "The secret to understanding Stonehenge lies in the stones themselves," he says.

Meanwhile, Chippindale sees no reason why both theories couldn't be correct. "I think it's unlikely that somewhere as elaborate and expensive as Stonehenge had a single purpose," he says. "It's entirely possible that Stonehenge was both a place of healing and a place for the dead."

Parker Pearson's findings will be the subject of a documentary to be aired on the National Geographic channel on June 1.

Common bacteria linked to cot death

* 00:01 30 May 2008
* NewScientist.com news service
*** Jason Palmer**

There is more reason than ever to believe that two common bacteria are part of the cause of sudden infant death syndrome (SIDS), commonly called cot death.

While many factors contributing to the risk for SIDS have been identified, the mechanism of its cause has remained a mystery. A link to bacterial infections was proposed decades ago, but evidence of the bacteria in SIDS victims has remained scarce.

Now, a team of researchers from the Great Ormond Street Hospital for Children has shown that specific bacteria are more prevalent in SIDS babies.

The team went over the results of autopsies of more than 500 infants who died aged between one week and one year. They then compared the rate of infection by the bacteria Staphylococcus aureus and Escherichia coli in infants whose cause of death was known, and those in SIDS babies.

What they found was that 26% of the autopsies in the explained cases showed infection by the bacteria, whereas in the SIDS cases, the rate of infection was nearly twice that.

Not a diagnostic

"What's good about this is it's a large study at one institution where all the cases were investigated in the same way, so it's enabled us to really provide harder evidence," says Marian Malone, one of the study's co-authors.

The prevalence of the bacteria is certainly indicative of a connection with cause of death, but their presence even in explained deaths means that a test for them cannot be used as a diagnostic – or as evidence for or against other explanations for deaths.

George Haycock, scientific adviser to the UK's Foundation for the Study of Infant Deaths , warns that there isn't just one answer to the SIDS mystery.

"This is certainly not the cause of SIDS, which is almost certainly multifactorial," he says. "Even in the cases where no cause can be identified, there may be multiple factors operating."

Toxin theory

The role of the bacteria in the so-called bacterial toxin theory could tie some of those multiple factors together. The idea is that the bacteria grow in the upper respiratory tract of babies, releasing toxins that are the ultimate cause of death.

"It's a theory that would fit the facts," Malone says. "We know that prone sleeping – sleeping on the front – can increase the number of pathogenic organisms in the upper airway. We know that if the mother has been smoking during pregnancy, it can alter the immune response [to toxins]."

Even the genetic differences among SIDS babies are related to immune response. The theory, Malone says, could tie a lot of things together.

"It's another piece of evidence fitting in with lots of other evidence that has been gathering, pointing to these bacteria," says Jim Morris, a pathologist at the Royal Infirmary, Lancaster, UK. "None of this is proof positive, but it's another important step to understanding what's going on."

Journal reference: The Lancet, vol 371, p 1848

US soldiers in high-tuberculosis areas face new epidemic: false positives

U.S. Army service members are increasingly deployed in regions of the world where tuberculosis (TB) is rampant, such as Iraq and Afghanistan, and the military now faces a growing medical problem. But it is not TB itself that is on the rise—instead, the problem lies with the growing number of "pseudoepidemics," or clusters of false-positives for TB that are the result of universal testing with a notoriously inaccurate tuberculin skin test (TST) and inconsistent procedures for interpreting those tests in low-risk populations.

These false positives tests have become more than a mere institutional inconvenience or a momentary medical scare for Soldiers being tested. They are a real financial and medical burden because they inappropriately diverting limited funds and resources.

A recent study, published in American Thoracic Society's first issue for June of the American Journal of Respiratory and Critical Care Medicine, describes eight outbreaks of false-positive TB tests between 1983 and 2005. The study was led by U.S. Army Major James Mancuso, M.D., of the Uniformed Services University of the Health Sciences.

Recent deployments to Iraq and Afghanistan, which are reported to have among the highest rates of active TB in the world, have raised concerns about TB exposure. However, many service members do not have sufficient contact with locals to raise their risk of contracting TB. As a consequence, "testing after recent deployments to the endemic and hyperendemic areas has occasionally resulted in large numbers of U.S. Army service members with [positive tests] and massive efforts aimed at preventing active TB," wrote Dr. Mancuso.

Because the positive-predictive value of a test—that is, the likelihood of a positive result indicating an actual case—is dependent on the prevalence of disease in a population. The lower the prevalence of a disease, and the higher the variability in the test and testing procedures, the less the positive-predictive value of a test will be. "This may dramatically reduce the positive-predictive value of the test to below 50 percent," said Dr. Mancuso.

Dr. Mancuso and his colleagues conducted outbreak investigations in deployed locations such as the Balkans and Afghanistan, where they collected and reviewed medical records of reported active and latent TB cases in deployed U.S. Army service members. They then obtained the medical histories of these soldiers, including prior diagnoses and treatments, determined current symptoms and interviewed the subjects to identify other possible risk factors. Finally, they retested all available skin test converters.

"Repeat testing of converters (positives) found that 30 to 100 percent were negative on retesting," wrote Dr. Mancuso. In one case, 95 percent of positive TB tests (38 of 40 tests) from Army National Guard servicemen in Kosovo were subsequently found to be negative, and the pseudoepidemic was primarily attributed to variability with the test administration and reading, as well as to the specific type of test used.

"The testing of [a] predominantly low-risk population leads to false-positive results in individuals and pseudoepidemics of false-positive TST conversions in U.S. Army populations," Dr. Mancuso concluded, recommending three actions to reduce the occurrence of false positive skin tests and these apparent outbreaks: test only truly high-risk personnel; standardize testing procedures; and use the more reliable of the TST tests, Tubersol, in lower-risk populations such as the U.S. Army.

"As always, an individualized assessment of each patient's risk of tuberculosis should be used to target testing and treatment of latent tuberculosis infection. In the absence of other risk factors, clinicians and public health officials should interpret reported skin test conversions after deployment with caution," he added.

Whole milk is effective and cost-effective as oral contrast agent

An item commonly found in many homes – whole milk – is just as effective, costs less and is easier on the patient than a diluted (0.1%) barium suspension that is also commonly used as an oral contrast agent in conjunction with CT to examine the gastrointestinal tract, a new study finds.

The study included 215 patients undergoing abdominal and pelvic CT, said Chi Wan Koo, MD, lead author of the study. All patients were given an IV contrast media; 115 were also given whole milk as an oral contrast agent; 100 received a 0.1% barium suspension. Two radiologists reviewed all the images and scored them based on degree of bowel distension and bowel wall visibility. Adequate bowel distension is necessary to optimize resolution of the bowel wall and contents, said Dr. Koo.

The study found that the images taken of patients who were given whole milk were just as useful as the images that were taken of patients given the diluted barium, she said.

In addition, patients were given a questionnaire, asking them how well they tolerated the oral contrast agents, and a cost comparison was done. “We found that milk was less expensive, it had better patient acceptance and fewer adverse symptoms,” Dr. Koo said.

Whole milk and 0.1% barium suspension are valuable in the diagnosis of small bowel disorders, such as ischemia, neoplasm and Crohn’s disease, said Dr. Koo. They are also useful in evaluating pancreatic and biliary abnormalities.

The study appears in the May issue of the American Journal of Roentgenology, published by the American Roentgen Ray Society.

Golf prolongs life

[PRESS RELEASE, 30 May 2008] Golf can be a good investment for the health, according to a new study from the Swedish medical university Karolinska Institutet. The death rate for golfers is 40 per cent lower than for other people of the same sex, age and socioeconomic status, which correspond to a 5 year increase in life expectancy. Golfers with a low handicap are the safest.

It is a well-known fact that exercise is good for the health, but the expected health gains of particular activities are still largely unknown. A team of researchers from Karolinska Institutet has now presented a study of the health effects of golf – a low-intensity form of exercise in which over 600,000 Swedes engage.

The study, which is published in Scandinavian Journal of Medicine & Science in Sports, is based on data from 300,000 Swedish golfers and shows that golf has beneficial health effects. The death rate amongst golfers is 40 per cent lower than the rest of the population, which equates to an increased life expectancy of five years.

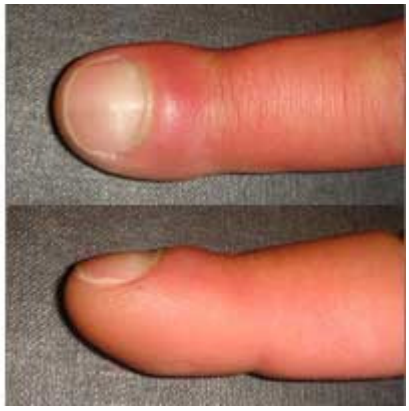
Professor Anders Ahlbom, who has led the study with Bahman Farahmand is not surprised at the result, as he believes that there are several aspects of the game that are proved to be good for the health.

"A round of golf means being outside for four or five hours, walking at a fast pace for six to seven kilometres, something which is known to be good for the health," he says. "People play golf into old age, and there are also positive social and psychological aspects to the game that can be of help."

The study does not rule out that other factors than the actual playing, such as a generally healthy lifestyle, are also behind the lower death rate observed amongst golfers. However, the researchers believe it is likely that the playing of the game in itself has a significant impact on health.

Golf players have a lower death rate regardless of sex, age and social group. The effect is greater for golfers from blue-collar professions than for those from white-collar professions. The lowest rates are found in the group of players with the lowest handicap (i.e. the best golfers).

"Maintaining a low handicap involves playing a lot, so this supports the idea that it is largely the game itself that is good for the health," says Professor Ahlbom.



Leeds medics solve an ancient riddle – and offer new tool for diagnosis

A puzzling medical condition, identified more than 2,000 years ago by Hippocrates, has finally been explained by researchers at the University of Leeds.

The phenomenon of "finger clubbing", a deformity of the fingers and fingernails, has been known for thousands of years, and has long been recognized to be a sign of a wide range of serious diseases – especially lung cancer.

"It's one of the first things they teach you at medical school," explained Professor David Bonthron of the Leeds Institute of Molecular Medicine. "You shake the patient by the hand, and take a good look at their fingers in the process."

Lung cancer, heart disease, hyperthyroidism, various gastrointestinal diseases and many other conditions all result in finger clubbing. But exactly why swollen, reddened fingers should be an indicator of serious illness has remained a mystery – until now.

"There are benign cases of clubbing, where it isn't associated with other illnesses, but particularly because of the link to lung cancer, it is generally regarded as rather sinister," said Bonthron. "You look at the range of conditions connected to finger clubbing and wonder what on earth they could have in common."

The researchers found clues in the medical literature, detailing past cases and previous research. "We knew that in cystic fibrosis patients who have undergone a lung transplant, their finger clubbing goes away. The same goes for empyema patients who have had their lungs drained. It suggested that impaired lung function was somehow crucial to finger clubbing – but we didn't understand how."

Prof Bonthron, Dr Chris Bennett of the Yorkshire Regional Genetics Service and their colleagues studied a group of patients suffering from inherited primary hypertrophic osteoarthropathy (PHO), a genetic disorder in which the finger clubbing is accompanied by painful joint enlargement and a thickening of the bone.

Their findings implicated a fatty compound called PGE2, which is produced naturally by the body to mediate the effects of internal inflammation. Crucially, once it has done its work, PGE2 is broken down by an enzyme 15-HPGD, produced in the lungs. The patients followed by the Leeds study were found to have a genetic mutation which prevented the production of 15-HPGD, resulting in up to ten times as much of the PGE2 in their systems.

"If you don't have this enzyme the PGE2 isn't broken down normally and simply builds up," said Bonthron, whose findings are published online this week in Nature Genetics.

In lung cancer patients, it is most likely overproduction of PGE2 by the tumour that causes the clubbing. In congenital heart disease, blood bypasses the lungs, where PGE2 is normally broken down by 15-HPGD.

The researchers have suggested that a straightforward urine test for levels of PGE2 may be a useful first step in the diagnosis of individuals with unexplained clubbing, and to understanding whether it is the symptom of something far more serious. The results also suggest that existing drugs such as aspirin, which are already used to prevent PGE2 production, may be effective in reducing the painful symptoms of finger clubbing.

It has taken 2,000 years to make the connection, but Bonthron adds: "Actually, when you look back, it's rather obvious. When we found this gene, everything else fell neatly into place – it was like a smack on the forehead."

Notes to editors

1. The above photographs show the classic symptoms of finger clubbing.

2. David Bonthron is Centenary Professor of Molecular Medicine at the University of Leeds.

Prevalence of pre-cancerous masses in the colon same in patients in their 40s and 50s

New findings point to potential to begin colon cancer screening at a younger age

The prevalence of pre-cancerous masses in the colon is the same for average-risk patients who are 40 to 49 years of age and those who are 50 to 59 years of age, reports a new study in Gastroenterology, the official journal of the American Gastroenterological Association (AGA) Institute.

Currently, standard protocol recommends screening patients age 50 and over for colon cancer based on the increasing incidence of colon cancer at that age. Because observational studies have shown that it takes a decade for pre-cancerous growths, or adenomas, to develop and progress to cancer, the increase in colon cancer prevalence in the over-50 age group, in fact, may be the result of undetected adenomas that were present in the individuals in their 40s.

Investigating this hypothesis, a team of researchers, led by Drs. Alfred I. Neugut and Andrew Rundle from Columbia University Medical Center, compared colonoscopy results, broken down by age group. Analyzing records from a centralized digital medical record system provided by EHE International, the team reviewed 553 screening colonoscopies for patients ages 40 to 49 and 352 screening colonoscopies for patients ages 50 to 59. Individuals who could be deemed "high-risk" because of a family history of colon cancer, a personal history of inflammatory bowel disease or any malignancy other than skin cancer were excluded from the sample.

Of the records reviewed, in the 40 to 49 age group, 79 patients, or 14 percent, had one or more adenoma. Similarly, the 50 to 59 age group had 56 patients, or 16 percent, with one or more adenoma.

"Our results support the theory that adenomas, which later may lead to cancer, form at an age earlier than we screen for today," said Alfred I. Neugut, MD, PhD, professor of medicine and epidemiology at Columbia University Medical Center and head of cancer prevention and control for the Herbert Irving Comprehensive Cancer Center of Columbia University Medical Center and New York-Presbyterian Hospital. "With this information in hand, it is logical to think that if we were to recommend screening for colon cancer at age 40, we may be able to decrease its prevalence even further and save more people from having to battle the disease."

Though the number of adenomas was relatively similar in the two age groups, there was a doubling in the prevalence of abnormal cell growth, or advanced neoplasia, in the 50 to 59 age group versus the 40 to 49 age group. While not statistically significant, in the 40 to 49 age group, 11 patients, or 2 percent, had an advanced neoplasm, and in the 50 to 59 age group, 13 patients, or 4 percent, had an advanced neoplasm.

"What this implies is that while the number of pre-cancerous growths is very similar in both age groups, there is a progression toward cancer in older patients," said Andrew Rundle, DrPH, assistant professor of epidemiology at Columbia's Mailman School of Public Health. "Abnormal cell growth is a warning sign of cancer, so the fact that there's an increase in advanced neoplasia in the older age group is in line with the increased colon cancer incidence we see in individuals over the age of 50. Detecting adenomas when patients are in their 40s could mean that we are able to drastically lower the prevalence of colorectal cancer. Additional studies need to be done to look specifically at this possibility and the cost-benefit of beginning screening at an earlier age."

EHE International, which sponsored the research, has been providing comprehensive physical exams for 95 years, and since 2002 has been using a digital electronic medical record system that can provide anonymous, de-identified data for biomedical research. "We are thrilled that the medical record data that we have accumulated over the years through our business can be used to conduct such important research and promote the greater good," said Deborah McKeever, president of EHE International.

Only one prior study has investigated the prevalence of colorectal adenomas in average-risk individuals aged 40 to 49 years in the U.S., and it reports very similar findings: an adenoma prevalence of 11 percent in the age group.

Altruism needs selfish genes to evolve after all

* Updated 16:23 30 May 2008
* NewScientist.com news service
*** Daniele Fanelli**

It's a problem that has been debated ever since Darwin: how have hundreds of species of insects and other animals evolved altruistic helpers that give up their own reproduction for the sake of others?

Recently, the orthodox explanation – that they favour their own genes indirectly by helping their kin – has been fiercely challenged by Edward O Wilson, one of the most prominent evolutionary biologists of our time.

But now a research team led by William Hughes, of Leeds University, UK, claims to have falsified Wilson's predictions, showing that genetic relatedness is really the key.

At the core of the dispute is the theory of kin selection, formalised in the 1960s by William Hamilton, accepted by the vast majority of modern biologists and defended by Richard Dawkins. According to Hamilton's rule, apparent acts of altruism – foregoing reproduction to help others, say – are actually self-serving, because they benefit the altruist's genes.

Wilson broke with this view, proposing that altruism evolved because it benefits groups, rather than genes. For such "group selection" to take place, he argued, animals don't need to be closely related, they only need to stick together and cooperate.

Multiple males

He argues that this is more likely to occur when individuals tend to remain in the nest they are born from. So the high relatedness observed in ants, bees and wasps – so-called eusocial species that have a queen and sterile workers – is a consequence, not a cause, of altruism.

If Wilson is right, then there should be no correlation between the degree of genetic relatedness within insect colonies and the level of social cooperation they show.

To test this, Hughes and colleagues looked at a behaviour that has fundamental consequences for colony kin structure – polyandry, which occurs when females mate with more than one male. This enhances female fitness by producing more variable offspring and is a common behaviour throughout the animal kingdom.

"Birds, reptiles, flies, butterflies, beetles – pretty much all species that have been looked at show some level of polyandry," says Hughes.

Ancestral monandry

Hughes and colleagues looked at the levels of polyandry in 267 species of eusocial ants, bees and wasps. The last common ancestor of these insects was solitary, and eusociality evolved independently on eight different occasions. By looking at how the species are related to each other over evolutionary time, the team could reconstruct the ancestral condition – monandry or polyandry – in each case.

The team found the ancestral condition was invariably monandry. And the same applies to termites, shrimps, ambrosia beetles and most other eusocial organisms.

"[In species excluding ants, bees and wasps] the data is much more limited, but it points in the same direction," says Hughes. "You always have ancestral monandry when eusociality evolves." In other words, close genetic relatedness is crucial to the evolution of altruism.

Eventually, once eusociality is evolved and established, insect queens start reaping the benefits of multiple mating, which has evolved several times as a secondary condition, says Hughes.

'Cut and dry'

Intriguingly, very high levels of polyandry are only observed in species where helpers have entirely lost the ability to reproduce, becoming permanently sterile castes. Again, this is exactly what kin-selection theory predicts, because only when eusociality has become irreversible, and workers have no other option but to help, can the leash of genetic relatedness loosen.

Hughes contents that these results would seem to settle the longstanding debate revived by Wilson.

"Wilson predicted that high relatedness evolves after eusociality. We show that it is ancestral. It's pretty cut and dry, really," says Hughes.

Wilson, however, does not agree that the debate has been resolved so cleanly.

"Hughes and colleagues did not prove the correlation of eusociality and ancestral monogamy, because they have no data on the many lines that did not evolve eusociality," he says.

"And they failed to mention other published explanations of multiple insemination in the later stages of eusociality. The weight of evidence favors the new explanation of close kinship as a consequence of eusociality, as laid out in my BioScience article."

Hughes accepts that there is much more to altruism than simple genetic benefits.

"It is good to be challenged about our hypotheses," says Hughes, "Hamiton's equations have three components in them but we have become very focused on relatedness. [Wilson] has done us a service in drawing attention back to ecological benefits and other components."

Journal reference: Science (DOI: 10.1126/science.1156108)

Immune cells 'vacuum up' Alzheimer's clumps

* 18:00 30 May 2008
* NewScientist.com news service

*** Alison Motluk**

Debris-gobbling immune cells can be enticed into the brain to eat away the amyloid plaques associated with Alzheimer's disease, according to a study in mice.

The study suggests a promising new approach in the fight against Alzheimer's – and several drug candidates are already on pharmaceutical company shelves, waiting to be tried out.

Richard Flavell at Yale University in New Haven, Connecticut, and his colleagues created a double transgenic mouse, dubbed Tg2576-CD11c-DNR. One gene predisposed it to develop amyloid plaques in its brain that mimic Alzheimer's disease, while another blocked the activity of TGF-beta, a cytokine.

The researchers had expected the double-transgenic mice to do even more poorly than their single-transgenic Alzheimer's cagemates. But as the animals got to old age – about 18 months – the Tg2576-CD11c-DNR mice performed significantly better at traversing through various mazes. When the researchers examined their brains, they found up to 90% less amyloid.

For reasons that are not entirely clear, selectively blocking TGF-beta allowed macrophages, immune cells that ingest unwanted materials, to get across the blood brain barrier and into the brain. There, they feasted on amyloid plaques. "It was like a vacuum cleaner," says Flavell.

Several drug candidates already exist that are known to block TGF-beta in a similar way. It's too early to know if such a drug would be able to roll back the symptoms. "But even to reverse the decline would be an improvement," says Flavell.

Journal reference: Nature Medicine, DOI: 10.1038/nm1781

Plant Foods For Preserving Muscle Mass

ScienceDaily (May 31, 2008) — Fruits and vegetables contain essential vitamins, minerals and fiber that are key to good health. Now, a newly released study by Agricultural Research Service (ARS)-funded scientists suggests plant foods also may help preserve muscle mass in older men and women.

The study was led by physician and nutrition specialist Bess Dawson-Hughes at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston, Mass.

The typical American diet is rich in protein, cereal grains and other acid-producing foods. In general, such diets generate tiny amounts of acid each day. With aging, a mild but slowly increasing metabolic "acidosis" develops, according to the researchers.

***A diet rich in alkaline-producing fruits and vegetables may help preserve muscle mass*. (Credit: Peggy Greb)**

Acidosis appears to trigger a muscle-wasting response. So the researchers looked at links between measures of lean body mass and diets relatively high in potassium-rich, alkaline-residue producing fruits and vegetables. Such diets could help neutralize acidosis. Foods can be considered alkaline or acidic based on the residues they produce in the body, rather than whether they are alkaline or acidic themselves. For example, acidic grapefruits are metabolized to alkaline residues.

The researchers conducted a cross-sectional analysis on a subset of nearly 400 male and female volunteers aged 65 or older who had completed a three-year osteoporosis intervention trial. The volunteers' physical activity, height and weight, and percentage of lean body mass were measured at the start of the study and at three years. Their urinary potassium was measured at the start of the study, and their dietary data was collected at 18 months.

Based on regression models, volunteers whose diets were rich in potassium could expect to have 3.6 more pounds of lean tissue mass than volunteers with half the higher potassium intake. That almost offsets the 4.4 pounds of lean tissue that is typically lost in a decade in healthy men and women aged 65 and above, according to authors.

Sarcopenia, or loss of muscle mass, can lead to falls due to weakened leg muscles. The authors encourage future studies that look into the effects of increasing overall intake of foods that metabolize to alkaline residues on muscle mass and functionality.

The study was published in the March issue of the American Journal of Clinical Nutrition.