

High caffeine intake can lead to arrhythmias

By Professor Anna Vittoria Mattioli

Barcelona, Spain, 30 August: Coffee is routinely consumed in countries within the Mediterranean basin. Coffee, an infusion of ground, roasted coffee beans, is the most widely consumed behaviourally active substance in the world. It contains several hundred different substances including, antioxidants, carbohydrates, lipids, vitamins, minerals, phenolic compounds and alkaloids. Nevertheless, the effects of coffee on the cardiovascular system have been mainly related to caffeine. Acute and chronic caffeine intake appears to have only minor negative consequence on health. However, high levels of caffeine intake have been related to ventricular arrhythmias.

Epidemiologic studies have already underlined the beneficial role of the Mediterranean dietary pattern on mortality, coronary artery disease, lipid metabolism and on blood pressure. The diet of people living in Mediterranean area, where olive oil is the principal source of dietary fat, encompasses all the beneficial dietary characteristics presented in previous studies. Little information is available on relationship between adherence to Mediterranean Diet and atrial fibrillation (AF).

"We aimed to investigate the relationship between diets and atrial fibrillation, one of the most common arrhythmias, and we focused on coffee and caffeine intake" explained Prof Mattioli from the University of Modena, Italy. "We selected patients presenting with a first detected episode of AF. Nutrition habits were investigated by a self administered food frequency questionnaire that included 116 items, followed by an interviewer-administered 24 h diet recall questionnaire."

The adherence to Mediterranean Diet was assessed using a Mediterranean Score. The Mediterranean Diet is usually represented in the form of a pyramid, the base of which refers to foods which are suggested to be consumed most frequently (non-refined cereals and products, olive oil, vegetables and fruits) and the top of the pyramid to those foods to be consumed rarely (red meat and meat products). The score ranged from 0 to 55. Higher values of score indicate greater adherence to the Mediterranean diet.

Interviewers investigated coffee consumption and other sources of caffeine (i.e. soda drinks, cola, chocolate, tea). Coffee consumption was specifically estimated and we evaluated: type of coffee consumed (filtered or boiled), number of daily cup of espresso coffee, American coffee, decaffeinated and cappuccino.

Coffee intake was divided in 4 categories: low habitual (from 1 cup/day), medium habitual (2-3 cups/day), heavy habitual (more than 3 cups/day) and non-habitual (0 cup/day).

Caffeine intake was estimated adding the caffeine from other sources evaluated as number of chocolate snacks, number of cans of cola soda usually consumed, intake of tea and type of tea.

Findings include:

* Total calorie intake was similar in patients with arrhythmia and in control patients. The intake of calories was normal in both groups.

* Adherence to Mediterranean Diet was significantly lower in patients that developed atrial fibrillation. Patients that developed arrhythmias achieved a total calories intake similar to patients that did not develop AF, but the quality of food was different and the Mediterranean diet score was lower. Patients with arrhythmia had higher consumption of red meat, and full fat dairy.

* Estimated intake of total antioxidants from food was lower in patients with atrial fibrillation.

* Source of antioxidants were different in patients with atrial fibrillation. Patients with atrial fibrillation had higher intake of antioxidants from coffee compared to other source (vegetables, fruits, wine).

* Patients with atrial fibrillation had higher intake of caffeine compare to control.

* Patients with high intake of caffeine and coffee are more likely to develop atrial fibrillation.

In this population the adherence to Mediterranean Diet is scarce. In addition, the antioxidant intake from coffee is higher than antioxidant intake from vegetables and fruits. High antioxidant levels in coffee were reported in several studies. A major issue is whether the antioxidants from coffee are bioactive. Many epidemiologic studies found that coffee is associated with reduced early oxidative stress. Thus, coffee may contain several bioactive compounds, some of which may be beneficial, whereas others may increase the risk of disease. A second point is the synergistic and antagonist interactions between food components of diet and the complex of nutrients intake.

"Our study suggests that high intake of coffee increase the risk of arrhythmias in people without known cardiac disease", concludes Prof Mattioli.

No evidence for the routine use of aspirin in people with asymptomatic vascular events

By Professor Gerald Fowkes

Barcelona, Spain, August 30: The routine use of aspirin for the primary prevention of vascular events in people with asymptomatic disease cannot be supported, according to results from the Aspirin for Asymptomatic

Atherosclerosis (AAA) study. The study is the first placebo-controlled randomised trial designed to determine the effect of aspirin in asymptomatic atherosclerosis as reflected by a low ankle brachial index (ABI). Results found no statistically significant difference in primary endpoint events between those subjects allocated to aspirin or placebo (HR 1.03, 95% CI 0.84-1.27).

Joint first author Professor Gerry Fowkes from the Wolfson Unit for Prevention of Peripheral Vascular Diseases in Edinburgh said: "It is possible that in the general population, aspirin could produce a smaller reduction in vascular events than this trial was designed to detect, but it is questionable whether such an effect, together with aspirin related morbidity, would justify the additional resources and health care requirements of an ABI screening programme."

The benefits of antiplatelet therapy in the prevention of future cardio- and cerebrovascular events is well established in patients with a clinical history of arterial vascular disease (secondary prevention); however, evidence in primary prevention is limited, with studies suggesting that any benefit of aspirin must be weighed against the risk of bleeding. The aim of the AAA trial was to determine the effectiveness of aspirin in preventing events in people with asymptomatic atherosclerosis detected by ABI screening.

The study recruited 28,980 men and women aged 50 to 75 years who were free of clinically evident cardiovascular disease in central Scotland; all were given an ABI screening test. Those with a low ABI (3350 subjects, ≤ 0.95 ABI) were entered into the trial and randomised to once daily 100 mg aspirin or placebo. Participants were followed up for a mean of 8.2 years and outcomes ascertained by annual contact, general practitioner records, linkage to discharges from Scottish hospitals, and death notification. The primary endpoint was a composite of initial fatal or non-fatal coronary event or stroke, or revascularisation. There were two secondary endpoints: all initial vascular events defined as a composite of a primary endpoint event or angina, intermittent claudication or transient ischaemic attack; and all-cause mortality.

Results showed that 357 participants had a primary endpoint event (13.5 per 1000 person years, 95%CI 12.2-15.0), 181 in the aspirin group and 176 in the placebo group. A vascular event comprising the secondary endpoint occurred in 578 participants, but again no statistically significant difference was found between the aspirin and placebo groups (288 vs 290 events). All-cause mortality was similar in both groups (176 v 186 deaths). An initial event of major bleeding requiring admission to hospital occurred in 34 (2%) of subjects in the aspirin group and 20 (1.2%) in the placebo group.

Commenting on the results (and on the use of ABI as a screening method), Professor Fowkes said: "Although the AAA trial was not of screening per se, the results would suggest that using the ABI as a tool to screen individuals free of cardiovascular disease in the community is unlikely to be beneficial if aspirin is the intervention to be used in those found to be at higher risk. Other more potent antiplatelets might be considered, but only if increased effectiveness in avoiding ischaemic events is not matched by increased bleeding."

** The ankle brachial index (ABI) is the ratio of systolic pressure at the ankle to that in the arm, and is used in vascular practice to confirm diagnosis and assess the severity of peripheral atherosclerosis in the legs. Lower levels of the ABI are also associated with higher rates of concomitant coronary and cerebrovascular disease and with the presence of cardiovascular risk factors.*

Opals set to shine with new grading technology

CSIRO and a consortium of Australian Opal miners (Opal Producers Australia Limited) have unveiled the world's first automated device to grade opals using image analysis, at the 2009 National Council of Jewellery Valuers forum in Sydney.

Ms Bischof said that opals have a unique range of colour characteristics that makes them by far the most difficult gemstone to appraise.

"Qualities such as 'flash', the way an opal reflects light and colour as it is rotated, can vary with human eyesight and lighting conditions," Ms Bischof said. "A person's judgment of an opal's colours, the brightness of those colours and the area each of them covers is a really difficult task, even for a skilled opal assessor. You really need objective image analysis and automation to assist with that."



The Gemmological Digital Analyzer (GDA) is the world's first automated device to grade opals using image analysis.

Credit: Chris Taylor

Incorporating the expert knowledge of over 60 opal industry professionals, CSIRO designed a GDA prototype with Australian company Applied Robotics. CSIRO then developed the complex mathematical algorithms to drive the image analysis system behind the GDA. A small camera inside the GDA takes 871 images of the stone as it rotates on a stage which moves 360 degrees horizontally and tilts 90 degrees vertically.

High powered computers linked to the GDA analyse the images and quantify the opal's gemmological characteristics, providing a classification grade based on colour, clarity, carat, cut and character and a summary graph showing proportions of the opal's colours. A database of information on the GDA graded opals will allow participating jewellers and industry organisations to accurately assign a dollar value to a particular grade of stone depending on the daily market price.

Director of Opal Producers Australia Limited and Lightning Ridge Opal miner Peter Sutton said the value of the Australian opal industry is estimated to be worth around \$50 million a year, according to the Australian Bureau of Statistics. "We suspect this figure is grossly underestimated because valuations for a single stone can sometimes vary by thousands of dollars," Mr Sutton said.

The demand and trade for other Australian commodities like wheat, coal and gold have benefited from the introduction of an independent grading system, ensuring fair prices for producers and the supply of a consistent quality product to customers.

"We wanted to create an objective grading system that would improve the demand for and value of the Australian Opal industry, giving miners a fair price and consumer's confidence to trade with grade quality assurance," Mr Sutton said. "This will be an independently-graded Australian opal product, which we will brand as Opallia."

NIH study reveals new genetic culprit in deadly skin cancer ***Sequencing work points to new target for melanoma treatment***

Drawing on the power of DNA sequencing, National Institutes of Health researchers have identified a new group of genetic mutations involved in the deadliest form of skin cancer, melanoma. This discovery is particularly encouraging because some of the mutations, which were found in nearly one-fifth of melanoma cases, reside in a gene already targeted by a drug approved for certain types of breast cancer.

In the United States and many other nations, melanoma is becoming increasingly more common. A major cause of melanoma is thought to be sun exposure; the ultraviolet radiation in sunlight can damage DNA and lead to cancer-causing genetic changes within skin cells.

In work published in the September issue of *Nature Genetics*, a team led by Yardena Samuels, Ph.D., of the National Human Genome Research Institute (NHGRI) sequenced the protein tyrosine kinase (PTK) gene family in tumor and blood samples from people with metastatic melanoma. The samples were collected by the study's coauthor Steven Rosenberg, M.D., Ph.D., a leading expert on melanoma and chief of surgery at the National Cancer Institute (NCI).

The PTK family includes many genes that, when mutated, promote various types of cancer. However, relatively little had been known about roles played by PTK genes in human melanoma. The NIH study was among the first to use large-scale DNA sequencing to systematically analyze all 86 members of the PTK gene family in melanoma samples.

The team's initial survey, which involved samples from 29 melanoma patients, identified mutations in functionally important regions of 19 PTK genes, only three of which had been previously implicated in melanoma. The researchers then conducted more detailed analyses of those 19 genes in samples from a total of 79 melanoma patients.

One of the newly implicated genes stood out from the rest. Researchers detected mutations in the ERBB4 gene (also known as HER4) in 19 percent of patients' tumors, making it by far the most frequently mutated PTK gene in melanoma. In addition, researchers found that many ERBB4 mutations were located in functionally important areas similar to those seen in other PTK oncogenes involved in lung cancer, brain cancer and gastric cancer.

Next, the researchers moved on to laboratory studies of melanoma cells with ERBB4 mutations. They found that these melanoma cells were dependent on the presence of mutant ERBB4 for their growth. What's more, the melanoma cells grew much more slowly when they were exposed to a chemotherapeutic drug known to inhibit ERBB4. The drug, called lapatinib (Tykerb), was approved by the Food and Drug Administration in 2007 for combination use in breast cancer patients already taking the drug capecitabine (Xeloda).

Encouraged by their study results, the researchers are planning a clinical trial using lapatinib in patients with metastatic melanoma harboring ERBB4 mutations. The clinical trial will be conducted under the direction of Dr. Rosenberg at the NIH Clinical Center. "This collaborative study represents an ideal example of how sophisticated genetic analyses can be translated to the benefit of cancer patients," said Dr. Rosenberg.

"We have found what appears to be an Achilles' heel of a sizable share of melanomas," said Dr. Samuels, who is an investigator in the Cancer Genetics Branch of the NHGRI's Division of Intramural Research. "Though additional work is needed to gain a more complete understanding of these genetic mutations and their

roles in cancer biology, our findings open the door to pursuing specific therapies that may prove useful for the treatment of melanoma with ERBB4 mutations."

In addition to ERBB4, the researchers identified two additional PTK genes, FLT1 and PTK2B, with a relatively high rate of mutations in melanoma. Each of these genes was mutated in about 10 percent of the tumor samples studied.

NHGRI Scientific Director Eric D. Green, M.D., Ph.D., pointed out how such research is helping to lay the groundwork for the era of personalized medicine. "We envision a day when each cancer patient will have therapies tailored to the specific genetic profile of his or her tumor. Ultimately, this should lead to more effective and less toxic approaches to cancer care," said Dr. Green, who directs the NIH Intramural Sequencing Center, which generated the DNA sequence data for the melanoma study.

In addition to NIH scientists, the team included a researcher from the Johns Hopkins Kimmel Cancer Center in Baltimore.

In May 2009, Dr. Samuel's group reported in *Nature Genetics* another large-scale DNA sequencing study of a different group of genes involved in melanoma, the matrix metalloproteinase (MMP) gene family. This earlier study found that one gene, MMP-8, thought to spur cancerous growth actually served to inhibit it. Those findings are now helping to shape melanoma treatment strategies aimed at MMP genes.

**New assessment quantifies risks and benefits of warfarin treatment for atrial fibrillation
Kaiser Permanente, Mass. General study finds benefits strongest for oldest patients and others at high stroke risk**

Warfarin therapy for patients with atrial fibrillation – the most common type of significant heart rhythm disorder – appears to be most beneficial for the oldest patients, those who have had a prior stroke and for patients with multiple risk factors for stroke, according to a new study by Kaiser Permanente and Massachusetts General Hospital researchers. This comparative effectiveness research study – among the first and largest to quantify warfarin's net clinical benefit, how much a treatment's potential benefits outweigh its risks, in the usual clinical care of patients with atrial fibrillation – appears in the September 1 *Annals of Internal Medicine*.

As part of the ongoing ATRIA (AnTicoagulation and Risk Factors In Atrial Fibrillation) study, researchers followed 13,559 adults with atrial fibrillation treated within Kaiser Permanente of Northern California from 1996 to 2003. To evaluate the risks and benefits of warfarin treatment and give patients and physicians quantitative guidance in making therapeutic decisions, the researchers analyzed rates of the two most significant adverse events associated with warfarin therapy – ischemic stroke, the type produced by arterial blockage, and intracranial hemorrhage, bleeding within and around the brain. For patients who did and did not take warfarin, the investigators balanced the reduction in ischemic stroke attributable to treatment against the increase in intracranial bleeding associated with warfarin. Since intracranial hemorrhages usually have worse outcomes than ischemic strokes, bleeding events were given greater weight in the comparison.

While warfarin therapy benefited most atrial fibrillation patients, the balance of benefits over risks was greatest in those at highest risk of stroke – those with multiple risk factors, those with a history of stroke and the oldest patients. The benefits of treatment increased strikingly with age, with no clear benefit in the average patient younger than 65 but a reduction of more than two strokes per 100 patients in those 85 and older.

Occurring when the upper chambers of the heart quiver instead of smoothly contracting, atrial fibrillation affects more than 2.3 million Americans. Because the heart rhythm disturbance promotes the formation of blood clots that can travel to the brain and block an artery, atrial fibrillation increases the risk of stroke fivefold. The condition is highly age-dependent and affects 10 percent of those over age 80. Researchers have long known that warfarin is effective in preventing such strokes, but the treatment can be difficult to control and often leads to hemorrhage. In fact, warfarin is associated with the most emergency admissions for drug-related adverse reactions. Balancing the benefits of warfarin against its most severe risks is critical to making the best therapeutic decisions for individual atrial fibrillation patients, explains the study's senior author Alan S. Go, MD, director of the Comprehensive Clinical Research Unit at the Kaiser Permanente Division of Research.

Daniel Singer, MD, of the Massachusetts General Hospital (MGH) Clinical Epidemiology Unit, the report's lead author, adds, "This comparative effectiveness study gives us more information about which atrial fibrillation patients are most likely to benefit from carefully administered warfarin therapy." He explains that, by assessing warfarin within a "real world" practice setting, the study provides a more contemporary assessment of the therapy's overall effects than do older clinical studies.

Go explains that Kaiser Permanente physicians partner with pharmacist-run anticoagulation clinics to provide thorough and nimble administration and careful monitoring of warfarin therapy for atrial fibrillation patients. This allows for delivery of high-quality anticoagulation therapy through frequent testing and

appropriate dose adjustment to account for changes in diet, medications and clinical status that may impact the therapy's narrow therapeutic window.

Singer adds, "One of our distinctive findings is that stroke risk continues to increase in patients age 85 and older and that warfarin provides substantial net protection for these elderly patients. A caution is that all these patients were presumably judged by their physicians to be reasonable candidates for warfarin therapy, so these results do not automatically apply to all elderly atrial fibrillation patients."

Additional researchers on the study are Yuchiao Chang, PhD, and Leila H. Borowsky, MPH, MGH Clinical Epidemiology; Margaret C. Fang, MD, MPH, University of California at San Francisco; and Niela K. Pomernacki, RD, and Natalia Udaltsova, PhD, Kaiser Permanente Division of Research. Funding for the study was provided by the National Institute on Aging, the National Heart, Lung and Blood Institute, and the Eliot B. and Edith C. Shoolman fund of the MGH.

Overdiagnosis since introduction of prostate cancer screening

The introduction of prostate-antigen screening, or PSA, has resulted in over 1 million additional men over the last 23 years being diagnosed and treated for prostate cancer—most of whom were likely overdiagnosed, researchers reported in a new study published online August 31 in the *Journal of the National Cancer Institute*.

Overdiagnosis has been associated with early diagnosis in prostate cancer, but there have been no previous national estimates of its magnitude.

Using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results program, H. Gilbert Welch, M.D., MPH, of the White River Junction VA and The Dartmouth Institute for Health Policy & Clinical Practice., and Peter C. Albertsen, M.D., of the University of Connecticut, examined age-specific prostate cancer incidence rates to determine the excess (or deficit) in the number of American men diagnosed and treated in each year after 1986. PSA screening was introduced in 1987.

According to the study, an additional 1.3 million men were diagnosed—that would otherwise have never been diagnosed absent screening - and more than 1 million have been treated since 1986.

"Given the considerable time that has passed since PSA screening began, most of this excess incidence must represent overdiagnosis," the authors write. "All overdiagnosed patients are needlessly exposed to the hassle factors of obtaining treatment, the financial implications of the diagnosis, and the anxieties associated with becoming a cancer patient..."

The increased diagnosis has been most dramatic among younger men: more than tripling since 1986 in men aged 50-59 (from 58.4 to 212.7 per 100,000) and more than a sevenfold increase in men under age 50 (from 1.3 to 9.4 per 100,000).

In an accompanying editorial, Otis W. Brawley, M.D., chief medical officer of the American Cancer Society, discusses how screening practices for prostate cancer have surged over the last 20 years, despite little evidence that it has saved lives.

According to Brawley, the highly pushed early-detection message has skewed public opinion and delegitimized the questions concerning screening, causing many men to be overdiagnosed. Mortality has decreased since the early 1990s, the editorialist points out, but reasons for this decline are unclear.

"We desperately need the ability to predict which patient has a localized cancer that is going to metastasize and cause suffering and death and which patient has a cancer that is destined to stay in the patient's prostate for the remainder of his life," he writes.

Aspirin works for primary prevention in moderate and high risk diabetics

By Professor Harald Darius

Barcelona, Spain, 31 August: The beneficial effects of aspirin in primary prevention of cardiovascular events i.e. stroke, MI and cardiac death are known and generally accepted. In a recent meta-analysis total cardiovascular event rate was shown to be reduced by 12% and the rate of myocardial infarctions by 18% (*Lancet* 2009; 373, 1849-60). This holds specifically true for individuals with a 10-year risk for cardiac death above 5% or a total cardiovascular event risk above 15%. Several scientific bodies including the ESC do recommend aspirin for primary prevention in this population, including all diabetics.

Recent trial results seem to contradict this general recommendation. Dr Hisao Ogawa et al. published the results of the Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) (*JAMA* 2008; 300, 2134-41) Trial showing no significant effect of aspirin on a combined endpoint of cardiovascular adverse events including fatal or nonfatal ischemic heart disease, fatal or nonfatal stroke and peripheral artery disease. However, the event rate in this trial was much lower than predicted and therefore the trial was largely underpowered to draw a meaningful conclusion. In addition, secondary endpoints focussing on more severe events like death, MI and stroke exerted a significant effect of aspirin in the entire patient cohort, as did the observation of the primary endpoint in diabetics above the age of 65 years.

The key role of antiplatelet therapy (mainly aspirin) for the secondary prevention of myocardial infarction and strokes is firmly established for high-risk patients with established arterial disease, and the proportional reductions in these cardiovascular events appear to be in the range of 20 to 25%, independent if the patients have diabetes or not. However, many young and middle-aged persons with diabetes do not have manifest arterial disease yet - although they are at a significant cardiovascular risk. Therefore, the substantial persons with uncertainty about the role of aspirin for the prevention of myocardial infarctions and strokes among apparently vascular healthy diabetes will remain until results of ongoing trials focussing on diabetics will be published in the years to come.

Until these results are available, the clinical strategy should include aspirin for primary prevention in all diabetics above the age of 65 years, or below 65 years if there is at least one additional cardiovascular risk factor present like obesity, hypertension or dyslipoproteinemia. In the case of a known vascular disease proven by the presence of atherosclerotic plaques in the coronary or carotid circulation, or a reduced ABI for the peripheral circulation, all diabetics should be offered a primary prevention with aspirin.

New sensitive markers to detect myocardial infarction

By Professor Christian Müller

Barcelona, Spain, 31 August: New biomarkers significantly improve the early detection of acute myocardial infarction (AMI). Recent studies reveal a novel and promising way for doctors to conclusively ensure that a patient is having or not having an AMI in a timely and accurate manner saving time and money. In the assessment of patients presenting with chest pain and suspected AMI doctors rely on detailed patient assessment, the ECG, and the measurement of cardiac troponins (specific markers for dying cells in the heart). AMI is the cause of death in more persons worldwide than any other disease. With effective treatment within our grasp, accurate and rapid diagnosis is of major medical and economic importance. With the development of blood tests depicting either cardiac troponin I or cardiac troponin T, the only current biomarkers thought to be unique to the heart, the diagnosis of AMI has been veritably revolutionised. In a patient presenting with chest pain, a rise in cardiac troponin has become a mandatory feature for the clinical diagnosis of AMI. Unfortunately, current cardiac troponin assays have one major limitation in common with their predecessor (CK-MB): it takes 3 hours after symptom onset until cardiac troponin becomes detectable. This is a major problem for doctors and causes diagnostic uncertainty particularly in patients presenting within the first hours from chest pain onset.

Recently, data from large multicenter studies have become available that demonstrate for the first time the impact of two novel biomarkers and therefore two novel approaches in the early diagnosis of AMI: sensitive cardiac troponin assays and copeptin, a marker of endogenous stress, in combination with standard cardiac troponin. Both approaches seem to largely overcome the sensitivity deficit of current standard cardiac troponin.

The more sensitive the cardiac troponin assay used, the smaller the number of dying myocardial cells necessary for this signal to be detected. Recent studies have clearly shown that sensitive cardiac troponin assays have a significantly higher diagnostic accuracy for the diagnosis of AMI and enable doctors to detect AMI already at presentation to the emergency department in the vast majority of patients.

More rapid diagnosis of AMI may reduce complications by allowing for earlier revascularization, earlier transfer to the coronary care unit, and earlier initiation of evidence-based treatment for AMI. In addition, the sensitive cardiac troponin assays may make it possible to reliably rule out the diagnosis of AMI in many patients on the basis of the initial measurement. The negative predictive value of the 99th percentile of the sensitive cardiac troponin assays, used as a single variable, was 97 to 99%. When sensitive cardiac troponin assays are used in conjunction with a clinical assessment and ECG, they will substantially reduce the percentage of patients in whom the diagnosis is uncertain after the first cardiac troponin measurement and for whom continuous ECG monitoring and serial blood sampling is necessary. The cost savings associated with this increase in early diagnostic accuracy might be substantial.

Similar findings were reported for the combination of copeptin and standard cardiac troponin. Copeptin, the C-terminal part of the vasopressin prohormone, is a marker of acute endogenous stress. If a patient suffering chest pains tested negative at presentation for both standard cardiac troponin and copeptin, which was the case in two-thirds of all patients studied, then there was a 99% probability that the patient was not having AMI, the study found. Only in the remaining minority of patients testing positive for either marker or both, would it be necessary to go the usual route of staying in the emergency room, monitoring and retesting a few hours later.

By looking at the copeptin levels in blood as a marker of acute endogenous stress, Tobias Reichlin, M.D., and co-workers from the Department of Internal Medicine, University Hospital Basel, Switzerland, sought to determine the incremental value of copeptin for a rapid rule out of AMI. Since the onset of chest pain associated with AMI is an enormous stress for the patient, copeptin levels were highest in patients presenting very early after the onset of symptoms.

Astronomers find coldest, driest, calmest place on Earth

The search for the best observatory site in the world has led to the discovery of what is thought to be the coldest, driest, calmest place on Earth. No human is thought to have ever been there but it is expected to yield images of the heavens three times sharper than any ever taken from the ground.

The joint US-Australian research team combined data from satellites, ground stations and climate models in a study to assess the many factors that affect astronomy – cloud cover, temperature, sky-brightness, water vapour, wind speeds and atmospheric turbulence.

The researchers pinpointed a site, known simply as Ridge A, that is 4,053m high up on the Antarctic Plateau. It is not only particularly remote but extremely cold and dry. The study revealed that Ridge A has an average winter temperature of minus 70°C and that the water content of the entire atmosphere there is sometimes less than the thickness of a human hair.

It is also extremely calm, which means that there is very little of the atmospheric turbulence elsewhere that makes stars appear to twinkle: "It's so calm that there's almost no wind or weather there at all," says Dr Will Saunders, of the Anglo-Australian Observatory and visiting professor to UNSW, who led the study.

"The astronomical images taken at Ridge A should be at least three times sharper than at the best sites currently used by astronomers," says Dr Saunders. "Because the sky there is so much darker and drier, it means that a modestly-sized telescope there would be as powerful as the largest telescopes anywhere else on earth."

They found that the best place in almost all respects was not the highest point on the Plateau – called Dome A – but 150km away along a flat ridge.

"Ridge A looks to be significantly better than elsewhere on the Antarctic plateau and far superior to the best existing observatories on high mountain tops in Hawaii and Chile," says Dr Saunders.

The finding is published today in the Publications of the Astronomical Society. Located within the Australian Antarctic Territory (81.5° S 73.5° E), the site is 144km from an international robotic observatory and the proposed new Chinese 'Kunlun' base at Dome A (80.37° S 77.53° E).

Interest in Antarctica as a site for astronomical and space observatories has accelerated since 2004 when UNSW astronomers published a paper in the journal Nature confirming that a ground-based telescope at Dome C, another Antarctic plateau site, could take images nearly as good as those from the space-based Hubble telescope.

Last year, the Anglo-Australian Observatory completed the first detailed study into the formidable practical problems of building and running the proposed optical/infra-red PILOT telescope project in Antarctica. The 2.5-metre telescope will cost over AUD\$10million and is planned for construction at the French/Italian Concordia Station at Dome C by 2012.

"Australia contains no world-class astronomical sites, and Australian astronomers face a choice between being minor players in telescopes in Chile or joining Chinese or European efforts to build the first major Antarctic observatory," says Dr Saunders.

How much omega-3 fatty acid do we need to prevent cardiovascular disease?

New research in the FASEB Journal identifies the 'Goldilocks dose' of DHA that is 'just right' for preventing oxidative stress in men

A team of French scientists have found the dose of DHA (docosahexaenoic acid) that is "just right" for preventing cardiovascular disease in healthy men. In a research report appearing in the September 2009 print issue of The FASEB Journal (<http://www.fasebj.org>), the scientists show that ***a 200 mg dose of DHA per day is enough to affect biochemical markers that reliably predict cardiovascular problems***, such as those related to aging, atherosclerosis, and diabetes. This study is the first to identify how much DHA is necessary to promote optimal heart health.

"This study shows that regularly consuming small amounts of DHA is likely to improve the health status of people, especially in regards to cardiovascular function," said Michel Lagarde, co-author of the study.

To determine the optimal dose of DHA, Lagarde and colleagues examined the effects of increasing doses of DHA on 12 healthy male volunteers between ages of 53 and 65. These men consumed doses of DHA at 200, 400, 800, and 1600 mg per day for two weeks for each dose amount, with DHA being the only omega-3 fatty acid in their diet. Blood and urine samples were collected before and after each dose and at eight weeks after DHA supplementation stopped. The researchers then examined these samples for biochemical markers indicating the effects of each dose on the volunteers.

"Now that we have a very good idea about how much DHA is just right, the next step is to try it out in an expanded clinical trial that involves many more people," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Until then, I'll stick with tasty foods that contain DHA, like fish, rather than getting a quick fatty-acid fix at the local vitamin store."

National guideline released for the treatment of hoarseness

New recommendations from ENT doctors on the management of a common voice problem in adults and children

Alexandria, Va. - The American Academy of Otolaryngology – Head and Neck Surgery Foundation (AAO-HNSF) will issue the first - and only - national clinical practice guideline to help healthcare practitioners identify and manage patients with hoarseness, also known as dysphonia. The guideline emphasizes evidence-based management of hoarseness by clinicians, and educates patients on the prevalence of this common vocal health issue.

"Hoarseness affects approximately 20 million people in the U.S. at any given time, and about one in three individuals will become hoarse at some point in their life," said Richard M. Rosenfeld, MD, MPH, an author of the guideline and chair of the AAO-HNSF Guideline Development Task Force. "In addition to the impact on health and quality of life, hoarseness leads to frequent healthcare visits and several billion dollars in lost productivity annually from work absenteeism."

The terms hoarseness and dysphonia are often used interchangeably, however, hoarseness is a symptom of altered voice quality and dysphonia is a diagnosis. Hoarseness (dysphonia) is defined as a disorder characterized by altered vocal quality, pitch, loudness, or vocal effort that impairs communication or reduces voice-related quality of life. Hoarseness may affect newborns, infants, children, and adults of any age. Individuals with hoarseness have impaired communication with their family and peers, which may result in depression, social isolation, missed work, lost wages, or reduced quality of life.

"Most hoarseness is caused by benign or self-limiting conditions, but it may also be the presenting symptom of a more serious or progressive condition requiring prompt diagnosis and management," said Seth R. Schwartz, MD, MPH, chair of the Hoarseness Guideline Panel. "This new guideline is intended to enhance diagnosis, promote appropriate therapy, improve outcomes, and to expand counseling and education for prevention."

Hoarseness is more common in women (50% higher than men), children (peak range 8-14 years), the elderly, and professional voice users (e.g., teachers, performers, telemarketers, aerobics instructors). In spite of how common the condition is, a recent survey by the AAO-HNS revealed that many Americans are unfamiliar with the possible causes and appropriate treatment for hoarseness. The survey revealed that almost half of adults are not aware that persistent hoarseness may be a symptom of cancer. Separate research cited in the guideline also found that only 5.9 percent of those with hoarseness seek treatment.

Recognizing that patients who do seek care may see many different types of healthcare providers, the guidelines are intended for all clinicians who are likely to diagnose and manage patients with hoarseness.

Key features of the new guideline include:

* Most, but not all, hoarseness is the result of benign underlying or self-limiting factors; however, clinicians should consider the possibility of a serious underlying condition (growth or tumor of the larynx) or medication side effects as a cause.

* Laryngoscopy is an office procedure to visualize the larynx (voice box and vocal cords) that should be performed if hoarseness persists or if the cause is uncertain.

* Imaging studies, such as a CT or MRI scans, should not be obtained for a primary complaint of hoarseness prior to visualizing the larynx; laryngoscopy is the primary diagnostic modality and should be done first.

* Anti-reflux medicines should not be prescribed for hoarseness unless there are (a) signs or symptoms of gastroesophageal reflux disease (GERD), such as heartburn or regurgitation, or (b) signs of inflammation of the larynx seen during laryngoscopy.

* Steroids or antibiotics given by mouth are not recommended for hoarseness and should not be used routinely.

* Voice therapy is a well-established intervention for hoarseness that can be performed at any age. Laryngoscopy should be performed prior to voice therapy and results communicated to the speech-language pathologist. Therapy for hoarseness usually includes one to two sessions per week for four to eight weeks.

* Surgery is not the primary treatment for most hoarseness, but may be indicated for suspected cancer, other tumors or growths, abnormal movement of the vocal cords, or abnormal tone of the vocal cord muscles.

* The risk of hoarseness may be reduced by preventive measures such as staying well-hydrated, avoiding irritants (especially tobacco smoke), voice training, and amplification during heavy voice use.

"In an era of health reform and comparative effectiveness research, well-crafted guidelines help improve quality, promote optimal outcomes, minimize harm, and reduce inappropriate variations in care," says Dr. Rosenfeld. "It is hoped that these guidelines will give clinicians the tools they need to spot an issue early, avoid poor outcomes, and reduce healthcare costs."

The guideline was created by a multidisciplinary panel representing neurology, speech-language pathology, professional voice teaching, family medicine, pulmonology, geriatric medicine, nursing, internal medicine, otolaryngology – head and neck surgery, pediatric medicine, and consumers.

What are the benefits of Tetris?

By Mark Yates BBC News

It's one of the world's most simple computer games - but, as a new report suggests, there could be more to Tetris than the idle act of fitting blocks together on a computer screen.

Computer games have changed beyond all recognition since those early days when blocky graphics would judder across a screen and explode with all the sonic impact of an egg box being crushed.

But while most of today's new games boast the production values of a Hollywood blockbuster, a handful of old favourites continue to defy their apparent sell-by date. There's Solitaire, the card game that comes pre-installed on every version of Windows.

And then there's Tetris, the creation of a Soviet computer programmer which requires players to move different shaped blocks into position so they form a straight line and then disappear from the screen. Despite its minimalism, this year Tetris celebrates its 25th birthday.

But while Tetris continues to win over new legions of entry-level computer gamers, it's also been drawing the interest of brain scientists. Some even suggest the game may actually be good for the health of the mind if not the body. While hours spent struggling to sink those breezeblocks render fingers sore and gnarled, there are scientific studies that point to wider benefits.

The latest inquiry comes from the Mind Research Network (MRN) - a brain research organisation based in the United States. Using little more than MRI brain scanners and game consoles, scientists have found that regular turns on Tetris caused the grey matter in a group of teenage girls to thicken.

Earlier this year, Oxford University reported that Tetris could reduce the flashbacks experienced in post-traumatic stress disorder (PTSD).

In the research published this week, 26 adolescents were asked to play Tetris for 30 minutes a day over a three-month period. Their brain power was then compared with a similar group who hadn't been playing the game.

The theory is that Tetris thickens the cerebral cortex - part of the brain that plays a key role in memory, attention, perceptual awareness, thought, language and consciousness.

"What we found was a change in the brain after playing Tetris," says Dr Richard Haier, a neurologist who led the project. "The thickness of the cerebral cortex actually increased, by less than half a millimetre.

Brain efficiency

"It used to be thought that the number of neurones [brain cells] in the brain was fixed after a certain age. This appears not to be true."

It's not the first time Dr Haier has seen research potential in playing Tetris, initially discovering the game in the early 1990s. "Back then we were trying to find out what happens if you practise something over time. We suspected that the brain efficiency was the key concept. "I was looking for a game that was suited to look at what happens to the brain when you practise a complex task. In 1991 no one had heard of Tetris. I went to the computer store to see what they had and the guy said, 'here try this it's just come in'.

"Tetris was the perfect game, it was simple to learn, you had to practise to get good and there was a good learning curve. Tetris is an excellent tool for neuroscience."

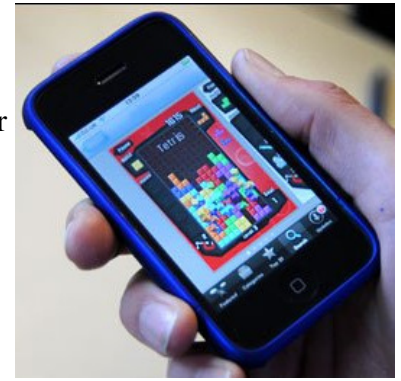
The link between computer games and boosting brain power is not new. Leading software companies like Nintendo have created their own brain-training games, such as MindFit, IQ Academy and Anagrammatic. These claim to sharpen up mental processes like memory, visual spatial awareness and concentration. But the apparent benefits of Tetris or other such games only go so far. What scientists have so far failed to find out is whether the new mental powers learnt from playing Tetris can help with anything other than... playing Tetris.

"The \$64,000 question is whether these brain changes are beneficial to activities other than playing Tetris. They are very important questions about the brain and learning."

Cabbie proof

Dr Chris Bird, a clinical neuroscientist at UCL, is cautious should anyone think Tetris is a short-cut to becoming brainier.

"If you practise something you are going to have to engage your brain in some way. By doing something again and again the parts of the brain involved in that operation will change," says Dr Bird. "It's the same with tests



on cab drivers in London who have to do the Knowledge [memorise every street in the capital]. These studies also show a decrease in other parts of the brain. "So while some parts of the brain show an increase in cells, there's a cost."

And one thing that Tetris doesn't seem to help is visual perception. Dr Bird cites a study from 2003 which assessed the benefits of action games, or "shoot 'em up" games, and found they helped improved a player's visual perception. In that research, Tetris was played by the control group - and those who played the puzzle game had not notably improved on the tests.

So what about hardened Tetris players themselves - do they see any knock-on benefits in other parts of their life?

Waste of time

Vincent Laurent, a member of *harddrop.com*, an online community of Tetris addicts, has been hooked on the game for 17 years. He said the attraction for him is its deceptive straightforwardness.

"Under a really simple and easy appearance, the game is incredibly deep and complex, it needs many years to assimilate every combination and keys to solve the problem.

"Today we have some versions of Tetris game which require five years to be finished, there is no more harder video game in the world than Tetris Grand Master 2 and Tetris Grand Master 3."

After spending much of his life glued to Tetris, Vincent, who is French, is in a strong position to judge whether it improved his mental skills.

"Honestly, with the level I have reached today, I prefer to think that I wasted my time," he laughs.

"I am sure it doesn't improve anything in the brain, except the Tetris skill itself. I can play today at more than three pieces per second, but I am slow in life, slow and a perfectionist. Tetris never helped me to think better or faster unfortunately."

Exercise alone shown to improve insulin sensitivity in obese sedentary adolescents New study isolates impact of exercise from diet and weight loss interventions

Chevy Chase, MD—A moderate aerobic exercise program, without weight loss, can improve insulin sensitivity in both lean and obese sedentary adolescents, according to a new study accepted for publication in *The Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM)*. Insulin is a hormone produced in the pancreas that permits glucose to enter cells to be used for energy or stored for future use by the body.

Because obese adolescents are resistant to insulin, in order to maintain normal blood sugar levels, they have to increase their production of insulin. Increased insulin production however, places higher demands on the pancreas. These higher demands can exhaust pancreatic beta cells to the point that they no longer produce sufficient amounts of insulin to keep blood sugar levels normal, which might subsequently lead to type 2 diabetes.

"Because weight loss can be difficult to achieve and maintain in obese sedentary children, the purpose of this study was to determine whether a controlled exercise program, without any diet intervention and with no intention of weight loss, would improve fat distribution and sensitivity to insulin," said Agneta Sunehag, MD, PhD, of Baylor College of Medicine and senior author of the study. "We found that a 12-week moderate aerobic exercise program consisting of four 30-minute workouts a week increased fitness and improved insulin sensitivity in both lean and obese adolescents."

In this study, 29 adolescents (14 lean and 15 obese) completed the 12-week moderate aerobic exercise program. During the exercise sessions, subjects worked out on a treadmill, elliptical or bicycle. The goal of each exercise session was to get the participants' heart rate to increase to at least 70 percent of their maximum capacity. Glucose and insulin concentrations were measured both before and after the exercise program. Cardiovascular fitness was determined using an oxygen consumption test which consists of measuring oxygen uptake of the participant during a treadmill exercise where speed and incline is increased every three minutes until the subject reaches his maximum exercise capacity.

"Many studies include both diet and exercise interventions, which makes it difficult to determine which intervention is most effective and best accepted by adolescents," said Sunehag. "Our findings show that exercise alone can increase fitness and improve insulin sensitivity, making an aerobic program like the one used in this study a potential useful tool in preventing obesity-related illnesses."

Other researchers working on the study include Gert-Jan van der Heijden of Baylor College of Medicine in Houston, Tex.; Gianna Toffolo and Erica Manesso of the University of Padova in Padua, Italy; and Pieter Sauer of the University of Groningen in The Netherlands.

The article, "Aerobic exercise increases peripheral and hepatic insulin sensitivity in sedentary adolescents," will appear in the November 2009 issue of JCEM.

Really?

The Claim: Chamomile Can Soothe a Colicky Baby.

By ANAHAD O'CONNOR

THE FACTS Colic - uncontrolled screaming and crying in an otherwise healthy infant - can be one of the most stressful parts of raising a newborn.

While its cause is uncertain, there is evidence that it stems in part from gastrointestinal discomfort. That may explain why chamomile tea, which according to research can ease intestinal spasms, has long been a home remedy for colic. Various studies have examined its usefulness, finding it simple, inexpensive and fairly effective.



Leif Parsons

One report by the American Academy of Pediatrics in 2007 reviewed two of those studies, including a randomized clinical trial that involved 68 colicky but otherwise healthy infants, ages 2 to 8 weeks. One group received either an herbal tea (served warm or cool) made primarily with German chamomile, and the other placebo tea. The scientists reported that each infant was offered either the tea or placebo with every bout of colic, up to 150 milliliters - a little more than half a cup - no more than three times a day. After a week, "parents reported that the tea eliminated the colic in 57 percent of the infants," the researchers reported, "whereas placebo was helpful in only 26 percent. No adverse effects were noted in either group."

Other studies have had similar results. Experts say allergic reactions to chamomile are rare, but one way to check is to swab a bit on the skin. If no redness develops, it should be safe.

THE BOTTOM LINE Research suggests chamomile may ease colic.

A Doomed Planet, and Scientists Are Lucky to Have Spotted It

By KENNETH CHANG

Were astronomers just lucky when they discovered the planet WASP-18b?

At first impression, the planet, described in the current issue of the journal *Nature*, fits a familiar profile for planets that have been discovered around other stars: big (about 10 times the mass of Jupiter), close to the parent star (about 1.9 million miles away, or just one-fiftieth of the distance between the Sun and Earth) and hot (3,800 degrees Fahrenheit). About one-quarter of the nearly 400 planets discovered so far have been such "hot Jupiters."

But as an international team of astronomers looked more closely, they became more surprised that they had seen WASP-18b at all. The tidal forces between a star and a planet dissipate energy, and WASP-18b is so close that it should fall into its host star in less than a million years — an eye blink on the cosmic scale. (Andrew Collier Cameron, a professor of astronomy at the University of St. Andrew and a member of the team, noted that with the impending fiery fate of the planet, it seemed appropriate that it was located in the constellation Phoenix.)

The star system is about a billion years old, the astronomers reported, so the chances that they observed WASP-18b on the cusp of oblivion is about 1 in 1,000.

In an accompanying commentary in *Nature*, Douglas P. Hamilton, a professor of astronomy at the University of Maryland, noted that this was roughly the same unlikely probability as drawing two red aces in a row from a full deck of cards. "Of those 400 objects, it's unique," Dr. Hamilton said. "It's the only planet that's going to be crashing into its star in one million years."

But luck is not the only possibility. Ignorance could be another. It might be that astronomers do not understand the dynamics of stellar tides. The rate of energy dissipation depends on how well the star vibrates - ringing like a bell or thumping like a chunk of wood. (If the star is ringing, less energy is dissipated, and WASP-18b would not be falling as quickly.) This difficult-to-measure quantity, which depends on turbulence inside the star, is not known for individual stars, not even for the Sun.

The answer does not have to wait a million years. In fact, astronomers just have to wait 5 to 10 years. WASP-18b already whips around the star every 22 hours, 35 minutes, 41.5 seconds — a year in less than an Earth day. If it is falling inward as fast as predicted, its day will shorten noticeably in the coming years.

H1N1 Pandemic Virus Does Not Mutate Into 'Superbug' in UMd. Lab Study First to Examine Potential Interactions with Seasonal Flu Strains

COLLEGE PARK, Md. - A laboratory study by University of Maryland researchers suggests that some of the worst fears about a virulent H1N1 pandemic flu season may not be realized this year, but does demonstrate the heightened communicability of the virus. Using ferrets exposed to three different viruses, the Maryland researchers found no evidence that the H1N1 pandemic variety, responsible for the so-called swine flu, combines in a lab setting with other flu strains to form a more virulent 'superbug.' Rather, the pandemic virus prevailed and out-competed the other strains, reproducing in the ferrets, on average, twice as much.

The researchers believe their study is the first to examine how the pandemic virus interacts with other flu viruses. The findings are newly published in an online scientific journal designed to fast-track science research and quickly share results with other investigators, PLOS Currents.

"The H1N1 pandemic virus has a clear biological advantage over the two main seasonal flu strains and all the makings of a virus fully adapted to humans," says virologist Daniel Perez, the lead researcher and program director of the University of Maryland-based Prevention and Control of Avian Influenza Coordinated Agricultural Project. "I'm not surprised to find that the pandemic virus is more infectious, simply because it's new, so hosts haven't had a chance to build immunity yet. Meanwhile, the older strains encounter resistance from hosts' immunity to them," Perez adds.

Some of the animals who were infected with both the new virus and one of the more familiar seasonal viruses (H3N2) developed not only respiratory symptoms, but intestinal illness as well. Perez and his team call for additional research to see whether this kind of co-infection and multiple symptoms may account for some of the deaths attributed to the new virus.

Among other research findings, the pandemic virus successfully established infections deeper in the ferret's respiratory system, including the lungs. The H1 and H3 seasonal viruses remained in the nasal passages.

"Our findings underscore the need for vaccinating against the pandemic flu virus this season," Perez concludes. "The findings of this study are preliminary, but the far greater communicability of the pandemic virus serves as a clearly blinking warning light."

Perez and his team used samples of the H1N1 pandemic variety from last April's initial outbreak of the so-called swine flu.

The research is funded by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

Essay

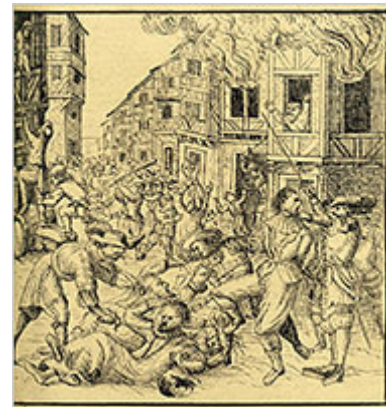
Finding a Scapegoat When Epidemics Strike

By DONALD G. McNEIL Jr.

Whose fault was the Black Death?

In medieval Europe, Jews were blamed so often, and so viciously, that it is surprising it was not called the Jewish Death. During the pandemic's peak in Europe, from 1348 to 1351, more than 200 Jewish communities were wiped out, their inhabitants accused of spreading contagion or poisoning wells.

The swine flu outbreak of 2009 has been nowhere near as virulent, and neither has the reaction. But, as in pandemics throughout history, someone got the blame - at first Mexico, with attacks on Mexicans in other countries and calls from American politicians to close the border.



DEMONIZED Above, a detail from the *Friese Chronicles* showing the 1349 massacre of Erfurt Jews in Germany, who were blamed for the Black Death. Yeshiva University Museum

In May, a Mexican soccer player who said he was called a "leper" by a Chilean opponent spat on his tormentor; Chilean news media accused him of germ warfare. In June, Argentines stoned Chilean buses, saying they were importing disease. When Argentina's caseload soared, European countries warned their citizens against visiting it.

"When disease strikes and humans suffer," said Dr. Liise-anne Pirofski, chief of infectious diseases at Albert Einstein College of Medicine and an expert on the history of epidemics, "the need to understand why is very powerful. And, unfortunately, identification of a scapegoat is sometimes inevitable."

A recent exhibition, "The Erfurt Treasure," at the Yeshiva University Museum in Manhattan, displayed a timely and depressing memento of this all too human habit. A chest with more than 600 pieces of gold jewelry, including a magnificent 14th-century wedding ring, was dug up during excavations in what was once a thriving Jewish quarter in Erfurt, Germany. It also held 3,141 silver coins, most with royal portraits; the last king depicted on them died in 1350.

That, said Gabriel M. Goldstein, the museum's associate director of exhibitions, strongly suggests the hoard was buried in 1349, the year the plague reached Erfurt.

"Why put such a huge investment portfolio in the ground and leave it for 700 years?" he asked. "There was a major uprising against Erfurt's Jews - records say 100 or 1,000 were killed. Seemingly, whoever hid it died and never came back."

Dr. Martin J. Blaser, a historian who is chairman of medicine at New York University's medical school, offers an intriguing hypothesis for why Jews became scapegoats in the Black Death: they were largely spared, in comparison with other groups, because grain was removed from their houses for Passover, discouraging the rats that spread the disease. The plague peaked in spring, around Passover.

But in every pandemic, the chain of causation is intricate. The historian William H. McNeill, author of “Plagues and Peoples,” suggests that ultimate blame may rest with Möngke Khan, grandson of Genghis, who in 1252 sent his armies as far south as present-day Burma, putting them in contact with rodents whose fleas played host to *Yersinia pestis*, the plague bacillus. After *Yersinia* returned with them to the flea-bitten marmots of the Eurasian steppes, it began creeping through the rodent burrows lining Mongol caravan routes, which stretched as far west as the Black Sea. That’s where plague-ridden rats boarded ships in the besieged Crimean port of Caffa in 1346, taking it to Europe.

But that lets off the hook the Indian or Egyptian sailors who had presumably first moved the wild black rat out of India 1,000 years earlier. And then, whom in prehistory does one blame for first carrying *Yersinia* north from its original home in the Great Lakes region of Africa?

It is not uncommon for ethnic groups to have religious or cultural customs that protect against disease - but whether it was originally intended to do that or not is often lost in time.

Manchurian nomads, Dr. McNeill said, avoided plague because they believed marmots harbored the souls of their ancestors, so it was taboo to trap them, although shooting them was permitted. But in the early 20th century, trapping by immigrants from China contributed to plague outbreaks.

And Tamils from India working as plantation laborers in Malaysia may have had less malaria and dengue than their Malay and Chinese co-workers did because they never stored water near their houses, leaving mosquitoes no place to breed.

The most visible aspect of blame, of course, is what name a disease gets. The World Health Organization has struggled mightily to avoid the ethnic monikers given the Spanish, Hong Kong and Asian flus, instructing its representatives to shift from “swine flu” to “H1N1” to “A (H1N1) S-O.I.V.” (the last four initials stand for “swine-origin influenza virus”) to, recently, “Pandemic (H1N1) 2009.”

Headline writers have rebelled, and ignored them.

Dr. Mirta Roses, director of the Pan American Health Organization, said that in the pandemic’s early days, she fought suggestions that it be named the Mexican flu or the Veracruz flu or the La Gloria flu after the country, state and town where it was discovered. “We try to avoid demonizing anyone and to keep the focus on the virus,” she said. “It helps reduce the level of panic and aggression.”

When Dr. Roses was a girl, growing up in a small town in Argentina, her neighbors blamed city dwellers for polio. One summer, families took turns with the local police staffing roadblocks to turn back buses from the capital.

“No one wanted the people from Buenos Aires,” she said, “because they were bringing polio.” (There was some logic in it. Polio, an intestinal virus, peaks in summer, and is more common in cities with overflowing sewers than in rural areas with outhouses.)

“It wasn’t until I grew up that I learned that that was no way to fight it,” she said. “It was vaccinating 99 percent of the children that stopped polio.”

By the old naming conventions, the 1918 Spanish flu probably ought to be known as the Kansas flu. According to “The Great Influenza: The Epic Story of the Deadliest Plague in History,” John M. Barry’s history of the epidemic, the first identifiable cases arose in Haskell County, in Kansas. They soon spread to Fort Riley, from there to other military bases, and then to Europe in troop ships. France, Germany and Britain had war censors controlling news reports; Spain did not. Spain got the blame.

The Spread of Black Death

Fleas and marmots carried the plague bacillus along Mongol caravan routes as far as the Black Sea, and shipboard rats carried the disease from there into Western Europe. Dashed lines show the advance of plague across the continent during the peak of the pandemic.



Source: “Plagues and Peoples” by William H. McNeill

THE NEW YORK TIMES

Most human diseases originate in animals. While culling animals sometimes makes sense as a public health measure - for example, culling chickens to stop an outbreak H5N1 avian flu - animals are also sometimes “punished” pointlessly. In May, the Egyptian government slaughtered thousands of pigs belonging to the Coptic Christian minority, despite international protests that doing so was racist against Copts and medically pointless because the disease was already in people. When the swine flu arrived anyway - in a 12-year-old American girl, the first confirmed case - the government vowed to hunt down the last few pigs hidden by poor families and kill them on the spot.

In Afghanistan, Khanzir, the country’s only pig, a curiosity in the Kabul Zoo, was quarantined to keep him away from the goats and deer he had formerly eaten with.

And during the spread of the avian flu around Asia, Thailand’s government shot open-billed storks in its cities and chopped down the trees they nested in, even though the flu had not been found in a single stork.

Though the truth is that diseases are so complex that pointing blame is useless, simply deflecting blame may be more efficient.

During the Black Death, Pope Clement VI issued an edict, or bull, saying Jews were not at fault. He did not, of course, blaspheme by blaming God. Nor did he blame mankind’s sins. That would have comforted the Flagellants, the self-whipping sect who were the bull’s real target; they often led the mobs attacking both Jews and the corrupt church hierarchy, and were considered heretics. Nor did it blame Möngke Khan or Yersinia pestis. It would be 500 years until the “germ theory” of disease developed.

No, the pope picked a target particularly tough to take revenge upon: a misalignment of Mars, Jupiter and Saturn.

Dog’s place and date of birth identified

Earlier studies of this field have shown that Eastern Asia is the place where the wolf was tamed to become the dog. More detailed information has not been available. Now researchers at KTH have succeeded in further specifying the birthplace of man’s best friend.

“For the first time in history it is now possible to provide a detailed picture of the dog including birthplace, point in time and the number of wolves that were tamed,” says Peter Savolainen, biology researcher at KTH.

Together with Swedish colleagues and a Chinese research group he has made a number of new discoveries concerning the history of the dog. These discoveries have recently been published in the scientific journal Molecular Biology and Evolution, and establish that the dog arrived 16 000 years ago in Asia, south of the Yangtze River in China. This is considerably earlier as concerns time and place than had previously been established.

“Our previous discoveries from 2002 have not been fully accepted; however with this new data acceptance will probably be greater. The picture is much more detailed,” Peter states.

The point in time when the dog emerged is well in line with the point when the population of this part of the world changed from hunting and gathering to farming as a way of life – this was 10 000 to 12 000 years ago.

According to Peter this research indicates that the dog has only one geographical origin, but is descended from a large number of animals. At least several hundred tame wolves, probably even more.

“Considering that it involved so many wolves, this indicates that this event was important and a major part of the culture,” he asserts. He adds that research results have produced several exciting theories such as the fact that the original dog, in contrast to its younger relatives in Europe who were used for herding and as guard dogs, probably ended up in people’s stomachs! The research result comes from genetical analysis of mitochondrial DNA from 1 500 dogs, from all over the earth.

Basics

Skipping Spouse to Spouse Isn’t Just a Man’s Game

By NATALIE ANGIER

In the United States and much of the Western world, when a couple divorces, the average income of the woman and her dependent children often plunges by 20 percent or more, while that of her now unfettered ex, who had been the family’s primary breadwinner but who rarely ends up paying in child support what he had contributed to the household till, climbs accordingly. The born-again bachelor is therefore perfectly positioned to attract a new, younger wife and begin building another family.

Small wonder that many Darwinian-minded observers of human mating customs have long contended that serial monogamy is really just a socially sanctioned version of harem-building. By this conventional evolutionary psychology script, the man who skips from one nubile spouse to another over time is, like the sultan who hoards the local maidenry in a single convenient location, simply seeking to “maximize his reproductive fitness,” to sire as many children as possible with as many wives as possible. It is the preferred male strategy, especially for powerful men, right? Sequentially or synchronously, he-men consort polygynously.

Women, by contrast, are not thought to be natural serializers. Sure, a gal might date around when young, but once she starts a family, she is assumed to crave stability. After all, she can bear only so many children in her lifetime, and divorce raises her risk of poverty. Unless forced to because some bouncer has abandoned her, why would any sane woman choose another trot down the aisle — for another Rachael Ray spatula set? Spare me extra candlesticks, I'm a one-trick monogamist.

Yet in a report published in the summer issue of the journal *Human Nature*, Monique Borgerhoff Mulder of the University of California, Davis, presents compelling evidence that at least in some non-Western cultures where conditions are harsh and mothers must fight to keep their children alive, serial monogamy is by no means a man's game, finessed by him and foisted on her. To the contrary, Dr. Borgerhoff Mulder said, among the Pimbwe people of Tanzania, whose lives and loves she has been following for about 15 years, serial monogamy looks less like polygyny than like a strategic beast that some evolutionary psychologists dismiss as quasi-fantastical: polyandry, one woman making the most of multiple mates.

In her analysis, Dr. Borgerhoff Mulder found that although Pimbwe men were somewhat more likely than their female counterparts to marry multiple times, women held their own and even outshone men in the upper Zsa Zsa Gabor end of the scale, of five consecutive spouses and counting. And when Dr. Borgerhoff Mulder looked at who extracted the greatest reproductive payoff from serial monogamy, as measured by who had the most children survive past the first five hazardous years of life, she found a small but significant advantage female. Women who worked their way through more than two husbands had, on average, higher reproductive success, a greater number of surviving children, than either the more sedately mating women, or than men regardless of wifetime total.

Provocatively, the character sketches of the male versus female serialists proved to be inversely related. Among the women, those with the greatest number of spouses were themselves considered high-quality mates, the hardest working, the most reliable, with scant taste for the strong maize beer the Pimbwe famously brew. Among the men, by contrast, the higher the nuptial count, the lower the customer ranking, and the likelier the men were to be layabout drunks.

"We're so wedded to the model that men will benefit from multiple marriages and women won't, that women are victims of the game," Dr. Borgerhoff Mulder said. "But what my data suggest is that Pimbwe women are strategically choosing men, abandoning men and remarrying men as their economic situation goes up and down."

The new analysis, though preliminary, is derived from one of the more comprehensive and painstaking data sets yet gathered of marriage and reproduction patterns in a non-Western culture. The results underscore the importance of avoiding the breezy generalities of what might be called *Evolution Lite*, an enterprise too often devoted to proclaiming universal truths about deep human nature based on how college students respond to their professors' questionnaires. Throughout history and cross-culturally, Dr. Borgerhoff Mulder said, "there has been fantastic variability in women's reproductive strategies."

Geoffrey F. Miller, an evolutionary psychologist at the University of New Mexico, agreed. "Evolutionary psychology and anthropology really need to take women's perspective seriously in all its dimensions," Dr. Miller said. "You can construe sequential relationships as being driven by male choice, in which case you'd call it polygyny, or by female choice, in which case you'd call it polyandry, but the capacity of women across cultures to dissolve relationships that aren't working has been much underestimated."

Pimbwe culture has been too disrupted over the years by colonialism and government interference to serve as a quaint museum piece of how our ancestors lived, but the challenges the people face are more survival-based than how to get your child into an elite preschool program. The Pimbwe live in small villages, have few possessions and eke out a subsistence living farming, fishing, hunting and gathering. Virtually all Pimbwe get married at least once, Dr. Borgerhoff Mulder said, and they do it without the blessing of judge, priest or Las Vegas. "Marriage is not formalized with any specific set of rituals," she said, "and marriages break up by one or another partner leaving."

Nor is there much formal sexual division of labor. "In terms of farming, men and women do pretty much the same tasks," Dr. Borgerhoff Mulder said. "The men will cook, do a lot with the kids."

Unlike in the West, where men control a far greater share of resources than women do, or in traditional pastoral societies like those found in the Middle East and Africa, where a woman is entirely dependent on the wealth of her husband and in divorce is not entitled to so much as a gimpy goat, Pimbwe women are independent operators and resourceful co-equals with men.

This does not mean that mothers can go it alone, however. Again in contrast to the contemporary West, childhood mortality remains a serious threat, and it takes the efforts of more than one adult to keep a baby alive. A good, hardworking husband can be a great asset - and so, too, may his relations. The evolutionary theorist

Sarah Blaffer Hrdy proposes that one reason the offspring of much-marrying Pimbwe women do comparatively well is that the children end up with a widened circle of caretakers. "The women are lining up more protection, more investment, more social relationships for their children to exploit," she said. "A lot of what some people would call promiscuous I would call being assiduously maternal."

The goose, like the gander, may find it tempting to wander if it means that her goslings will fly.

Daylight-saving time leads to less sleep, more injuries on the job

Mining injuries more frequent, severe after lost hour, according to national survey

WASHINGTON – Every March, most Americans welcome the switch to daylight saving time because of the longer days, but also dread losing an hour of sleep after they move their clocks forward. Now a new study shows that losing just an hour of sleep could pose some dangerous consequences for those in hazardous work environments.

The findings are reported in the September issue of the *Journal of Applied Psychology*, which is published by the American Psychological Association.

"One hour of lost sleep may not seem like a lot. But our findings suggest it could have an impact on people's ability to stay alert on the job and prevent serious injuries." said the article's lead author, Christopher Barnes, PhD. Barnes and co-author David Wagner, PhD, were both doctoral students in organizational behavior at Michigan State University when they conducted this research.

They analyzed the number of injuries reported to the Mine Safety and Health Administration from 1983 to 2006. The U.S. Department of Labor requires all mine operators to investigate and report all mining-related injuries. The researchers also looked at the number of work days employees missed as a result of their injuries. Across the 24 years, there were 576,292 reported injuries on the job.

On average, there were 3.6 more injuries on the Mondays following the switch to daylight saving time compared to other days, and 2,649 more days of work were lost as a result of those injuries. That's approximately a 68 percent increase in lost work days. In their analysis, the researchers controlled for weekends and holidays. Work experience did not appear to play a role in the number of injuries suffered.

The researchers also confirmed that people do sleep less in the days after they're forced to turn their clocks forward. They looked at data from the Bureau of Labor Statistics' American Time Use Survey, which measures the amount of time Americans spend engaged in various activities, including sleep. For this study, the researchers looked at data from 14,310 interviews from 2004 to 2006. Results showed that after the switch to daylight saving time, people slept an average of 40 minutes less on the Sunday night they switched to daylight saving time.

The researchers did not find any significant changes in the number and severity of workplace injuries on the Mondays after the switch to standard time, when people gained an hour. Further analysis of the American Time Use Survey showed that people had a much easier time adjusting their sleep schedules and did not, on average, sleep less or more after they changed to standard time. These findings would help explain why there were no significant effects, according to Barnes.

The study could have some important practical implications for employers, Barnes said. "We think managers and organizations can use this information to help improve safety in the days following the switch to daylight saving time," he said. "They can schedule particularly dangerous work on other days, perhaps later in the week after employees have had more time to adjust their sleep schedules." Another suggestion would be to implement extra safety precautions on those days.

Article: "Changing to Daylight Saving Time Cuts Into Sleep and Increases Workplace Injuries," Christopher M. Barnes, PhD, and David T. Wagner, PhD, Michigan State University; Journal of Applied Psychology, Vol. 94, No. 5.

(Full text of the article is available from the APA Public Affairs Office and at <http://www.apa.org/journals/releases/apl9451317.pdf>)

Trauma 411: Prolonged Surgery Should be Avoided in Certain Cases

Timing is what matters in treating orthopaedic injuries in trauma patients

Rosemont, IL Trauma patients who sustain multiple fractures are often in serious condition when they arrive at the emergency department. A review article published in the September 2009 issue of the *Journal of the American Academy of Orthopaedic Surgeons (JAAOS)* explains that trauma patients who have several orthopaedic injuries and are considered to be in unstable condition should only have a few hours of surgery when first arriving at the hospital. This principle is known as 'damage control'.

The benefits of initially limiting time in the operating room for patients with life-threatening injuries include:

- * less blood loss during surgery;
- * fewer complications in the intensive care unit;
- * less stimulation to the immune system; and

* higher patient survival rates.

According to lead author Hans-Christoph Pape, MD, Chairman of Orthopaedic/Trauma Surgery at the University of Aachen in Aachen, Germany, data shows that too many surgeries and blood loss can weaken the immune system and can lead to a higher likelihood of experiencing complications after surgery.”

“If a patient has just a couple of fractures it is of course useful to operate right away,” says Dr. Pape. “However, if a patient has life-threatening injuries for example, more than three fractures and perhaps a lacerated liver, it is often too dangerous to do all the surgery right away.”

In trauma patients with life-threatening injuries, Dr. Pape and his colleagues found:

* It often is best to use an external fixator (where pins in the bone are connected by an external bar) to stabilize an orthopaedic injury to stop initial pain and bleeding.

* Two or three days later, once the patient is stable, data suggests this period to be a more ideal time to begin other more invasive and time-consuming operations.

Pape and his colleagues analyzed data from several trauma registries in Germany. They compared patient outcomes in about 21,000 trauma patients with the amount of hours each patient had spent in the operating room. “We found that patients with life-threatening injuries, such as chest contusions or liver lacerations in association to multiple bone fractures, and who have surgery for six or more hours do not always do as well,” says Dr. Pape. “If you limit the amount of time in the operating room to less than three hours, patients appear to do better.”

In the more severe cases, study authors say it is ideal to taper the amount of surgery. It is important to monitor blood pressure, pulmonary function and immune function to see if patients are stable enough to undergo further surgery.

The benefit of scheduling surgery to repair fractures over the span of several days is that it allows the trauma patient to recover from every surgical procedure before moving forward with the next one.

Timing is key in patients with life-threatening injuries. “There needs to be close communication between the orthopaedic surgeon, the general surgeon and ICU staff,” says Dr. Pape. “All members of the care team need to re-evaluate the patient throughout the process to see if it is safe to fix the next fracture.”

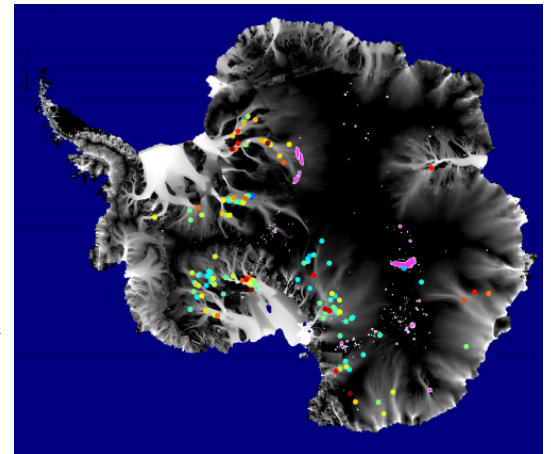
Disclosure: Hans-Christophe Pape, MD, has received nothing of value and does not hold stock in a commercial company or institution related directly or indirectly to the subject of this article.

Map characterizes active lakes below Antarctic ice

Lakes in Antarctica, concealed under miles of ice, require scientists to come up with creative ways to identify and analyze these hidden features. Now, researchers using space-based lasers on a NASA satellite have created the most comprehensive inventory of lakes that actively drain or fill under Antarctica's ice. They have revealed a continental plumbing system that is more dynamic than scientists thought.

"Even though Antarctica's ice sheet looks static, the more we watch it, the more we see there is activity going on there all the time," said Benjamin Smith of the University of Washington in Seattle, who led the study.

Unlike most lakes, Antarctic lakes are under pressure from the ice above. That pressure can push melt water from place to place like water in a squeezed balloon. The water moves under the ice in a broad, thin layer, but also through a linked cavity system. This flow can resupply other lakes near and far.



Dots represent the locations where scientists have identified 124 active lakes below the ice sheet in Antarctica. Warmer colors (orange and red) depict lakes with larger water volumes while cooler colors (green and blue) depict lakes with smaller volumes. Purple areas show the locations of previously known inactive lakes. Credit: Ben Smith, University of Washington

Understanding this plumbing is important, as it can lubricate glacier flow and send the ice speeding toward the ocean, where it can melt and contribute to sea level change. But figuring out what's happening beneath miles of ice is a challenge.

Researchers led by Smith analyzed 4.5 years of ice elevation data from NASA's Ice, Cloud and land Elevation satellite (ICESat) to create the most complete inventory to date of changes in the Antarctic plumbing system. The team has mapped the location of 124 active lakes, estimated how fast they drain or fill, and described the implications for lake and ice-sheet dynamics in the *Journal of Glaciology*.

What Lies Beneath

For decades, researchers flew ice-penetrating radar on airplanes to "see" below the ice and infer the presence of lakes. In the 1990s, researchers began to combine airborne- and satellite-based data to observe lake locations on a continent-wide scale.

Scientists have since established the existence of about 280 "subglacial" lakes, most located below the East Antarctic ice sheet. But those measurements were a snapshot in time, and the question remained as to whether lakes are static or dynamic features. Were they simply sitting there collecting water?

In 2006 Helen Fricker, a geophysicist at the Scripps Institution of Oceanography, La Jolla, Calif., used satellite data to first observe subglacial lakes on the move. Working on a project to map the outline of Antarctica's land mass, Fricker needed to differentiate floating ice from grounded ice. This time it was laser technology that was up to the task. Fricker used ICESat's Geoscience Laser Altimeter System and measured how long it took a pulse of laser light to bounce off the ice and return to the satellite, from which she could infer ice elevation. Repeating the measurement over a course of time revealed elevation changes.

Fricker noticed, however, a sudden dramatic elevation change -- over land. It turned out this elevation change was caused by the filling and draining of some of Antarctica's biggest lakes.

"Sub-ice-sheet hydrology is a whole new field that opened up through the discovery of lakes filling and draining on relatively short timescales and involving large volumes of water," said Robert Bindshadler, a glaciologist at NASA's Goddard Space Flight Center in Greenbelt, Md., who has used ICESat data in other studies of Antarctica. "ICESat gets the credit for enabling that discovery."

Networking in the Antarctic

But were active lakes under the ice a common occurrence or a fluke?

To find out, Ben Smith, Fricker and colleagues extended their elevation analysis to cover most of the Antarctic continent and 4.5 years of data from ICESat's Geoscience Laser Altimeter System (GLAS). By observing how ice sheet elevation changed between the two or three times the satellite flew over a section every year, researchers could determine which lakes were active. They also used the elevation changes and the properties of water and ice to estimate the volume change.

Only a few of the more than 200 previously identified lakes were confirmed active, implying that lakes in East Antarctica's high-density "Lakes District" are mostly inactive and do not contribute much to ice sheet changes.

Most of the 124 newly observed active lakes turned up in coastal areas, at the head of large drainage systems, which have the largest potential to contribute to sea level change.

"The survey identified quite a few more subglacial lakes, but the locations are the intriguing part," Bindshadler said. "The survey shows that most active subglacial lakes are located where the ice is moving fast, which implies a relationship."

Connections between lakes are apparent when one lake drains and another simultaneously fills. Some lakes were found to be connected to nearby lakes, likely through a network of subglacial tunnels. Others appeared to be linked to lakes hundreds of miles away.

The team found that the rate at which lake water drains and fills varies widely. Some lakes drained or filled for periods of three to four years in steady, rather than episodic, changes. But water flow rates beneath the ice sheet can also be as fast as small rivers and can rapidly supply a lubricating film beneath fast-flowing glaciers.

"Most places we looked show something happening on short timescales," Smith said. "It turns out that those are fairly typical examples of things that go on under the ice sheet and are happening all the time all over Antarctica."

Biased parrots pass tests with flying colours

* 00:01 02 September 2009 by Gaia Vince

Being strongly right- or left-handed might be a sign of intelligence – for bird brains, at least.

Ambidextrous parrots are a lot less smart than their left- or right-biased counterparts, say Maria Magat and Culum Brown at Macquarie University in Sydney, Australia, who set the birds problem-solving tasks.

Magat and Brown worked with eight species of Australian parrot, some of which are primarily left-biased – gang-gang cockatoos, for instance, are 100 per cent left-footed – others right-biased and the rest "ambidextrous". The species included cockatiels and budgerigars, which use only their beaks to feed: the biologists determined their side preference by noting which eye they preferred for looking at food.

Then they timed the birds at various tasks, including foraging for different seeds sprinkled in a tray of pebbles and raising a hanging seed basket up to their beaks using their claws.

Parrots that had a strong bias towards using one side or the other were faster at the tasks than species that showed no preference between left or right. But it made no difference whether the species was strongly "right-footed" or "left-footed".

Split brains

All animals have cerebral lateralisation, meaning that their brains are divided into two hemispheres responsible for processing different tasks. Strongly lateralised individuals are strongly "handed" – or strongly "footed" in the case of birds.

"Our study shows that strong lateralisation improves problem-solving ability and foraging in birds, which is an evolutionary advantage," says Brown.

"It allows each side of the brain to become specialised at different tasks, so, for instance, the right side of the parrot's brain can process foraging tasks without being slowed by interference from the left side of the brain."

Humans are less strongly lateralised than gang-gang cockatoos – 95 per cent of us are right- or left-handed – but Brown reckons that handedness is likely to be advantageous. "People who are strongly right- or left-handed are probably smarter than ambidextrous people," he says.

Side and skill

Similar traits have been seen in New Caledonian crows, says Alex Kacelnik, a behavioural ecologist at the University of Oxford. "Crows are supremely skilled in use of tools and are also extremely lateralised at individual level, meaning that each individual prefers to use either the left or the right side of their beaks to hold tools."

But Kacelnik says that Brown and Magat's study simply shows a correlation between lateralisation and skill, not that lateralisation causes greater skill. "For instance, an untrained person may pick an unfamiliar surgical tool indifferently between the two hands, but a well-trained surgeon will have developed a strong preference for doing it in the most efficient manner. This yields a correlation between laterality and skill, but not because more lateralised individuals make better surgeons, but because practice of surgery promotes lateralisation."

Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2009.1397

The Race to Be an Early Adopter of Technologies Goes Mainstream, a Survey Finds

By JENNA WORTHAM

For decades, the adoption and use of the latest technologies was limited to a subculture: Whether called "tech enthusiasts" or "gadget geeks," the implication was that most of the world got along fine with older, established products and services, while a smaller group pursued the most leading-edge technology.

But according to a study released Wednesday by Forrester Research, a marketing firm based in Cambridge, Mass., a shift has taken place. What used to be the pursuit of a few has become decidedly mainstream. We're all gadget geeks now.

According to the study, which surveyed 53,668 households in the United States and Canada by mail, half of all American adults are gamers. Sixty-three percent of American households have a broadband Internet connection. Three-quarters of American households have cellphones and PCs. And nearly 10 million American households, out of nearly 118 million, added an HDTV in the last year, a jump of 27 percent over 2007.

"There's really no group out of the tech loop," said Jacqueline Anderson, an analyst with Forrester who was one of the study's authors. "America is becoming a digital nation. Technology adoption continues to roll along, picking up more and more mainstream consumers every year."

High-definition television sets were one of the fastest-growing consumer technologies in 2008. Over the next five years, the company forecasts, nearly 39 million households in the United States will get their first high-definition set, bringing total market penetration for HDTV to nearly 70 percent.

The study also found that despite the recession, online spending remained strong, with older consumers leading the charge. On average, those consumers spent \$560 in the last three months, although "20 percent of that group spent more than \$1,000 online in the last three months," Ms. Anderson said. Given the tumultuous economic climate, "that's a lot of money," she said.

Ms. Anderson also pointed out that families were a big driver behind the widespread adoption of technologies. The popularity of video game consoles like the Nintendo Wii, which took a decidedly different approach from other game-console makers by appealing to nongamers and families, created an opening for more digital entertainment to enter the home.

Families are also more likely to have gadgetry like MP3 players, digital cameras and digital camcorders. "They have little kids so they want to catalog those memories," Ms. Anderson said. In addition, 86 percent of families with children had mobile phones but were also more likely to use mobile phones with more features like music and video playback.

The study also suggests a growing reliance on the Internet for commerce, communication, entertainment and social lives, said Charles S. Golvin, an analyst with Forrester Research, and a co-author on the study.

"The digitization of our daily lives has been steadily ramping up over the past decade," Mr. Golvin said.

One area that appears to be slower to catch on is home networks. The survey found that 33 percent of households in the United States with an Internet connection reported having a home network, up from 28 percent a year ago. Although Ms. Anderson says that figure is relatively high, the adoption is still lower compared with the adoption of other home technologies.

“The barrier to entry for a home network is a lot higher than for an HDTV, where all you have to do is buy one,” she said. “There are more components and you have to understand how to connect them. Many people had the components for a home network before but didn’t necessarily understand what it meant to put them together or why they’d want to,” she said. In the next five years, the company forecasts, more than 30 million households will install a home network, bringing market penetration to just over 50 percent.

Already, Mr. Golvin says, more people are migrating away from the home and office to use the Web and turning toward their smartphones. About 15 percent of cellphone owners were using the Internet on their phones in 2008, the study found, showing that, for a growing number of Americans, there is an increasing “expectation that all the same services and resources are available to us no matter where we are,” he said.

Vitamin C deficiency impairs early brain development

New research at LIFE – Faculty of Life Sciences at University of Copenhagen shows that vitamin C deficiency may impair the mental development of new-born babies.

In the latest issue of the well-known scientific journal The American Journal of Clinical Nutrition, a group of researchers headed by professor Jens Lykkesfeldt shows that guinea pigs subjected to moderate vitamin C deficiency have 30 per cent less hippocampal neurones and markedly worse spatial memory than guinea pigs given a normal diet. Like guinea pigs, human beings are dependent on getting vitamin C through their diet, and Jens Lykkesfeldt therefore speculate that vitamin C deficiency in pregnant and breast-feeding women may also lead to impaired development in foetuses and new-born babies.



Guinea pigs - like humans - are dependent on getting sufficient vitamin C through their diet. Studies show that new-born guinea pigs subjected to vitamin C deficiency have a markedly worse memory than guinea pigs given enough vitamin C. Maybe this also applies to human beings?

The brain retains vitamin C

Several factors indicate that the neonatal brain, in contrast to other tissue, is particularly vulnerable to even a slight lowering of the vitamin C level. The highest concentration of vitamin C is found in the neurons of the brain and in case of a low intake of vitamin C, the remaining vitamin is retained in the brain to secure this organ. The vitamin thus seems to be quite important to brain activity. Tests have shown that mouse foetuses that were not able to transport vitamin C develop severe brain damage. Brain damage which resembles the ones found in premature babies and which are linked to learning and cognitive disabilities later in life.

Vitamin C, or L-ascorbic acid, is essential for a number of bodily functions. In the adrenal glands, vitamin C is required for the production of the hormone adrenaline which the body uses in stress situations and for physical activities. Vitamin C is also necessary to form the protein collagen which is an important constituent part of sinews, gum, cartilage and bones. Vitamin C is also vital to the immune system. Humans and guinea pigs are among the few mammals that cannot produce vitamin C themselves but are entirely dependent on having it supplied through their diet.

Widespread vitamin C deficiency

In some areas in the world, vitamin C deficiency is very common – population studies in Brazil and Mexico have shown that 30 to 40 per cent of the pregnant women have too low levels of vitamin C, and the low level is also found in their foetuses and new-born babies. It is not yet known to what extent new-born babies in Denmark or the Western World suffer from vitamin C deficiency but a conservative estimate would be 5 to 10 per cent based on the occurrence among adults.

“We may thus be witnessing that children get learning disabilities because they have not gotten enough vitamin C in their early life. This is unbearable when it would be so easy to prevent this deficiency by giving a vitamin supplement to high-risk pregnant women and new mothers” says Jens Lykkesfeldt whose research group is currently studying how early in pregnancy vitamin C deficiency affects the embryonic development of guinea pigs and whether the damage may be reversed after birth.

[Read more in the scientific article *Vitamin C deficiency in early postnatal life impairs spatial memory and reduces the number of hippocampal neurones in guinea pigs in the online edition of American Journal of Clinical Nutrition*](#)

Resident duty-hour reform associated with increased complication rate

Rosemont, Ill. -- A new study finds a 2003 reform of the length of resident on-duty hours has led to an increase in the rate of perioperative (the span of all three phases of surgery: before, during and after) complications for patients treated for hip fractures. Among other restrictions, this reform limited the resident workweek to 80 hours. The resulting complications vary significantly, with an increasing rate of worse outcomes seen in teaching hospitals, according to a study published in the September 2009 issue of the Journal of Bone and Joint Surgery (JBJS).

"The data suggests a statistically significant increase in selected complications after implementation of the duty-hour reforms in teaching hospitals, where residents help deliver care, compared to non-teaching hospitals. This may go against common assumptions regarding outcomes as they relate to the length of resident hours," said study lead author James M. Browne, MD, an orthopaedic surgeon currently completing a fellowship in Rochester, Minnesota. The study was performed at Duke University Medical Center.

On July 1, 2003, The Accreditation Council for Graduate Medical Education implemented a resident duty-hour reform for all medical and surgical residents, including orthopaedic resident surgeons, in the U.S. Dr. Browne and his co-authors at Duke reviewed data from teaching and nonteaching hospitals for 48,430 patients treated for hip fractures in a nationwide inpatient sample database, reviewing two groups:

- * the first from 2001 and 2002 before resident duty-hour reform; and
- * the second in 2004 and 2005 after reform.

This study sought to measure changes in the rate of patient death or resulting in-hospital complications since this reform. No increase in death rates was found, but an increase in resulting negative outcomes was found in teaching hospitals compared to nonteaching hospitals. The undesired results included increases in the rate of:

- * pneumonia,
- * hematoma,
- * transfusion,
- * renal complications, and
- * nonroutine discharge.

In addition to an increase in the rate of medical complications, the study also notes an increase in length and cost of stay in teaching hospitals.

"I think it would be premature for a patient to make any medical decisions based on the results of this study. What this data does tell us is that this issue needs to be examined further. Remember, this is limited to hip fracture outcomes tracked during a limited time period and does not take into account any improvements in delivery of care since 2005." said Dr. Browne.

A recent report from the Institute of Medicine proposes further limitations on resident work hours.

"Surgeons and policy-makers need more data to understand the full impact of these duty hour changes on our patients. As we consider any kind of reform, we must continue to keep the safe delivery of care that results in successful patient outcomes as our number one priority," said Dr. Browne.

Disclosure: *The authors did not receive any outside funding or grants in support of their research for or preparation of this work. One or more of the authors, or a member of his or her immediate family, received, in any one year, payments or other benefits in excess of \$10,000 or a commitment or agreement to provide such benefits from commercial entities (Zimmer, DePuy, and Wright Medical).*

UAB Researchers Find Possible Use for Kudzu, the Vine That Ate the South

- Kudzu is potential dietary supplement
- Southeastern nuisance vine may lower blood sugar, blood pressure, cholesterol
- Long used as herbal medicine in Asia

BIRMINGHAM, Ala. - Kudzu, the fast-growing vine that has gobbled up some 10 million acres in the Southeast, may prove to be a valuable dietary supplement for metabolic syndrome, a condition that affects 50 million Americans, say researchers at the University of Alabama at Birmingham (UAB).

In findings published in the latest Journal of Agriculture and Food Chemistry, the researchers say studies on animal models showed that substances called isoflavones found in kudzu root improved regulation of contributors to metabolic syndrome, including blood pressure, high cholesterol and blood glucose. One particular isoflavone, called puerarin and found only in kudzu, seems to be the one with the greatest beneficial effect.

"Our findings showed that puerarin helps to lower blood pressure and blood cholesterol," said J. Michael Wyss, Ph.D., a professor of in the UAB Department of Cell Biology and lead author on the study. "But perhaps the greatest effect we found was in its ability to regulate glucose, or sugar, in the blood."

An excessive amount of glucose in the blood is linked to both diabetes and obesity. Wyss says puerarin seems to regulate glucose by steering it to places where it is beneficial, such as muscles, and away from fat cells and blood vessels.

Wyss and colleagues added a small amount of kudzu root extract to the diets of lab rats for about two months. Compared to a control group that did not get the extract, the rats had lower cholesterol, blood pressure, blood sugar and insulin levels. No side-effects were noted.

"We need to better understand the mechanism by which kudzu root has these effects and then conduct human trials before we can recommend it as a supplement," Wyss said. "We also need a better understanding of who would most benefit. Is this something that children should take or perhaps those at risk for stroke or heart disease?"

"Puerarin, or kudzu root, may prove to be a strong complement to existing medications for insulin regulation or blood pressure, for example," said Jeevan Prasain, Ph.D., an assistant professor in the UAB Department of Pharmacology and Toxicology and a study co-author. "Physicians may be able to lower dosages of such drugs, making them more tolerable and cheaper."

Kudzu has long been used as a dietary supplement in Asian countries, most commonly as a tea or a powder. The climate of the American Southeast is ideal for kudzu, which is native to China and Japan and was brought to the United States in the 1930s for erosion control. Kudzu vines can grow as much as a foot per day during the summer and can overwhelm trees, power poles and buildings if left unchecked.

This research was supported by the National Center for Complementary and Alternative Medicine and the Office of Dietary Supplement Grants, parts of the National Institutes of Health. Collaboration came from the UAB departments of Cell Biology and Pharmacology and Toxicology, the Purdue-UAB Botanicals Center and the Department of Biology, Luther College, Decorah, Iowa.

Europe's oldest stone hand axes emerge in Spain

Findings suggest that tool advance occurred by 900,000 years ago, much earlier than previously thought.

By Bruce Bower

Europe's Stone Age has taken an edgy turn. A new analysis finds that human ancestors living in what is now Spain fashioned double-edged stone cutting tools as early as 900,000 years ago, almost twice as long ago as previous estimates for this technological achievement in Europe.

If confirmed, the new dates support the idea that the manufacture and use of teardrop-shaped stone implements, known as hand axes, spread rapidly from Africa into Europe and Asia beginning roughly 1 million years ago, say geologist Gary Scott and paleontologist Luis Gibert, both of the Berkeley Geochronology Center in California.

Evidence of ancient reversals of Earth's magnetic field in soil at two archaeological sites indicates that hand axes date to 900,000 years ago in one location and to 760,000 years ago in the other, Scott and Gibert report in the Sept. 3 *Nature*. Until now, most researchers thought that hand axes unearthed at these sites were made between 500,000 and 200,000 years ago.



access

First tool ***Researchers say that a stone hand ax, shown here from both sides, that was previously found in a Spanish rock shelter dates to 900,000 years ago, making it the oldest such implement in Europe. Michael Walker***

Other European hand ax sites date to no more than 500,000 years ago. In contrast, hand axes date to roughly 1.7 million years ago in eastern Africa. And age estimates of 1.2 million years and 800,000 years for hand axes from two Israeli sites indicate that this tool-making style spread out of Africa long before the origin of *Homo sapiens* around 200,000 years ago. Excavations in southern China have also yielded 800,000-year-old hand axes (SN: 3/4/00, p. 148). Fossils from ancient human ancestors have not been found with the Israeli and Chinese artifacts.

Earlier analyses of magnetic reversals in soil at other sites in southern Spain indicate that single-edged stone tools appeared there around 1.3 million years ago, Gibert says (SN: 1/4/97, p. 12). Population movements back and forth between Africa and Europe must have occurred at that time, possibly via vessels across the Strait of Gibraltar, he hypothesizes.

"Then at 900,000 years ago, we now have the oldest evidence of hand axes in Europe, which represents a second migration from Africa that brought a new stone-tool culture," Gibert says.

Scott and Gibert's "surprisingly old ages" for the Spanish hand axes bring the chronology of ancient Europe's settlement in line with that of Asia, remarks archaeologist Wil Roebroeks of Leiden University in the

Netherlands. Europe contains relatively few stone-tool sites from around 1 million years ago, making it difficult to reconstruct the timing of ancient population pulses into the continent, Roebroeks says.

Although new estimated ages for soil layers at the Spanish sites appear credible, the suggestion that hand axes there are by far the oldest in Europe "is extremely daring, to put it mildly," comments archaeologist Robin Dennell of the University of Sheffield in England. In his view, the precise depth of the hand axes when they were unearthed several decades ago remains unclear. It's possible that these finds actually came from soil layers that Scott and Gibert place at no more than 600,000 years old, Dennell says.

Scott and Gibert first identified the geological position of specific magnetic reversals in sediment at an ancient lakeshore near the Spanish sites. Dates for these reversals have already been established in previous studies. The researchers compared these magnetic shifts to those at the hand ax sites to date the tools.

These data provide minimum ages for the Spanish finds. "Older ages are possible but would be odd," Gibert says.

HPV vaccine could prevent breast cancer: Australian research

Vaccinating women against the human papillomavirus (HPV) may prevent some forms of breast cancer and save tens of thousands of lives each year, new Australian research suggests.

Using genetic probes, researchers at the University of New South Wales tested cancerous breast cells and found several strains of HPVs known to have a high risk of initiating cancer of the cervix. HPV has a causal role in 90-95 per cent of cervical cancers.

The research was conducted by a team from the UNSW School of Biotechnology and Biomolecular Sciences, led by Visiting Professor James Lawson, and is published in the British Journal of Cancer.

The team confirmed the presence of high-risk HPV in the nuclei of breast cancer epithelial cells in five (39 per cent) of 13 ductal carcinoma in situ and three (21 per cent) of 14 invasive ductal carcinoma (IDC) breast cancer specimens. Non-invasive or in situ cancers are those confined to the milk-making glands and do not spread to other parts of the breast or body. Invasive cancers such as IDC are more serious and account for 70-80 percent of all breast cancers.

"The finding that high risk HPV is present in a significant number of breast cancers indicates they may have a causal role in many breast cancers," says UNSW researcher, Dr Noel Whitaker, a co-author of the new report. "Confirming a cancer-causing role for HPV in some breast cancers establishes the possibility of preventing some breast cancers by vaccination against HPV," he says.

The idea that HPV has an involvement in breast cancer is controversial. Scientific reports from 15 countries around the world have identified the presence of high-risk types of HPV in breast tissue and breast cancer specimens. But those studies have also showed widely varying results, with the prevalence of HPV-positive breast cancer in ranging from as low as four per cent to as high as 86 per cent, and have been clouded by difficulties in detecting the virus in breast specimens.

As well, the genetic probe technique used – polymerase chain reaction (PCR) – has been criticized for its propensity for contamination. The technique is based on taking small genetic samples and rapidly copying them to provide a large enough sample to study.

The UNSW researchers addressed these issues by using a technique (in situ PCR) that avoids cross-contamination and that provides evidence about whether HPV genetic material is present in the nuclei of human breast cancer specimens. They validated their findings by looking for "telltale" changes linked to HPV such as enlarged nucleus surrounded by a characteristic "halo". The researchers are working on a new method that will make testing even quicker, cheaper and simpler.

Globally 1.1 million women were diagnosed with breast cancer and more than 500,000 women lost their life to the disease in 2004. Australia data reveals that 12,265 women were diagnosed with breast cancer in 2005, and 2,618 women died from breast cancer in 2006. During the past quarter century 213,658 Australian women were diagnosed with breast cancer (1982 – 2005) and 63,632 died from the disease (1981 – 2006).

That late-night snack: Worse than you think

Eat less, exercise more. Now there is new evidence to support adding another "must" to the weight-loss mantra: eat at the right time of day.

A Northwestern University study has found that eating at irregular times -- the equivalent of the middle of the night for humans, when the body wants to sleep -- influences weight gain. The regulation of energy by the body's circadian rhythms may play a significant role. The study is the first causal evidence linking meal timing and increased weight gain.

"How or why a person gains weight is very complicated, but it clearly is not just calories in and calories out," said Fred Turek, professor of neurobiology and physiology in the Weinberg College of Arts and Sciences and director of the Center for Sleep and Circadian Biology. "We think some factors are under circadian control.

Better timing of meals, which would require a change in behavior, could be a critical element in slowing the ever-increasing incidence of obesity." The findings could have implications for developing strategies to combat obesity in humans, as the United States and the world battle what has been called an "obesity epidemic." More than 300 million adults worldwide are obese, including more than a third of American adults.

Details of the obesity study, which was led by Turek, will be published online Sept. 3 by the journal *Obesity*. "One of our research interests is shift workers, who tend to be overweight," said lead author Deanna M. Arble, a doctoral student in Turek's lab. "Their schedules force them to eat at times that conflict with their natural body rhythms. This was one piece of evidence that got us thinking -- eating at the wrong time of day might be contributing to weight gain. So we started our investigation with this experiment."

Simply modifying the time of feeding alone can greatly affect body weight, the researchers found. Mice that were fed a high-fat diet during normal sleeping hours gained significantly more weight (a 48 percent weight increase over their baseline) than mice eating the same type and amount of food during naturally wakeful hours (a 20 percent increase over their baseline). There was no statistical difference between the two groups regarding caloric intake or the amount of activity.

Over a period of six weeks, both groups of mice were allowed to eat as much high-fat diet as they wanted during their daily 12-hour feeding phase. (Much like many humans, mice have a preference for high-fat food.) Since mice are nocturnal, the 12-hour feeding phase was during the day for those fed during normal sleeping hours and during the night for those fed during naturally wakeful hours. Food was not provided during the other 12 hours of their day.

Our circadian clock, or biological timing system, governs our daily cycles of feeding, activity and sleep, with respect to external dark and light cycles. Recent studies have found the body's internal clock also regulates energy use, suggesting the timing of meals may matter in the balance between caloric intake and expenditure.

The researchers next plan to investigate the molecular mechanisms behind their observation that eating at the "wrong" time can lead to weight gain.

The title of the Obesity paper is "Circadian Timing of Food Intake Contributes to Weight Gain." In addition to Turek and Arble, other authors of the paper are Joseph Bass, Aaron D. Laposky and Martha H. Vitaterna, all from Northwestern.

World-first swine-flu vaccine trial reveals one dose provides 'strong immune response' Pilot Leicester study suggests one dose of vaccine may be sufficient

Results from the first swine-flu vaccine trials taking place in Leicester reveal a strong immune response after just one dose. The pilot study, run by the University of Leicester and Leicester Hospitals, was trialled with 100 healthy volunteers, aged between 18 and 50.

Dr Iain Stephenson, who led the trial at the Leicester Royal Infirmary, said: "The clinical trial of Novartis MF59-adjuvanted cell-based A (H1N1) vaccine indicates that the "swine flu" vaccine elicits a strong immune response and is well-tolerated.

"Results showed that the serum antibody responses were highest among subjects who received two doses of vaccine, however a single vaccine dose also induced responses associated with protection against influenza.

"The findings showed that it is possible to induce protective antibody against A(H1N1) infection within two weeks of administration of a single low-dose adjuvanted vaccine."

Non-adjuvanted formulations were not evaluated in this part of the study and will be evaluated shortly

The trial evaluated the tolerability and immunogenicity of the vaccine, and tested different schedules of vaccination, in terms of time between vaccinations. The vaccine schedule was one or two doses of 7.5µg MF-59 adjuvanted surface-antigen A/California/2009 vaccine derived from cell-culture.

Dr. Stephenson, of the Department of Infection, Immunity and Inflammation at the University of Leicester is a clinical senior lecturer at the University, and a consultant in infectious diseases at the University Hospitals of Leicester NHS Trust. He said: "The aim of the trial was to find out how many doses and what type of vaccine is needed to give protection. These initial results should help to plan vaccination campaigns in the autumn, including doses and timings. We concluded that the MF59-adjuvanted A(H1N1) vaccine of low antigen content was well tolerated and generated antibody responses associated with protection against influenza, even after a single dose."

"The results suggest that one vaccine dose may be sufficient to protect against the A(H1N1) swine flu, rather than two. Larger trials are already underway around the world. Timings on when the vaccine will be available to governments will depend on the results of these clinical trials, and approvals by regulatory authorities" The research found the vaccine is well tolerated with pain at the injection site the most frequent adverse event.

Additional pivotal trials with both cell culture and traditional egg based vaccines under way around the world that will include more than 6000 adults and children.

Previous research had indicated that two doses of the vaccine would be needed against swine flu. You can access earlier stories here:

<http://www2.le.ac.uk/ebulletin/news/press-releases/2000-2009/2009/08/nparticle.2009-08-11.3248230936>

Three human genes evolved from junk

* 03 September 2009 by Michael Le Page

AT LEAST three human genes evolved "from scratch" via mutations in non-coding stretches of DNA, a process thought to be virtually impossible until recently. The genes evolved since human and chimp lineages split and so are unique to us.

The three new genes seem to have arisen as a result of mutations in non-coding sequences of DNA

It is tempting to speculate that uniquely human genes drive uniquely human traits, says Aoife McLysaght of the Smurfit Institute of Genetics at Trinity College Dublin, who discovered the three genes with her colleague David Knowles. But that would be premature: "There is no clue about the function at all yet."

What is extraordinary about the genes is their evolutionary past. Most new genes arise when existing ones are duplicated and the copies slowly acquire different functions. The three new genes, called *CLLU1*, *C22orf45* and *DNAH10OS*, suddenly sprang into existence as a result of mutations in DNA sequences that did not previously code for proteins.

While comparing human, chimp and macaque DNA, McLysaght's team stumbled upon human genes that stood out because they seemed to have no equivalents in the other species. The short proteins the three genes code for have been found in blood samples from healthy people, and the genes are also present in all human genomes sequenced so far, suggesting they have vital functions in humans.

In the other primates, the equivalent DNA sequences contained differences that would halt protein production early on, so the sequences are non-coding in these species. Crucially, chimps, gorillas, gibbons and macaques share some of these differences, meaning that, in our shared ancestor, these sequences were non-coding as well. The researchers conclude that three of these non-coding sequences must have mutated in humans and become capable of coding for the short proteins at some point since we diverged from chimps six million years ago (Genome Research, DOI: 10.1101/gr.095026.109). While at least half the non-coding DNA in humans is junk with no function, it is not clear whether the non-coding DNA from which the genes evolved had any function.

Such "de novo" gene evolution was once thought impossible because random mutations are highly unlikely to produce a DNA sequence that encodes a protein of any length, let alone a protein that will be translated by cells and do anything useful. But in 2006, several de novo genes were discovered in fruit flies. Since then, it's become clear that genes do continually evolve in this way.

Part of the explanation might be that biological systems are very noisy: even though most of our DNA is junk, most of it still gets transcribed into RNA at times, and some of that RNA probably reaches cells' protein-making machinery. This means that when mutations do throw up sequences capable of encoding proteins, some may get "tested" and useful ones selected for. As more primate genome data becomes available, McLysaght estimates a further 15 human genes will turn out to have evolved de novo.

She now plans to find out what the three genes she found do, but it won't be easy. The conventional method for discovering what genes do is to disable them in mice to see what the effect is - the trouble is that no animals besides humans have these genes.

Reboot for UK's 'oldest' computer

Britain's oldest original computer, the Harwell, is being sent to the National Museum of Computing at Bletchley where it is to be restored to working order.

The computer, which was designed in 1949, first ran in 1951 and was designed to perform mathematical calculations; it lasted until 1973. When first built the 2.4m x 5m computer was state-of-the-art, although it was superseded by transistor-based systems. The restoration project is expected to take a year.

The system was built and used by staff at the Atomic Energy Research Establishment in Harwell, Oxfordshire.

Speaking to BBC News, Dick Barnes, who helped build the original Harwell computer, said the research was - officially at least - for civilian nuclear power projects. "Officially it was to help with general background atomic theory and to assist in the development of civilian power," he said. "Of course, it [the Atomic Energy Research Establishment] had connections to the nuclear weapons programme," he added.



The Harwell computer was still in use in 1973

Although not the first computer built in the UK, the Harwell had one of the longest service lives.

Built by a team of three people, the device was capable of doing the work of six to ten people and ran for seven years until the establishment obtained their first commercial computer.

"We didn't think we were doing anything pioneering at the time," said Mr Barnes.

"We knew the Manchester Baby and Cambridge's EDSAC were already up and running. Both these projects had large teams and we felt like a poor relation. "Looking back, hardly any of us were computer literate and it's astonishing that we managed stored computing at all," he said.

The Harwell machine is recognisably modern in that unlike some of its predecessors such as Colossus it used a single memory to store data and programs.

Kevin Murrell, director of The National Museum of Computing at Bletchley Park, said it had some of the characteristics of contemporary machines.

"The machine was a relay-based computer using 900 Dekatron gas-filled tubes that could each hold a single digit in memory - similar to RAM in a modern computer - and paper tape for both input and program storage."

Time line

Retired from service at Harwell, the system was offered as a prize for colleges, with Wolverhampton and Staffordshire Technical College (later Wolverhampton University) taking ownership and renaming it as the WITCH (Wolverhampton Instrument for Teaching Computing from Harwell). It was used in computer education until 1973. It then went on display at Birmingham Science Museum, before being put in storage at Birmingham City Council Museums' Collection Centre. Now it is being sent to the National Museum of Computing in Bletchley, where a team are set to restore it to working order.

Mr Barnes said the prospect of seeing the Harwell computer up and running after more than 36 years was "very exciting". "I still don't know how they managed to find so many spare parts, but I think they have a very good chance of getting it going again," he said.

There are several significant predecessors to the Harwell computer: The Ace (parts of which are on display in London's Science Museum), the Electronic Delay Storage Automatic Calculator (EDSAC) which was broken up, and Manchester's Small-Scale Experimental Machine (SSEM) nicknamed Baby, which has been rebuilt but not using original parts.

Gorilla sexual intrigue could explain human monogamy

* 12:13 02 September 2009 **by Ewen Callaway**

Female gorillas use sex as a tactic to thwart their rivals, new research suggests. Pregnant apes court their silverback male to stop other females conceiving.

"It seems to us that mating is another tactic that females use to compete with each other – in this case to gain favour with another male," says Diane Doran-Sheehy, a primatologist at Stony Brook University in New York.

Her team chronicled the sex lives of five female western lowland gorillas and one silverback almost every day for more than three years. "We wondered if, basically, [pregnant] females can mimic [ovulating] females and dupe the male into mating with them and distract him from what those other girls are doing," Doran-Sheehy says. This kind of competitive behaviour may even help explain how humans evolved into a mostly monogamous species, she says.

Pleased to meet you

However, Homo sapiens and Gorilla gorilla aren't the only apes who engage in recreational sex. Bonobos treat coitus like a handshake, while female chimpanzees mate during pregnancy and outside fertile periods, or oestrus, to gain support from males and to protect against infanticide. "All of the males think they could be the father of your offspring," Doran-Sheehy says.

Yet paternity isn't an issue for silverback gorillas, which usually enjoy exclusive access to a harem of females. "It doesn't have all that much to do with the males," Doran-Sheehan says. "It's what's going on with the females in the group."

Her team recorded most copulations and all births among a human-habituated group of gorillas at the Mondika research centre in the Republic of Congo for 1147 days between September 2003 and January 2007.

All five females gave birth to one infant during the study and all engaged in sex after pregnancy, the researchers found. However, females seemed to time such post-conceptive romps with the fleeting fertility of another female.

Strategic sex

For instance, after one female, MK, became pregnant she mated with the silverback during three consecutive oestrus cycles of another gorilla, EB, who left the group afterwards. With only lactating – and therefore

sexually inactive – females remaining, MK ceased offering herself to the silverback. Another female named UG mated throughout her pregnancy, almost always when another female was trying to become pregnant.

The silverback seemed none the wiser. Unlike male mountain gorillas, which prefer to mate with fertile females, Doran-Sheehy's silverback went for higher-ranking females, fertile or not.

Such prestige could be one reason why pregnant females fake oestrus: group sizes are limited, and females must curry favour with a male to stick around.

By delaying the pregnancy of others, females could also gain a reproductive advantage over competitors, says Tara Stoinski, a primatologist at Zoo Atlanta in Georgia, who found that pregnant female gorillas in captivity also time their sexual advances to coincide with those of other females. "I agree with Diane's assertion that females are competing with each other."

Journal reference: American Journal of Primatology, DOI: 10.1002/ajp.20743

YouTube videos yield clues to brain injury symptom

University of Kentucky researcher identifies 'fencing response' in knockout hits

LEXINGTON, Ky. (Sept. 2, 2009) – Brain injury researchers at the University of Kentucky have spent hundreds of hours watching YouTube videos of people getting smacked, punched and knocked in the head during sporting events and recreational activities. But those researchers weren't goofing off on the Internet; they were doing hard science.

Led by Jonathan Lifshitz, assistant professor in the UK Spinal Cord & Brain Injury Research Center, the team was collecting data to document a visible, involuntary response to head trauma. Their findings could have immediate value in helping coaches make educated, objective decisions about whether to return an athlete to play after a blow to the head.

"As basic scientists, we all hope that our research we do in the laboratory translates into the clinics," Lifshitz said in a television interview with WTVQ-36 in Lexington. "In this case, we hope it translates onto the sidelines."

Lifshitz describes the response, dubbed the "fencing response," as a forearm posture that resembles the *en garde* position in competitive sword fighting. It also can appear as a defensive boxing pose. The fencing response – which has also been observed in rats under experimental conditions – indicates damage to blood vessels and neurons in a critical brainstem region that controls balance, Lifshitz said.

In the course of their research, the team reviewed some 2,000 "knockout" videos on YouTube, eventually narrowing their sample to three dozen that showed moderate-to-severe impacts to the head, where the person receiving the blow did not immediately get up. Of those, two-thirds exhibited a clear fencing response. The response was noted particularly in football and mixed martial arts, Lifshitz said.

"The fencing response frequently takes place before the player even hits the ground," Lifshitz said.

Among the videos the team reviewed was the head-to-head collision of Baltimore Raven Willis McGahee and Pittsburgh Steeler Ryan Clark in a Jan. 18 AFC playoff game. McGahee's immediate fencing response is clearly visible in the video.

Moderate-to-severe head trauma can cause permanent brain damage or death if ignored by medical staff. Unfortunately, sometimes these injuries are not readily apparent. The fencing response provides an immediate visual cue that could help injured players get the attention they need, Lifshitz said.

"The observation of the fencing response can help coaches and trainers make immediate and future return-to-play decisions," Lifshitz said. "But the response is not universal. The absence of a fencing response should not be taken as a sign that no injury has occurred."

The findings were published Aug. 18 in the scholarly journal Medicine and Science in Sports and Exercise.

Boron-based compounds trick a biomedical protein

University of Oregon chemists, biologists team to boost boron's expanding use in medicine

Chemists and biologists have successfully demonstrated that specially synthesized boron compounds are readily accepted in biologically active enzymes, a move that, they say, is a proof of concept that could lead to new drug design strategies.

In June 2008, University of Oregon chemist Shih-Yuan Liu reported in the Journal of the American Chemical Society his lab's synthesis of boron-nitrogen compounds with electronic and structural similarities to fundamentally important benzene molecules. That synthesis suggested a new tool for possible use in biomedical research as well as in materials science.

What Liu's lab created were benzene surrogates known as 1,2-dihydro-1,2-azaborines that possess electron-delocalized structures consistent with aromaticity -- a core concept in chemistry where rings of atoms exhibit unexpected stability.

Now, in the Sept. 1 issue of *Angewandte Chemie*, a weekly journal of the German Chemical Society, Liu and colleagues show that their synthesized compounds indeed are accepted in non-polarized hydrophobic pockets of a well-studied enzyme, a member of the lysozyme family discovered by Alexander Fleming in 1921 and used widely in biomedical research.

The "proof of concept" was completed in the Institute of Molecular Biology lab of the UO physicist Brian W. Matthews, where Liu's synthesized compound was treated with T4 lysozymes, crystallized and examined with high-resolution X-ray crystallography.

"I feel this is a fairly big step forward," Liu said. "Our compounds bind efficiently to the T4 lysozyme and behave as hydrophobic arene molecules similar to natural systems. Our compound actually has polar features, so it was questionable that it would bind to the enzyme's hydrophobic pocket, but it did and very similarly to the way carbon molecules would bind."

In essence, Liu and colleagues have potentially put boron, a commonly occurring essential nutrient in plants -- but seemingly "bypassed by nature in evolution" of other living things, Liu said -- into play as an alternative to carbon in manufacturing target-specific pharmaceuticals. The use of boron in the biomedical field is not new but its acceptance has been hampered by instability, but interest has risen in the last decade, Liu said.

An analysis of boron's medical potential appeared in the February issue of *EMBO Reports*. Boron is being studied by a number of drug manufacturers. It currently is used as an antibacterial drug component and as part of a therapy for multiple myeloma. The advance by Liu's lab strengthens the case that boron-based molecules can be used as new pharmacophores, or as markers of drugs in living tissue, and to improve long-stymied attempts to develop boron-neutron capture therapies to produce inhibiting agents for cancer treatment.

"This research provides the first experimental evidence that enzymes in our bodies cannot distinguish between our artificial compound versus the all-carbon systems," Liu said. "We can trick the enzymes to believing they are accepting the real thing."

The National Institutes of Health funded the research. Co-authors were Liu's chemistry doctoral student Adam J.V. Marwitz, Matthews and Lijun Liu, a research associate in the Matthews lab.

New study shows those blinded by brain injury may still 'see'

Except in clumsy moments, we rarely knock over the box of cereal or glass of orange juice as we reach for our morning cup of coffee. New research at The University of Western Ontario has helped unlock the mystery of how our brain allows us to avoid these undesired objects.

The study, led by Canada Research Chair in Visual Neuroscience Mel Goodale, lead author Chris Striemer and colleagues in Western's Department of Psychology, has been published in the current issue of the prestigious *Proceedings of the National Academy of Sciences*.

"We automatically choose a path for our hand that avoids hitting any obstacles that may be in the way," says Goodale. "Every day, we perform hundreds of actions of this sort without giving a moment's thought as to how we accomplish these deceptively simple tasks."

In the study, a patient who had become completely blind on his left side following a stroke to the main visual area of the brain was asked to avoid obstacles as he reached out to touch a target in his right -- or 'good' -- visual field. Not surprisingly, he was able to avoid them as any normal-sighted individual would.

Amazingly, however, when obstacles were placed on his blind side, he was still able to avoid them -- even though he never reported having seen them.

"The patient's behaviour shows he is sensitive to the location of obstacles he is completely unaware of," Striemer says. "The patient seemed to be as surprised as we were that he could respond to these 'unseen' obstacles," Goodale adds.

These findings provide compelling evidence for the idea that obstacle avoidance depends on ancient visual pathways in the brain that appear to bypass the main visual areas that allow us to perceive the world. Thus, even when the part of the brain that gives us our visual experience is damaged, other parts of the brain still maintain a limited ability to use visual information from the eyes to control skilled movements of the limbs.

Additional experiments in Goodale's lab at the world-renowned Centre for Brain & Mind have shown that these primitive visual pathways work only in real-time and do not have access to memories, even of the short-term variety. As an example, they provided an obstacle in the patient's blind field but delayed his reach by two seconds. With this short delay, he no longer showed any sensitivity to the object's location.

The study's results have important implications for our understanding of what gets lost and what gets spared following damage to the brain's main visual pathways, and point the way for new approaches to rehabilitation.

Avastin dramatically improves response, survival in deadly recurrent glioblastomas

The targeted therapy Avastin, alone and in combination with the chemotherapy drug CPT-11, significantly increased response rates, progression-free survival times and survival rates in patients with a deadly form of brain cancer that had recurred.

Patients with recurrent glioblastoma have a grim prognosis, and conventional treatments were typically limited to largely ineffective and highly toxic chemotherapies. Only about 5 percent of patients respond to further treatment – meaning their tumors shrink by 50 percent or more. And only 15 to 20 percent of patients make it to the six month mark before their disease progresses again. Survival is limited to six to seven months.

But a randomized Phase II study of Avastin alone and Avastin given with CPT-11 have improved those statistics, dramatically increasing response rates, progression-free survival times and overall survival. Early results from the study prompted the U.S. Food and Drug Administration to agree to an accelerated approval of Avastin in May 2009 for use in patients with recurrent glioblastomas, said Dr. Timothy Cloughesy, director of the Neuro-Oncology Program at UCLA's Jonsson Comprehensive Cancer Center and senior author of the study. The program allows provisional approval of medicines for cancer or other life-threatening diseases.

The study, conducted at 11 centers across the county, was published this week in the early online version of the Journal of Clinical Oncology.

"This is a huge breakthrough for us. In all the years we've been treating recurrent glioblastomas using conventional and investigational agents, we've never had anything like the responses we're seeing with Avastin," said Cloughesy, who also is a professor of neurology. "You just don't get these kinds of responses in this patient population. We're seeing dramatic improvements."

The two-armed study enrolled 167 patients with recurrent glioblastoma. One arm evaluated Avastin used as a single agent, the other Avastin given with CPT-11. An independent radiological facility was used to measure tumor responses, Cloughesy said.

In the Avastin only arm, 28.2 percent of patients responded to the treatment, meaning their tumors shrunk by 50 percent or more, a significant increase from the historic 5 percent response rates. Of the 80 patients, 42.6 percent surpassed the six month mark without their disease progressing, up from the historic 15 to 20 percent of patients. Survival was 9.2 months, a slight increase of the typical six to seven month survival time.

In the arm studying Avastin with CPT-11, 37.8 percent of patients responded to the treatment, while 50.3 percent surpassed the six month progression-free survival mark. Overall survival was 8.7 months, a little less than the Avastin only study.

Cloughesy believes the study shows the apparent power of Avastin when used alone in treating deadly brain cancers for which few effective treatments now exist.

"I think what this tells us is that the majority of the effects we're seeing are due to the Avastin," he said.

In addition, Avastin was well tolerated. While some serious side effects were noted – brain hemorrhage, strokes and heart attacks – they were seen in a very small number of patients. Avastin also appeared to reduce brain swelling, allowing patients to significantly lower the steroid dose they had to take, eliminating a number of debilitating side effects.

"Because their brain swelling went down and they could lower their doses of steroids, some patients saw a marked improvement in function," Cloughesy said.

About 20,000 patients will be diagnosed with glioblastoma this year, of those 14,000 will die.

The last new systemic therapy for recurrent glioblastoma was approved in 1976. Until Avastin, all other experimental therapies tested in this type of cancer failed to meet the FDA guidelines for approval. It's vital that less toxic, more effective therapies are found to fight glioblastoma, Cloughesy said, both when it recurs and when it is first diagnosed. Studies are underway now to see if the study results can be validated in patients with newly diagnosed glioblastomas.

A significant study finding was that Avastin was nearly as effective alone as it was when given with chemotherapy, but was much better tolerated. In consultation with their doctor, a patient facing less than a year to live might opt for Avastin alone to promote better quality of life and avoid the toxic side effects of chemotherapy.

Avastin is an angiogenesis inhibitor, meaning it cuts off the independent blood supply that a tumor develops to feed and oxygenate itself. A molecularly targeted therapy, Avastin neutralizes vascular endothelial growth factor (VEGF), a chemical signal that stimulates the growth of new blood vessels, or angiogenesis. In addition to recurrent glioblastoma, Avastin has been approved for use in metastatic colorectal, breast and kidney cancers as well as non-small cell lung cancer. In addition to UCLA's Jonsson Cancer Center, other institutions participating in the study included the University of California, San Francisco, M.D. Anderson, Dana Farber, Memorial Sloan-Kettering, Duke University, Henry Ford Hospital, the University of Virginia, the University of Chicago, Evanston Northwestern Healthcare and the University of Utah Hospital. The study was funded by Genentech, which manufactures Avastin.

Skin Deep
Plastic Surgery May Also Ease Migraines
By **CATHERINE SAINT LOUIS**

MANY of the nearly 30 million Americans who suffer from migraines end up feeling like guinea pigs. Chronic patients - those who are laid low 15 or more days a month — often cycle through drug after drug in search of relief. They also contend with side effects like mental sluggishness and stomach upset. Treatment involves guesswork because doctors have not pinpointed what causes migraines, nor do they know which drugs will best help which patients. “It can be a merry-go-round going from medication to medication in pursuit of control,” said Dr. Roger K. Cady, the vice president of the board for the National Headache Foundation, a nonprofit organization devoted to patient education.

No wonder that earlier last month, news of a surgical “cure” that touts a high success rate ricocheted worldwide. The double-blind study, published in the journal *Plastic and Reconstructive Surgery*, found that more than 80 percent of patients who underwent surgery in one of three “trigger sites” significantly reduced their number of headaches compared with more than 55 percent of the group who had sham surgery. More than half of the patients with the real surgery reported a “complete elimination” of headaches compared with about 4 percent of the placebo group.

Forehead lifts are cosmetic procedures that plastic surgeons typically perform to smooth furrowed brows. But a decade ago, after some of his patients reported that their migraines improved post-operation, Dr. Bahman Guyuron, a plastic surgeon and the lead author of the study, began to search for a surgical solution that could address migraine trigger points - which he defines as where the headache begins and settles - in the forehead, temples and the back of the head.

Headache specialists tend to be neurologists or internists, so Dr. Guyuron’s work has not always been taken seriously. “If I had a neurologist tell me there’s a new way of doing a facelift, I would have been very skeptical about it also,” said Dr. Guyuron, the chairman of the plastic surgery department at University Hospitals Case Medical Center in Cleveland. “But honestly I would have had an open mind.”

In the last month, the press has made much of the fact that a single operation could relieve migraines and turn back the clock in one fell swoop. But it is the potential that surgery for migraines may offer a viable alternative to drugs that has migraine specialists intrigued. “A very large subset became headache-free and remained headache-free for a year - that is a fantastic result,” said Dr. Richard B. Lipton, the director of the Montefiore Headache Center in the Bronx.

Especially considering that in the field of migraines, success is defined “as a reduction of 50 percent of attacks,” Dr. Cady said. Going from 10 episodes monthly to 5 is a welcome change, he added, but “it’s still a lot of migraines.”

The theory behind the surgery is that because some migraines are caused when sensitive nerve branches are squeezed and irritated by muscles, deactivating those muscles could bring prolonged relief. In the off-label use of Botox for migraines, those same muscles - when paralyzed with Botox injections - have eased headaches in some patients for roughly three months. Forehead lifts, Dr. Guyuron reasoned, might result in a longer-lasting, perhaps permanent, alleviation of pain. Only study participants who responded positively to Botox were offered the surgery. (Dr. Cady cautioned that the research on Botox as a treatment for chronic headaches is not yet ironclad. Allergan, Botox’s maker, is pursuing the approval of Botox as a treatment for chronic migraines by the Food and Drug Administration.)

Many headache specialists, Dr. Lipton and Dr. Cady included, emphasize that this migraine surgery isn’t applicable to most sufferers. “Folks who are appropriate for this procedure - they are the tip of the iceberg, not the vast majority,” said Dr. Jennifer S. Kriegler, a neurologist who is one of the study’s authors and who works at the Cleveland Clinic’s headache center.

At this stage, suitable candidates are those who endure frequent migraines and have failed more tried-and-true methods of controlling their headaches, several doctors said. The bottom line, Dr. Lipton explained, is if you can’t identify a point of irritation and “if you don’t respond to Botox, we don’t know if this treatment works for you.”

Some doctors fear that the surgery may be offered to inappropriate patients before further research confirms its efficacy for a broader group of patients. “I don’t want us to overshoot and start doing widespread surgeries in not very well selected patients until we are convinced this is broadly effective,” said Dr. F. Michael Cutrer, the chief of the headache division in the neurology department at the Mayo Clinic in Rochester, Minn. “You can always stop a medication but you can’t reverse a surgery.”

As word of the surgery spreads, Dr. Cutrer said that he anticipated pleas for referrals to the few plastic surgeons nationwide who offer the operations, but that “until we maybe have studies that are a bit larger, and some

longer follow-up I'm going to be very cautious." So far, Dr. Guyuron has trained roughly 150 doctors, and other plastic surgeons are refining their own migraine operations, even though they barely advertise.

Two years ago, an aunt told Shannon Byrne, from Mayfield Heights, Ohio, about Dr. Guyuron's migraine surgery. Ms. Byrne said that she had already spent a decade on "every single medication you can think of." Still, pain hammered her head more days than not. "You're willing to try anything," she said. Dr. Guyuron's surgery, which she had 18 months ago, was a godsend. The migraines that led to her dropping out of college and to a stroke at 20 are gone. "My dad told me not to worry about the money," Ms. Byrne, now 22, said of the thousands paid out of pocket.

A classic forehead lift for cosmetic effect differs significantly from surgery for migraine sufferers. The latter removes frown muscles more thoroughly and entails padding nerves with fatty tissue, said Dr. David A. Branch, a plastic surgeon in Bangor, Me., who performs migraine operations.

Sometimes, migraine surgery doesn't involve the forehead at all. It varies according to where the patient's trigger sites are: forehead, temples or back of the head. If Dr. Guyuron operates on the temples, the eyebrows are rejuvenated, he said. It is only the surgery at the back of the head that has no added perk, he said.

It's unclear whether or not the migraine sufferers whose pain had disappeared a year post-operation will remain headache-free for life.

"My goal is zero headaches," said Dr. Jeffrey E. Janis, a plastic surgeon in Dallas, who has performed roughly 100 operations in the last five years after training with Dr. Guyuron. "I might be able to achieve that in some, not in all." Complete elimination is "a pretty strong claim after one year of follow-up," Dr. Cutrer said.

As a way of dampening expectations, Dr. Kriegler, who has referred patients to Dr. Guyuron, frequently tells them: "Once a migraineur, always a migraineur."

Guatemala Mayan city may have ended in pyramid battle

By Sarah Grainger

EL MIRADOR, Guatemala (Reuters) - One of Guatemala's greatest ancient Mayan cities may have died out in a bloody battle atop a huge pyramid between a royal family and invaders from hundreds of miles away, archaeologists say.

Researchers are carrying out DNA tests on blood samples from hundreds of spear tips and arrowheads dug up with bone fragments and smashed pottery at the summit of the El Tigre pyramid in the Mayan city of El Mirador, buried beneath jungle vegetation 8 km from Guatemala's border with Mexico.



A partially uncovered Maya temple is seen at the El Mirador archaeological site in the Peten jungle, Guatemala. One of Guatemala's greatest ancient Mayan cities may have died out in a bloody battle atop a huge pyramid between a royal family and invaders from hundreds of miles away, archaeologists say. REUTERS/Daniel LeClair

Many of the excavated blades are made of obsidian which the archaeologists have traced to a source hundreds of miles away in the Mexican highlands. They believe the spears belonged to warriors from Teotihuacan, an ancient civilization near Mexico City and an ally of Tikal, which was an enemy city of El Mirador.

"We've found over 200 of the obsidian tips alone, as well as flint ones, indicating there was a tremendous battle," said excavation leader Richard Hansen, a senior scientist in Idaho State University's anthropology department who is pushing the pyramid battle theory.

"It looks like this was the final point of defense for a small group of inhabitants," told Reuters.

El Mirador is one of the biggest ancient cities in the Western Hemisphere and is thought to have been home to between 100,000 and 200,000 people at its height. Historians believe it was built up from around 850 BC and flourished for hundreds of years before it was mysteriously abandoned in 150 AD.

Many archaeologists think the size and elaborate stucco decoration of the buildings in the city are to blame as the inhabitants used up stone, trees and lime plaster in their construction until their resources were entirely depleted.

Hansen's team believes a group of some 200 people, thought to be the last remnants of the royal family, stayed in the ruined metropolis until they were attacked by warriors from Teotihuacan.

They believe the invaders were allies of Tikal, around 60 km to the southeast, which resented being dwarfed by the enormous pyramids of El Mirador and was eager to make sure the enemy never recovered. They think Teotihuacan warriors trapped the survivors in a siege before a bloody battle that sealed the city's fate.

MODERN THREAT

Hansen's archaeologists found graffiti they believe was left by Teotihuacan fighters who smashed up carved Maya monoliths and left crudely etched skull drawings, known as Tlalocs, on the rock as proof of their victory.

"The Tlaloc is the war god image of the highland Mexicans (and we found it) crudely pecked on these monuments, suggesting that perhaps a hostile event had taken place here," Hansen said.

The team sent excavated spear tips to a lab in Missouri where scientists are trying to extract blood samples for DNA tests. They expect to find one DNA type in blood on the obsidian objects and a different type on the Maya-made flint fragments, suggesting a battle between two racial groups.

El Mirador is home to one of the world's biggest pyramids by volume, La Danta, named after the tapirs that roam the dense jungle that hid the pre-Columbian treasures for decades until the site was discovered in the early 20th century. American archeologists who made an aerial survey of the El Mirador Basin in Guatemala's northern Peten region in the 1930s mistook the tree- and vegetation-covered pyramid for a volcano.

Hansen has worked with teams digging at El Mirador for some 30 years. The site is at risk from looters, poachers and loggers trying to make a living out of the forest, as well as drug traffickers seeking to move cocaine into Mexico.

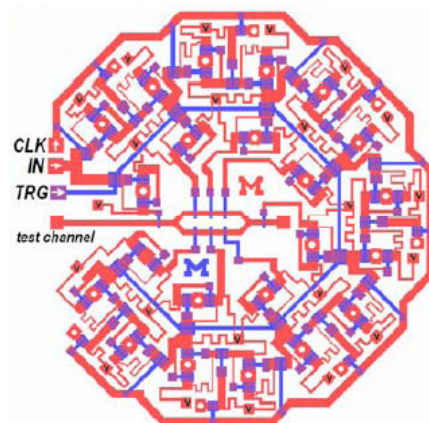
Last year, President Alvaro Colom announced the creation of a huge park in the Peten region to encompass both El Mirador and the already excavated Tikal, a popular tourist site. The park will include a silent propane-powered train to lug tourists to the El Mirador ruins, currently only accessible by helicopter or a two-day hike through the jungle.

New microprocessor runs on thin air

* 17:25 03 September 2009 by Colin Barras

There's no shortage of ways to perform calculations without a standard electronic computer. But the latest in a long line of weird computers runs calculations on nothing more than air.

The complicated nest of channels and valves (see image) made by Minsoung Rhee and Mark Burns at the University of Michigan, Ann Arbor, processes binary signals by sucking air out of tubes to represent a 0, or letting it back in to represent a 1. A chain of such 1s and 0s flows through the processor's channels, with pneumatic valves controlling the flow of the signals between channels.



A schematic of the 8-bit air-powered processor, click "1 more image" below to see the finished thing (Image: Royal Society Chemistry/Rhee/Burns)

Valve computer

Each pneumatic valve is operated by changing the air pressure in a small chamber below the air channel, separated from the circuit by a flexible impermeable membrane. When the lower chamber is filled with air the membrane pushes upwards and closes the valve, preventing the binary signal flowing across one of the processor's junctions. Sucking out the air from the chamber reopens the valve by forcing the membrane downwards, letting the signal move across the junction.

The two researchers used the valve-controlled channels to produce a variety of logic gates, flip-flops and shift registers, which they linked together to create a working 8-bit microprocessor. That means that the longest discrete pieces of data it can handle are eight binary digits long, like the processors used in 1980s consoles such as the Nintendo Entertainment System. It's even possible to watch the pneumatic components in action, because the valve membranes reflect light strongly whenever they are forced downwards (see movie).

Lab helper

But the air processor is far from just being a computational curiosity, say Rhee and Burns: it has the potential to improve the "lab-on-a-chip" devices tipped to automate complex chemistry tasks and improve disease testing, DNA profiling and other lab jobs.

These pocket-scale microfluidic devices are yet to be much practical use, say the Michigan team, perhaps because they typically require a large number of bulky and expensive off-chip components to control their operation.

Using logic circuits is one way to bring most of those controls onto the lab-on-a-chip itself and reduce running costs. But because many microfluidic systems have no electronic components, adding standard electronic valves to the device would require a new fabrication process, says Burns.

"Many microfluidic systems use pneumatic valves to control liquid flow, so adding the pneumatic control circuits should be relatively simple and inexpensive," he says.

Although the device still requires an off-chip vacuum source to operate, the volume of the microprocessor is so small that the required vacuum can be generated by a hand pump.

Versatile approach

Andrew de Mello, a microfluidics expert at Imperial College London, UK, thinks that the simplified method of operation could lead to useful microfluidic devices for developing countries. "The fact that you can generate that vacuum from a hand pump means these devices are low power, and suited for remote locations," he says.

However, the device is unlikely to have applications beyond its use in microfluidics – the "air" or "vacuum" signals are very sluggish compared with the lightning-quick flow of electrons through a standard circuit.

"Shrinking the device would mean that the signals would travel shorter distances and thus operate at higher 'clock speeds'," says Burns. *Journal reference: Lab on a Chip, DOI: 10.1039/b904354c*

Discovery of HIV's weak spot boosts vaccine quest

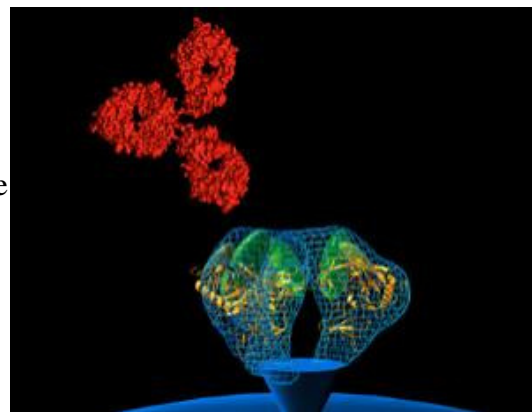
* 19:32 03 September 2009 by **Andy Coghlan**

The discovery of antibodies that bind to a hitherto unknown "weak spot" on HIV has revived hopes that a potent vaccine is within reach.

Now that the weak spot – common to many strains – has been discovered, researchers can aim for vaccines that trick people into making their own antibodies to target it.

"It's the discovery of the target that's the key thing," says Wayne Koff, senior vice president of research and development at the International AIDS Vaccine Initiative in New York, and a key member of the team reporting the breakthrough.

Vaccine developers have been beset by one failure after another. One explanation for the failures is that HIV rapidly mutates to escape detection by the immune system. As a result, many of the mutated strains are no longer recognised by antibodies. But lab tests show the new antibodies bind to many more strains and variants of HIV than usual, potentially giving patients protection against any strains that infect them, or any new mutants that evolve in their own bodies.



Two new antibodies (represented by red structure above) have been found that bind to a weak spot on HIV (lower structure) (Illustration: Christina Corbaci and Rob Pejchal)

Binding site

Led by Dennis Burton of the Scripps Research Institute in La Jolla, California, the team screened blood from 1800 infected individuals for antibodies.

They found that about 10 per cent of the donors made so-called "broadly-neutralising antibodies" (bNAbs) that recognise multiple strains of HIV. Eventually the researchers whittled these down to two extremely potent antibodies – both from the same African donor – that massively outperformed the others.

One, codenamed PG9, neutralised 127 of 162 HIV strains and the other, codenamed PG16, neutralised 119.

More importantly, detailed lab analyses revealed exactly which part of the virus the antibodies recognised, and it turned out to be a region hitherto unrecognised as a binding site.

Linked units

It was a region on gp120, the protein that forms "spikes" on the surface of the virus, and which enables the virus to bind to and infect a cell. Even more important, the binding site was on a variant of gp120 that consists of three linked units of gp120 – a so-called trimer.

This variant is the way gp120 appears on the virus itself and on infected cells – and therefore the way it will appear to someone's immune system. By contrast, most previous searches for potent antibodies have focused on whether they attach to a single unit of gp120, called a monomer. In lab tests, neither of the new antibodies bound to the monomer, demonstrating that their potency would have been missed if they'd been subjected to this standard screening test.

Common element

Now, thanks to the antibodies, researchers have realised that the trimer is a viral weak spot because it's indispensable to the virus. So unlike many other targets on the virus, it's shared by many, if not all, strains of HIV. "The key is the trimer," says Koff. "Our hypothesis now is that if you bind to the trimer, you neutralise the virus, as that's how it appears on the surface of the virus."

The antibodies are only a starting point, however, and the race is on now to develop synthetic vaccines that have the same shape as the "weak spot", or epitope, so people receiving vaccinations make antibodies that recognise it when the real virus comes along.

More weak spots

"The identity of this epitope is a major advance and will lead many groups to explore ways to produce new vaccines," says Dan Barouch of the Beth Israel Deaconess Medical Center in Boston, Massachusetts, and leader

of a recent study exploring why one of the leading vaccine candidates was a failure. "It shows exactly the site on HIV that broadly neutralising antibodies can target."

Koff says follow-up studies are now under way at IAVI's Neutralizing Antibody Center at Scripps – due to open officially on 24 September – to screen for more broadly neutralising antibodies, hopefully revealing yet more sites on the viral anatomy that are indispensable.

"The expectation is that we'll find more," he says. "We hope there will be a number of sites that are vulnerable, and we'll know that in a few months' time."

It is impossible to predict when the first vaccines targeting "weak spots" might go into trials. But Koff says: "We're cautiously optimistic we're now turning in the right direction."

Journal reference: Science (DOI: 10.1126/science.1178746)

Syracuse University research team discovers switch that causes the body to produce cancerous cells

A team of Syracuse University researchers discovered a second molecular switch within the Mixed Lineage Leukemia protein complex that they believe could be exploited to prevent the overproduction of abnormal cells that are found in several types of cancer, including leukemia.

The paper was designated as the "Paper of the Week" in the September 4 issue of the *Journal of Biological Chemistry* (JBC), published by the American Society for Biochemistry and Molecular Biology. Only the top 1 percent of the more than 6,600 articles published each year in JBC receives this prestigious designation.

The research team is led by biologist Michael Cosgrove, assistant professor in SU's College of Arts and Sciences. Anamika Patel, a post-doctoral researcher in Cosgrove's lab, who is being featured on JBC's website, did much of the experimental work for the paper.

During the course of their research to better understand MLL, a protein switch that helps regulate the formation of white blood cells, Cosgrove's research group discovered a new molecular switch within the MLL complex, which they labeled W-RAD.

"We thought that MLL was the only switching mechanism present in this protein complex," Cosgrove said. "However, we discovered the complex is really two switches."

In normal cells, MLL combines with four proteins that comprise the W-RAD group to create a molecular switch that controls DNA packaging events required to form white blood cells. When the MLL switch is broken, white blood cells do not mature properly, resulting in a dangerous proliferation of abnormal cells.

Similarly, the proteins that form the W-RAD complex are overproduced in several types of cancer cells, but until now, scientists did not know the function of these proteins. Cosgrove's group discovered that the W-RAD proteins form a new kind of switch—one that has never been seen before.

"The W-RAD switching mechanism signals the cell to create multiple copies of cancer cells," Cosgrove says. "If we can find a way to turn off this switch, we might be able to slow or stop the production of abnormal cells and convert them to normal cells."

Anticancer compound found in American mayapple Mayapple shows potential as cash crop in US

VERONA, MS—A common weed called American mayapple may soon offer an alternative to an Asian cousin that's been harvested almost to extinction because of its anti-cancer properties. The near-extinct Asian plant, *Podophyllum emodi*, produces podophyllotoxin, a compound used in manufacturing etoposide, the active ingredient in a drug used for treating lung and testicular cancer. *Podophyllum emodi* is a cousin of the common mayapple weed found in the United States.

Podophyllotoxin is found in Indian mayapple (*Podophyllum emodii* Wall.), American mayapple (*Podophyllum peltatum* L.), and other species. Podophyllotoxin and its derivatives are used in several commercially available pharmaceutical products such as the anticancer drugs etoposide, teniposide, and etopophos, which are used in the treatment of small-cell lung cancer, lymphoblastic leukemia, testicular cancer, and brain tumors. Podophyllotoxin derivatives are also used for the treatment of psoriasis and malaria, and some are being tested for the treatment of rheumatoid arthritis. Currently, podophyllotoxin is produced commercially using the roots and rhizomes of Indian mayapple, an endangered species harvested from the wild in India, Pakistan, Nepal, and China.

Researchers at Mississippi State University and the University of Mississippi recently set out to identify American mayapple types with high podophyllotoxin content. Valtcho D. Zheljzkov and colleagues at Mississippi State University published the research results in *HortScience*. According to Zheljzkov; "The objective of this study was to estimate podophyllotoxin concentration in American mayapple across its natural habitats in the eastern United States and to identify high podophyllotoxin types that could be used for further selection and cultivar development."

Mayapple has been long been grown as a cash crop in Europe and Russia, but has never been introduced or domesticated in the United States, although the idea was suggested by researchers more than 30 years ago. Previous research demonstrated that American mayapple leaves contain podophyllotoxin, making way for the development of American mayapple as a high-value crop for American growers. Zheljzkov explained that, until now, there has been no comprehensive study on the genetic resources of American mayapple colonies across the United States. "We hypothesized that there might be great variation with respect to podophyllotoxin content within American mayapple across the eastern United States."

The researchers studied the effect of location, plant nutrient concentration, and phytoavailable nutrients in soil on podophyllotoxin concentration in American mayapple across its natural habitats in the eastern United States. The study was the largest of its kind ever conducted; American mayapple leaves were collected from 37 mayapple colonies across 18 states.

This groundbreaking study confirmed that mayapple colonies in the eastern part of the United States can be used for the development of high podophyllotoxin cultivars, which could subsequently provide the base for commercial production of podophyllotoxin in the United States. The results from this study will help to develop a Geographic Information System (GIS) map of the genetic resources of American mayapple in the U.S.

The complete study and abstract are available on the ASHS Hortscience electronic journal web site:

<http://hortsci.ashspublications.org/cgi/content/abstract/44/2/349>

Smoke no longer found in European hospitals

Tobacco use is prohibited in hospitals in many European countries, although levels of compliance with this regulation differ. A study carried out by researchers from the Catalan Institute of Oncology (ICO) has shown for the first time that exposure to environmental tobacco smoke in European hospitals is "low", and "without any notable differences" between them.

Europe wants to see smoking in all closed public places banned by 2012. However, to date only 10 European countries – Spain is not among them – are applying this regulation comprehensively. Now a research study has described the levels of environmental tobacco smoke in European hospitals and has shown for the first time that exposure is "low" and "without any notable differences between them".

The study, carried out in 2001 in 30 hospitals throughout seven European countries (Germany, Austria, Belgium, France, Greece, Romania and Spain) measured levels of particulates with a diameter of 2.5 microns (known as PM2.5) ($\mu\text{g}/\text{m}^3$) or below, which indicate the presence of environmental tobacco smoke, at six standard sites in each hospital.

Esteve Fernández, lead author of the study and a researcher at the ICO, tells SINC "it is important to measure compliance with laws by regularly measuring levels of environmental tobacco smoke". To do this, the experts suggest that national and European regulations to control tobacco addiction should ban smoking in health establishments without any exceptions.

In total, 199 PM2.5 measurements were taken, 30 of them in the vestibules of main hospital entrances, 29 in casualty department waiting rooms, 22 in medical hospitalisation units, 27 in cafeterias, 22 on fire escape stairways, 22 in general surgery hospitalisation units, and 39 in other places, including eight smokers' areas (in Belgium and Greece).

The results, which have appeared recently in the European Respiratory Journal, show that the average level of PM2.5 micro particles in all the countries was $3.0\mu\text{g}/\text{m}^3$, with half of the measurements being between 2.0 and $7.0\mu\text{g}/\text{m}^3$. Eleven of the measurements (5.5%) revealed levels of particulates of more than $25.0\mu\text{g}/\text{m}^3$, which is the limit recommended by the World Health Organisation (WHO) for external air quality.

Most of the countries studied had introduced specific smoking bans in health establishments at the time of the study, although some of these bans allowed smoking in certain places, or even in the cafeterias.

References: E. Fernández, C. Martínez, M. Fu, J.M. Martínez-Sánchez, M.J. López, G. Invernizzi, A. Ouranou, B. Dautzenberg y M. Nebot. "Second-hand smoke exposure in a sample of European hospitals". European Respiratory Journal; 34: 111 julio de 2009.

Fear of insurance rejection deters potentially life saving genetic tests for bowel cancer

An Australian study of families with genetic risk of bowel cancer has found that 50 percent of participants declined genetic testing when informed of insurance implications.

"This indicates that people have a significant fear of insurance discrimination which impacts their decision to have potentially life saving genetic testing," says co-lead author Dr Louise Keogh, of the University of Melbourne's Key Centre for Women's Health in Society.

The population-based study was led by researchers from the University of Melbourne and the Cancer Council Victoria, and published in the prestigious Medical Journal of Australia today.

Researchers identified 106 people from 25 families in which there were genetic mutations that increase the risk of bowel cancer. All were offered the chance to learn their own individual genetic information at a Familial Cancer Clinic. "When we told participants about the life insurance implications of genetic testing, the number declining genetic testing more than doubled from 20 per cent to 50 per cent," Dr Keogh said.

"In Australia, while genetic information has no implications for health insurance, it can affect life, trauma, disability and sickness and accident insurance policies," says co-lead author Christine van Vliet, School of Medical Sciences, University of New South Wales.

"However this is not the case in all countries. Since we know all people have some genes which predispose to disease, it is important that the Australian life insurance industry does not deter people from learning about their genetic risks," she says.

Bowel cancer is the second most common cancer for men and women in Australia. One in every 3,000 Australians carry a genetic mutation that places them at high risk of bowel cancer.

"For those at high genetic risk, screening for and removal of polyps reduces the risk of bowel cancer by more than 50 percent," says Associate Professor Mark Jenkins of the University of Melbourne's School of Population Health and senior author on the paper.

"Insurance-related apprehension about genetic testing could have troubling public health consequences. Screening people at high genetic risk of bowel cancer is a highly cost effective way to reduce deaths due to bowel cancer," he says.

Dr Louise Keogh says that now that we know insurance policies are adversely affecting health decision-making, it is time to act. "We call on the Federal Government and the Australian insurance industry to look at what other countries have done and reconsider the use of genetic information where genetic testing has the potential to reduce morbidity and mortality," she says.

People with a strong family history of bowel cancer and concerned about the possibility of having inherited a high risk can obtain a referral from a GP to visit a Family Cancer Clinic.

For more information contact Rebecca Scott University of Melbourne Mobile: +613 8344 0181

Universal translator for web browsers

EVER wondered what the Arabic or Chinese press are saying about the issues of the day? Finding out just got a lot easier, at least for those using the Firefox web browser.

A new plug-in identifies the language used on a web page and automatically provides a translation, leaving the layout of the page unchanged.

The plug-in, designed by the San Francisco-based Worldwide Lexicon project, recognises over 40 languages. Users start by telling the software which language they prefer. When a page written in a different language loads, the software searches for translations provided by the project's community of volunteers. If none is available it uses an online services such as Google Translate.

[A test version of the plug-in is available at the Firefox website.](#)

Observatory

Breath Sensor Identifies Signs of Lung Cancer

By HENRY FOUNTAIN

The breath of people with lung cancer is different from that of healthy people - it contains higher concentrations of alkanes and other volatile organic compounds.

Researchers have known this for years, and have tried to develop breath-sensing systems that could diagnose the disease, as an alternative to CT scans and other current diagnostic methods. The systems have tended to be costly, requiring complicated equipment and techniques to concentrate the compounds so they reach detectable levels.

Gang Peng of the Israel Institute of Technology in Haifa and colleagues have now developed what they say is an inexpensive, portable sensor technology that can quickly distinguish between the breath of lung cancer patients and healthy people.

The sensor, described in Nature Nanotechnology, uses tiny particles of gold, five billionths of a meter in diameter, that are capped with organic compounds chosen for their ability to react with four of the volatile compounds found in higher concentrations in the breath of lung cancer patients. When the particles are deposited in a thin film between two electrodes, they act as an electrical resistor.

The researchers found that when an array of nine resistors was exposed to exhaled breath, the resistance changed as compounds in the breath reacted with the compounds on the gold particles. The patterns of the changes in the array differed depending whether the subjects had lung cancer or not.

The researchers are continuing to develop the system, and say that a similar approach may work for the diagnosis of other diseases as well.

Vital Signs

Awareness: Clinical Trial Rule Is Widely Ignored

By **RONI CARYN RABIN**

Many researchers are ignoring a 2005 requirement that they register proposed clinical trials in a government database as a condition for publishing their results in medical journals. And the journals are publishing the papers anyway, a new study reveals.

The study, a review of 323 articles published last year in leading medical journals, found that only 147 of the clinical trials - 45.5 percent - were properly registered before the end of the trial in a way that clearly stated the main outcomes being assessed. Even among the articles that were registered, almost a third had discrepancies between the outcomes described in the registry and the ones ultimately reported.

Of the trials that were not registered properly, 89 - more than half - were never entered in the National Institutes of Health's clinical trials registry. The report appears in the Sept. 2 issue of *The Journal of the American Medical Association*.

"We're asking people to tell readers honestly and transparently, 'What did you do, and what did you find?'" said an author of the paper, David Moher, senior scientist at the Ottawa Hospital Research Institute in Canada.

Dr. Moher added that bias could easily be introduced when investigators changed the primary outcome they were measuring - moving the goalpost, so to speak. That might happen, for example, if a clinical trial is designed to determine whether a drug increases survival rates but investigators change the primary outcome to assessing if the drug improves quality of life.

Using waste to recover waste uranium

Using bacteria and inositol phosphate, a chemical analogue of a cheap waste material from plants, researchers at Birmingham University have recovered uranium from the polluted waters from uranium mines. The same technology can also be used to clean up nuclear waste. Professor Lynne Macaskie, this week (7-10 September), presented the group's work to the Society for General Microbiology's meeting at Heriot-Watt University, Edinburgh.

Bacteria, in this case, *E. coli*, break down a source of inositol phosphate (also called phytic acid), a phosphate storage material in seeds, to free the phosphate molecules. The phosphate then binds to the uranium forming a uranium phosphate precipitate on the bacterial cells that can be harvested to recover the uranium.

This process was first described in 1995, but then a more expensive additive was used and that, combined with the then low price of uranium, made the process uneconomic. The discovery that inositol phosphate was potentially six times more effective as well as being a cheap waste material means that the process becomes economically viable, especially as the world price of uranium is likely to increase as countries move to expand their nuclear technologies in a bid to produce low-carbon energy.

As an example, if pure inositol phosphate, bought from a commercial supplier is used, the cost of this process is £1.72 per gram of uranium recovered. If a cheaper source of inositol phosphate is used (eg calcium phytate) the cost reduces to £0.09 for each gram of recovered uranium. At 2007 prices, uranium cost £0.211/g; it is currently £0.09/g. These prices make the process economic overall because there is also an environmental protection benefit. Use of low-grade inositol phosphate from agricultural wastes would bring the cost down still further and the economic benefit will also increase as the price of uranium is forecast to rise again.

"The UK has no natural uranium reserves, although a significant amount of uranium is produced in nuclear wastes. There is no global shortage of uranium but from the point of view of energy security the EU needs to be able to recover as much uranium as possible from mine run-offs (which in any case pollute the environment) as well as recycling as much uranium as possible from nuclear wastes," commented Professor Macaskie, "By using a cheap feedstock easily obtained from plant wastes we have shown that an economic, scalable process for uranium recovery is possible".

Largest ever Alzheimer's gene study unveils dementia mysteries

Professor Julie Williams British scientists have discovered two new genes associated with Alzheimer's disease, while French colleagues uncovered a third.

The results, from the largest ever Alzheimer's genome-wide association study (GWAS) involving 16,000 individuals, are published in *Nature Genetics*. They are the first new genes found to be associated with the common form of Alzheimer's disease since 1993.

The Alzheimer's Research Trust spoke of "a leap forward for dementia research", the MRC's Sir Leszek Borysiewicz praised "a huge step towards achieving an earlier diagnosis of Alzheimer's", and the Welsh First Minister Rhodri Morgan hailed the Cardiff-led study as "a real feather in the cap of Welsh science".

The study was funded by the Wellcome Trust, Medical Research Council, Alzheimer's Research Trust and Welsh Assembly Government among others. The UK-led research involved scientists from universities in

Cardiff, London, Cambridge, Nottingham, Southampton, Manchester, Oxford, Bristol and Belfast, who collaborated with Irish, German, Belgian, Greek and American institutions.

Previously only one gene, APOE4, had been associated with Alzheimer's disease. This study reveals two further genes, CLU and PICALM, are related to the disease. This is expected to provide scientists with a much clearer route to developing new treatments.

The paper's lead-author, Prof Julie Williams, Chief Scientific Adviser to the Alzheimer's Research Trust, said: "Both CLU and PICALM highlight new pathways that lead to Alzheimer's disease. The CLU gene produces clusterin which normally acts to protect the brain in a variety of ways. Variation in this gene could remove this protection and contribute to Alzheimer's development. PICALM is important at synapses - connections between brain cells - and is involved in the transport of molecules into and inside of nerve cells, helping form memories and other brain functions. We know that the health of synapses is closely related to memory performance in Alzheimer's disease, thus changes in genes which affect synapses are likely to have a direct effect on disease development."

"This research is changing our understanding of what causes the common form of Alzheimer's disease and provides valuable new leads in the race to find treatments and possibly cures."

"It also shows that other genes can be identified using this method, and the group are already planning a larger study involving 60,000 people, which can be achieved within the next year."

Rebecca Wood, Chief Executive of the Alzheimer's Research Trust, which part-funded the study, said: "These findings are a leap forward for dementia research. At a time when we are yet to find ways of halting this devastating condition, this development is likely to spark off numerous new ideas, collaborations and more in the race for a cure.

"The work of Professor Williams and colleagues shows how British researchers lead the world in the struggle to understand and defeat dementia. With the right support for scientists, we can offer hope to the 30 million people worldwide who live with dementia.

The First Minister for Wales, Rhodri Morgan, said: "This major breakthrough in the battle to understand and develop treatments for Alzheimer's is good news for the 37,000 people in Wales and their carers who are affected by Alzheimer's or other forms of dementia. It is a real feather in the cap of Welsh science that this important global study has been led by a Welsh scientist, Professor Julie Williams and that the Welsh Assembly Government was able to give financial support for her work. World-class research like this will help lead to improved treatment for this distressing disease, and may one day even mean we can cure dementia."

Sir Leszek Borysiewicz, Chief Executive of the Medical Research Council, said: "Funding work on neurodegenerative diseases is a priority for us and MRC investment in this kind of innovative research is crucial in piecing together the Alzheimer's puzzle. This study is a huge step towards achieving an earlier diagnosis of Alzheimer's and improving the lives of the many people affected by the disease."

The team shared their data with a further French-led study, also published in Nature Genetics, which has revealed compelling evidence for a third gene associated with Alzheimer's called CR1.

The only other genes that have been connected to Alzheimer's disease are in extremely rare cases of familial Alzheimer's disease, which is inherited in less than 1% of cases.

Piece from childhood virus may save soldiers' lives

Research presented Sept. 6 at European complement conference

A harmless shard from the shell of a common childhood virus may halt a biological process that kills a significant percentage of battlefield casualties, heart attack victims and oxygen-deprived newborns, according to research presented Sunday, September 6, 2009, at the 12th European meeting on complement in human disease in Budapest, Hungary.

Introducing the virus's shell in vitro shuts down what's known as the complement response, a primordial part of the immune system that attacks and destroys the organs and vascular lining of people who have been deprived of oxygen for prolonged periods, according to researchers at Children's Hospital of The King's Daughters (CHKD) and Eastern Virginia Medical School (EVMS), in Norfolk, Va.

The complement response kicks in after the victim has been revived, in what is known as a reperfusion injury. It does its work slowly but unrelentingly, killing soldiers, infants or heart attack victims over the course of days.

"To find a way to manipulate the complement system pharmacologically has been like a search for the Holy Grail," said one of the lead researchers, Dr. Kenji Cunnion, an infectious disease physician at CHKD and an associate professor of pediatrics at EVMS.

While Cunnion and Neel Krishna, Ph.D., a pediatric virologist at CHKD and assistant professor of microbiology at EVMS, focus on pediatric research, they see clear military applications.

"The complement reaction is one of the major causes of death of the battlefield," said Krishna. "By the time you get a victim to the hospital, it may be too late."

Dr. L.D. Britt, M.D., MPH, Brickhouse professor and chairman of surgery at EVMS, agrees.

"Hemorrhagic shock is the leading cause of death in combat trauma and reperfusion injury plays a significant role both in increased mortality and increased brain damage," said Britt, senior consultant to the military on combat trauma. "This research could help save the lives of soldiers, as well as the lives of other trauma victims who have been without oxygen for extended periods."

Britt has joined Cunnion in Krishna in seeking a grant from the Department of Defense to expedite research and development.

The complement system ranks as one of the oldest biological mechanisms in life's evolution and exists in almost identical form in everything from seagulls to starfish.

Essentially, the complement system recognizes and destroys potentially toxic substances that gain entry into an organism's bloodstream. When a starfish loses a limb, for instance, the complement system sends a contingent of killer cells to block and attack anything that tries to work its way inside.

In human evolution, complement provided an essential natural defense.

"Up until 100 years ago, the vast majority of humans died from infectious diseases," said Cunnion. "Nobody died of old age and almost nobody lived long enough to die of a heart attack."

Thanks to modern medicine, people now live long enough to die from trauma, such as car accidents, or from conditions, such as heart attack and stroke, that can leave cells throughout the body starved for oxygen. Cells deprived of oxygen often undergo biochemical changes, essentially marking themselves for death. When blood flow and oxygen are restored, these changes trigger the complement cascade. The marauding cells unleashed by complement cascade are indiscriminate, killing not only the cell with the biochemical marker but innocent bystander cells as well.

"It's like throwing a grenade," said Krishna.

A patient, who has suffered survivable brain damage from oxygen deprivation, might die over several days as swaths of cells are destroyed by this seemingly unstoppable reaction. Animal research has shown that stopping this complement reaction significantly reduces brain damage.

The complement system is so complex that research scientists spend entire careers studying it, publishing in journals that specialize in this primordial defense mechanism.

In the case of Cunnion and Krishna, discovering how to shut down the complement system resulted from happenstance. As they worked in neighboring labs, they noticed a similarity in the structure of molecules Cunnion used in his experiments and the protein shell of the astrovirus Krishna studied. They wondered what would happen if they introduced the astrovirus shell into an assay routinely used in Cunnion's lab to assess complement activation.

"It was kind of a shot in the dark," Krishna said. "We didn't expect anything to happen."

The complement reaction completely stopped.

The presentation in Hungary, "Human Astrovirus Coat Protein Binds C1q and MBL and Inhibits the Classical and Lectin Pathways of Complement Activation," highlights not only the discovery, but research published in Current Topics in Complement II and the Journal of Virology, describing precisely how this tiny piece of protein halts the complement cascade in its tracks.