

Biblical plagues really happened say scientists

The Biblical plagues that devastated Ancient Egypt in the Old Testament were the result of global warming and a volcanic eruption, scientists have claimed.

By Richard Gray, Science Correspondent

Researchers believe they have found evidence of real natural disasters on which the ten plagues of Egypt, which led to Moses freeing the Israelites from slavery in the Book of Exodus in the Bible, were based.

But rather than explaining them as the wrathful act of a vengeful God, the scientists claim the plagues can be attributed to a chain of natural phenomena triggered by changes in the climate and environmental disasters that happened hundreds of miles away.

They have compiled compelling evidence that offers new explanations for the Biblical plagues, which will be outlined in a new series to be broadcast on the National Geographical Channel on Easter Sunday.

Archaeologists now widely believe the plagues occurred at an ancient city of Pi-Rameses on the Nile Delta, which was the capital of Egypt during the reign of Pharaoh Rameses the Second, who ruled between 1279BC and 1213BC. The city appears to have been abandoned around 3,000 years ago and scientists claim the plagues could offer an explanation.

Climatologists studying the ancient climate at the time have discovered a dramatic shift in the climate in the area occurred towards the end of Rameses the Second's reign. By studying stalagmites in Egyptian caves they have been able to rebuild a record of the weather patterns using traces of radioactive elements contained within the rock. They found that Rameses reign coincided with a warm, wet climate, but then the climate switched to a dry period.

Professor Augusto Magini, a paleoclimatologist at Heidelberg University's institute for environmental physics, said: "Pharaoh Rameses II reigned during a very favourable climatic period. "There was plenty of rain and his country flourished. However, this wet period only lasted a few decades. After Rameses' reign, the climate curve goes sharply downwards. "There is a dry period which would certainly have had serious consequences." The scientists believe this switch in the climate was the trigger for the first of the plagues.

The rising temperatures could have caused the river Nile to dry up, turning the fast flowing river that was Egypt's lifeline into a slow moving and muddy watercourse. These conditions would have been perfect for the arrival of the first plague, which in the Bible is described as the Nile turning to blood.

Dr Stephan Pflugmacher, a biologist at the Leibniz Institute for Water Ecology and Inland Fisheries in Berlin, believes this description could have been the result of a toxic fresh water algae. He said the bacterium, known as Burgundy Blood algae or *Oscillatoria rubescens*, is known to have existed 3,000 years ago and still causes similar effects today. He said: "It multiplies massively in slow-moving warm waters with high levels of nutrition. And as it dies, it stains the water red." The scientists also claim the arrival of this algae set in motion the events that led to the second, third and fourth plagues – frogs, lice and flies.

Frogs development from tadpoles into fully formed adults is governed by hormones that can speed up their development in times of stress. The arrival of the toxic algae would have triggered such a transformation and forced the frogs to leave the water where they lived. But as the frogs died, it would have meant that mosquitoes, flies and other insects would have flourished without the predators to keep their numbers under control. This, according to the scientists, could have led in turn to the fifth and sixth plagues – diseased livestock and boils

Professor Werner Kloas, a biologist at the Leibniz Institute, said: "We know insects often carry diseases like malaria, so the next step in the chain reaction is the outbreak of epidemics, causing the human population to fall ill."

Another major natural disaster more than 400 miles away is now also thought to be responsible for triggering the seventh, eighth and ninth plagues that bring hail, locusts and darkness to Egypt.

One of the biggest volcanic eruptions in human history occurred when Thera, a volcano that was part of the Mediterranean islands of Santorini, just north of Crete, exploded around 3,500 year ago, spewing billions of tons of volcanic ash into the atmosphere. Nadine von Blohm, from the Institute for Atmospheric Physics in Germany, has been conducting experiments on how hailstorms form and believes that the volcanic ash could have clashed with thunderstorms above Egypt to produce dramatic hail storms.

Dr Siro Trevisanato, a Canadian biologist who has written a book about the plagues, said the locusts could also be explained by the volcanic fall out from the ash. He said: "The ash fall out caused weather anomalies, which translates into higher precipitations, higher humidity. And that's exactly what fosters the presence of the locusts." The volcanic ash could also have blocked out the sunlight causing the stories of a plague of darkness.

Scientists have found pumice, stone made from cooled volcanic lava, during excavations of Egyptian ruins despite there not being any volcanoes in Egypt. Analysis of the rock shows that it came from the Santorini

volcano, providing physical evidence that the ash fallout from the eruption at Santorini reached Egyptian shores.

The cause of the final plague, the death of the first borns of Egypt, has been suggested as being caused by a fungus that may have poisoned the grain supplies, of which male first born would have had first pickings and so been first to fall victim.

But Dr Robert Miller, associate professor of the Old Testament, from the Catholic University of America, said: "I'm reluctant to come up with natural causes for all of the plagues. The problem with the naturalistic explanations, is that they lose the whole point. "And the whole point was that you didn't come out of Egypt by natural causes, you came out by the hand of God."

The Ten Plagues of the Bible will be shown at 7pm on Sunday 4 April on the National Geographic Channel

Hyenas' laughter signals deciphered

Acoustic analysis of the 'giggle' sound made by spotted hyenas has revealed that the animals' laughter encodes information about age, dominance and identity. Researchers writing in the open access journal BMC Ecology recorded the calls of 26 hyenas in captivity and found that variations in the giggles' pitch and timbre may help hyenas to establish social hierarchies.

Frédéric Theunissen, from the University of California at Berkeley, USA, and Nicolas Mathevon, from the Université Jean Monnet, St. Etienne, France worked with a team of researchers to study the animals in a field station at Berkeley. Theunissen said, "The hyena's laugh gives receivers cues to assess the social rank of the emitting individual. This may allow hyenas to establish feeding rights and organize their food-gathering activities."

The researchers found that while the pitch of the giggle reveals a hyena's age, variations in the frequency of notes can encode information about dominant and subordinate status. These vocalizations are mainly produced during food contests by animals that are prevented from securing access to a kill, and have been considered a gesture of submission.

Theunissen and colleagues also suggest that the giggle may be a sign of frustration and that it may be intended to summon help. He said, "Lions often eat prey previously killed by hyenas. A solitary hyena has no chance when confronted by a lion, whereas a hyena group often can 'mob' one or two lions and get their food back. Giggles could therefore allow the recruitment of allies. Cooperation and competition are everyday components of a hyena's life. When hearing a giggling individual, clan-mate hyenas could receive information about who is getting frustrated (in terms of individual identity, age, status) and decide to join the giggler, or conversely to ignore it or move away". The researchers plan to further test these hypotheses with playback experiments in the field.

Microbes reprogrammed to ooze oil for renewable biofuel

Using genetic sleight of hand, researcher Xinyao Liu and professor Roy Curtiss at Arizona State University's Biodesign Institute have coaxed photosynthetic microbes to secrete oil—bypassing energy and cost barriers that have hampered green biofuel production. Their results appear in this week's advanced online issue of the Proceedings of the National Academy of Sciences or PNAS.

The challenges of developing a renewable biofuel source that is competitive with the current scalability and low-cost of petroleum have been daunting. "The real costs involved in any biofuel production are harvesting the fuel precursors and turning them into fuel," said Roy Curtiss, director of the Biodesign Institute's Center for Infectious Diseases and Vaccinology and professor in the School of Life Sciences. "By releasing their precious cargo outside the cell, we have optimized bacterial metabolic engineering to develop a truly green route to biofuel production."

Photosynthetic microbes called cyanobacteria offer attractive advantages over the use of plants like corn or switchgrass, producing many times the energy yield with energy input from the sun and without the necessity of taking arable cropland out of production.

Lead author Xinyao Liu and Curtiss, applied their expertise in the development of bacterial-based vaccines to genetically optimize cyanobacteria for biofuel production. Last year, they were able to modify these microbes, priming them to self-destruct and release their lipid contents. In the group's latest effort however, the energy-rich fatty acids were extracted without killing the cells in the process. "In China, we have a saying," Liu says. "We don't kill the hen to get the eggs." Rather than destroying the cyanobacteria, the group has ingeniously reengineered their genetics, producing mutant strains that continuously secrete fatty acids through their cell walls. The cyanobacteria essentially act like tiny biofuel production facilities.

Liu realized that if cyanobacteria could be cajoled into overproducing fatty acids, their accumulation within the cells would eventually cause these fatty acids to leak out through the cell membrane, through the process of diffusion. To accomplish this, Liu introduced a specific enzyme, known as thioesterase, into cyanobacteria.

The enzyme is able to uncouple fatty acids from complex carrier proteins, freeing them within the cell where they accumulate, until the cell secretes them. "I use genes that can steal fatty acids from the lipid synthesis pathway," Liu explains noting that thioesterase acts to efficiently clip the bonds associating the fatty acids with more complex molecules. This use of modified thioesterases to cause secretion of fatty acids was first described for *Escherichia coli* by John Cronan of the University of Illinois more than a decade ago.

A second series of modifications enhances the secretion process, by genetically deleting or modifying two key layers of the cellular envelope—known as the S and peptidoglycan layers—allowing fatty acids to more easily escape outside the cell, where their low water solubility causes them to precipitate out of solution, forming a whitish residue on the surface. Study results show a 3-fold increase in fatty acid yield, after genetic modification of the two membrane layers.

To improve the fatty acid production even further, the group added genes to cause overproduction of fatty acid precursors and removed some cellular pathways that were non-essential to the survival of cyanobacteria. Such modifications ensure that the microbe's resources are devoted to basic survival and lipid production.

Liu emphasizes that the current research has moved along at a lightening clip, with only about 6 months passing from the initial work, through production of the first strains—a fact he attributes to the formidable expertise in the area of microbial genetic manipulation, assembled at the Biodesign Institute. "I don't think any group would have the capacity to do this as fast," he said.

Professor Roy Curtiss agrees, noting that "the seminal advance has been to combine a number of genetic modifications and enzyme activities previously described in other bacteria and in plants in the engineered cyanobacteria strains along with the introduction of newly discovered modifications to increase production and secretion of fatty acids.

The results to date are encouraging and we are confident of making further improvements to achieve enhanced productivity in strains currently under construction and development. In addition, optimizing growth conditions associated with scale-up will also improve productivity."

The team, which includes researchers Daniel Brune and Wim Vermaas, is also optimistic that significantly higher fatty acid yields will be obtainable, as research continues.

The research opens the door to practical use of this promising source of clean energy.

Acupuncture calms highly anxious dental patients

Acupuncture in the management of anxiety related to dental treatment: A case series

Acupuncture can calm highly anxious dental patients and ensure that they can be given the treatment they need, suggests a small study published in *Acupuncture in Medicine*. A visit to the dentist provokes extreme fear and anxiety in an estimated one in 20 people, and can put them off going altogether, a condition termed odontophobia. And up to a third of patients report moderate anxiety at the prospect of dental treatment, studies show.

The authors base their findings on 16 women and four men from eight dental practice lists. Each of the patients was moderately or extremely anxious about going to the dentist for treatment, as assessed by a validated questionnaire - the Back Anxiety Inventory (BAI). All were in their 40s and had been trying to deal with this problem for between two and 30 years.

The BAI score was assessed before and after five minutes of acupuncture treatment, targeting two specific acupuncture points (GV20 and EX6) on the top of the head. The acupuncture was carried out by the dentists themselves, all of whom are members of the British Dental Acupuncture Society.

The average BAI score of 26.5 fell to 11.5, and all 20 patients were able to undergo their planned treatment, whereas before this had only been possible in six - and then only partially and after a great deal of effort on the part of both dentist and patient.

The authors point out that several attempts have been made to conquer this type of anxiety, including sedatives, relaxation techniques, behavioural therapies, biofeedback and hypnosis. The research indicates that these do help, but they are time consuming and require considerable levels of psychotherapeutic skills, if applied properly, say the authors.

They caution that further larger studies are needed to confirm the value of acupuncture in these sorts of cases, but suggest that acupuncture "may offer a simple and inexpensive method of treatment."

Beta-blockers 'cut cancer spread'

Blood pressure drugs may be able to reduce the ability of breast cancer to spread around the body, researchers have told a European conference.

A joint UK and German study found that cancer patients taking beta-blockers had a lower risk of dying.

The drugs may block hormones that trigger the spread of cancer cells. However, experts stressed that more evidence from bigger studies would be needed before the drug could be given as part of routine treatment.

Breast cancer, which affects more than 30,000 people in the UK each year, is most easily tackled when tumours are confined to the breast only.

When cancer cells migrate to other parts of the body, and start growing, a process known as metastasis, the likelihood of successful treatment begins to fall. The biological processes which trigger metastasis are still not fully understood.

The latest research, presented at the European Breast Cancer Conference in Barcelona, builds on earlier laboratory studies which suggest that the ability of cancer cells to increase in number and spread is boosted by the presence of stress hormones.

Beta-blockers attach themselves to the same receptors on cancer cells used by these hormones, potentially reducing their ability to stimulate the cell and trigger spread. They are already taken by approximately two million people in the UK.

To test this theoretical cancer-fighting ability, Dr Des Powe, from Queen's Medical Centre, Nottingham, in collaboration with Professor Frank Entschladen from Witten University in Germany, looked at three groups of breast cancer patients, a total of 466 people.

The first group had high blood pressure, also called hypertension, and were taking beta-blockers, the second had high blood pressure, but were taking something different for it, while the third had no blood pressure problems.

In the 43 who were taking beta-blockers, there was a significant reduction in both cancer metastasis, and new tumours within the breast. Overall they had a 71% lower chance of dying from breast cancer compared with the other groups.

Small-scale research

Dr Powe said: "It is reasonable to speculate, therefore, that some non-hypertensive women with breast cancer will respond favourably to beta-blocker treatment, though doses and side-effects would need to be investigated in clinical trials." However, he said that the study was "relatively small" and its results would need to be reproduced in a larger group of patients.

"We are very encouraged by these first results which have already shown that by using a well-established, safe and cost effective drug, we can take another step on the road towards targeted therapy in breast cancer."

Meg McArthur, from Breakthrough Breast Cancer, welcomed the findings: "Although this is early stage research, these results show that beta blockers could play a role in reducing the risk of metastatic breast cancer. This is a positive step forward as it could potentially lead to survival improvements for people affected with this condition. "However, as the study is quite small, we would like to see further research in this area."

Study shows that mutations in 1 gene cause many cancers

COLUMBUS, Ohio – An important gene that normally protects the body against cancer can itself cause a variety of cancers depending on the specific mutation that damages it, according to a new study by investigators at the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC-James).

The study examined mutations in a gene called PTEN. People who inherit a mutated copy of this gene have Cowden syndrome, a condition that carries a high risk of cancer in a number of organs, including the breast, thyroid and ovary. In addition, PTEN is frequently mutated in normal body cells leading to prostate, lung and pancreatic cancers.

Why people with Cowden syndrome develop different cancers, or cancers that are more severe in some than in others, is unknown, though the cause is often attributed to the natural genetic differences that exist between individuals.

This animal study, however, linked specific mutations in the gene to distinct kinds of cancer in organs targeted by the syndrome.

"We showed that the mutations themselves play a critical role in driving the cancers that occur in certain organs in people with Cowden syndrome," says principal investigator Gustavo Leone, associate professor of molecular virology, immunology and medical genetics at the OSUCCC-James.

"Together, our findings demonstrate that specific inherited PTEN mutations have a strong influence in the variable predisposition to cancer of patients with Cowden syndrome."

The findings, published in the March 16 issue of the Proceedings of the National Academy of Sciences of the United States of America, suggest that testing for specific PTEN mutations might predict the kind and severity of cancer that will develop in people with the syndrome.

Furthermore, because PTEN is the second most commonly mutated gene in human cancer overall, the same mutations might predict severity in sporadic tumors, as well.

"Mutations in this gene also play a role in developmental disabilities and perhaps in autism, so this mouse model might be useful for studies in those conditions, as well," says co-principal investigator Michael Ostrowski, professor and chair of molecular and cellular biochemistry at Ohio State.

For this study, Leone, Ostrowski and their colleagues developed three strains of genetically identical mice, each of which had one of three specific PTEN mutations found in people with Cowden syndrome. This left each strain with a different version of the PTEN protein. The study showed that each version functioned in a different way, and each influenced cancer development to a different degree.

Mutation 1 disabled the protein altogether and often caused cancer in the animals, while mutation 2 produced a protein that was more active than the normal PTEN protein, and sometimes caused cancer. Mutation 3 altered the protein in ways that should have made it more cancer-causing but also made it more fragile, so less of the protein was present to cause problems. This mutation sometimes didn't cause cancer at all.

Using a database of more than 400 patients with Cowden syndrome, the researchers found that patients with these same mutations have cancer in the corresponding organs as the mice. The mice also showed equivalent gender differences in tumor development, with females developing more thyroid tumors, and males developing more adrenal gland and stomach tumors.

The researchers are now investigating why patients may experience differences in cancer severity even when they have the same mutation.

Funding from the National Cancer Institute, the American Cancer Society, the Susan Komen Foundation, the Evelyn Simmers Foundation, and the U.S. Department of Defense supported this research.

Leone is the recipient of the Pew Charitable Trusts Scholar Award and the Leukemia and Lymphoma Society Scholar Award.

Hormone replacement in joint fluid has potential regenerative effect

German researchers determined that concentrations of the sex hormones, testosterone in men and estrogen in women, may have a positive effect on the regenerative potential of cartilage tissue. The study suggests hormone replacement in the joint fluid of men and women might be beneficial in treating late stages of human osteoarthritis (OA) by regenerating damaged tissue. Details of this evidence-based study appear in the April issue of *Arthritis & Rheumatism*, a journal published by Wiley-Blackwell on behalf of the American College of Rheumatology.

Free moving (diarthrodial) joints, such as the knee and hip, produce smooth and painless limb movement when there is adequate transmission of forces between the bones and joint (articular) cartilage. Disturbances in joint architecture due to trauma, abnormal load, endocrine diseases (diabetes, hypothyroidism) or inflammatory conditions may result in OA. Worldwide estimates say 9.6% of men and 18% of women 60 years or older have OA symptoms and the World Health Organization (WHO) projects that by 2020, OA will be the fourth leading cause of disability.

Nicolai Miosge, M.D., Ph.D., and colleagues from the August University in Goettingen, Germany examined the regenerative potential of chondrogenic progenitor cells (CPCs) that are present in arthritic tissue during the late stages of OA. The research team speculated that these CPCs might be influenced by sex steroids, and therefore hormone replacement therapy directed to the joint fluid could be beneficial in restoring damaged tissue. Tissue samples from 372 patients who underwent total knee replacement were analyzed. The mean age was 71 years of age for men and 72 years for women, with women representing 64.25% of participants.

Estrogens are known to influence bone metabolism and researchers found that 17β -estradiol (E2), which increases calcium deposition in both sexes, was present in the joint fluid of study participants. CPCs positive for estrogen receptors (ER α and ER β) as well as androgen receptors were present in the OA tissue as well. Both estrogen and testosterone influenced the expression of all 3 receptor genes and the CPCs by regulating gene expression.

Researchers found late-stage OA cartilage populated with elongated cells that were not present in healthy connective tissue. Upon investigation of the elongated cells, the team identified a unique progenitor cell population (CPCs). "We were able to isolate CPCs in 95.48% of female patients and 96.97% of male patients, making these cells a good target for future therapeutic intervention for a very large number of OA patients," Dr. Miosge said. "Hormone replacement therapy in joint fluid may help mitigate the effects of OA and further investigation is needed," concluded Dr. Miosge.

*Article: "Sex Differences of Chondrogenic Progenitor Cells in Late Stages of Osteoarthritis." Sebastian Koelling and Nicolai Miosge. *Arthritis & Rheumatism*; Published Online: March 30, 2010 (DOI: 10.1002/art.27311); Print Issue Date: April 2010.*

Brain estrogen shows promise as schizophrenia treatment

An estrogenic drug that influences neurotransmitter and neuronal systems in the brain is showing promise as an effective therapy for women who suffer from schizophrenia. A study has found that Raloxifene - a synthetic estrogen currently used to treat osteoporosis - has beneficial effects on postmenopausal women with

schizophrenia, with a test group experiencing a more rapid recovery from psychotic and other symptoms compared to control groups.

Research project leader and Director of the Monash Alfred Psychiatry Research Centre (MAPrc) Professor Jayashri Kulkarni said women in the trial who were given 120mg a day of the unique selective estrogen receptor modulator had a significantly greater improvement in psychosis symptoms compared with those on placebos and lower doses. "The results were very promising. Under daily treatment with this 'brain estrogen', the women in the study had improvement in their key psychosis symptoms and also experienced enhanced memory and higher learning capacity," Professor Kulkarni said.

"Many patients in this study had longstanding, persistent schizophrenia, so we are delighted that they experienced improvements in their mental well-being. We will continue to investigate the efficacy of Raloxifene which is a currently available treatment for osteoporosis in postmenopausal women."

"Unlike estradiol, the standard estrogen found in the oral contraceptive pill or hormone replacement treatment, this type of estrogen did not have the side effects on breast, uterus and ovarian tissue that we worry about with other forms," Professor Kulkarni said.

While the findings were still tentative given the relatively small sample size, the research team is cautiously optimistic that ongoing trials will further confirm the positive therapeutic potential of the drug for postmenopausal women, and potentially for other cohorts.

Professor Kulkarni said the findings, published in *Psychoneuroendocrinology*, would offer hope to the hundreds of thousands of women in Australia who suffer from schizophrenia. "Our results indicate that this therapy really could revolutionise treatment options for women with schizophrenia. While at this stage we are just investigating its use in postmenopausal women, we are planning further research using hormone treatments in younger women and men suffering from psychotic illnesses," Professor Kulkarni said.

"One in five of us will experience a mental illness at some point in our lives. These conditions have a huge impact not only the sufferer, but on their families and Australian communities, so it is critical that governments and the private sector invest in research to develop effective treatment options."

Professor Kulkarni pioneered research into hormonal factors and treatments in psychosis after assessing epidemiological studies that indicated gender differences in the age and onset of schizophrenia, and from clinical observations that symptoms were more severe in women during premenstrual, perimenopausal and postnatal phases. The current study follows on from previous trials of estrogen and anti-estrogen treatment for women and men with a variety of mental illnesses.

Doctors report alarming increase in mumps-related testicle problems among young males

Urologists at a leading Irish hospital have reported an alarming increase in the number of teenage boys and young men developing mumps orchitis, in a paper published in the April issue of the urology journal BJUI.

They are urging colleagues to offer the MMR vaccine to unvaccinated males in the 15-24 age group and educate them about the condition, which causes one or both testicles to swell and can lead to fertility problems.

Mr Niall Davis, a Urology Research Registrar, teamed up with colleagues at the Mater Misericordiae University Hospital, Dublin, to carry out an extensive review of five decades' worth of research and statistics.

"Boys who did not receive the measles-mumps-rubella (MMR) vaccine during the mid 1990s are now collecting in large numbers in secondary schools and colleges and this provides a perfect breeding ground for the virus" he says. "It's estimated that as many as 40 per cent of males who develop mumps after puberty can suffer from orchitis. This is of considerable concern as epidemics of mumps orchitis are now being reported more frequently in many countries worldwide."

During the pre-vaccine era, mumps was most likely to affect children aged between five and seven, with epidemics happening every four to five years. Globally 290 cases per 100,000 population were diagnosed between 1977 and 1985. Since the introduction of the MMR in 1968, there has been a dramatic reduction in cases, with the USA reporting a 99 per cent fall.

But 15 years ago there was a global shortage of the MMR vaccine and media scares about links to autism, inflammatory bowel disease and Crohn's disease led to reduced uptake, despite subsequent reviews that concluded that such links did not exist.

In some urban parts of the UK, uptake fell from 91 per cent to 58 per cent and public concern linking MMR to autism still remains high.

"It is those unvaccinated boys that we are now seeing in our urology department" says Mr Davis. "It's estimated that as many as 42 per cent of patients with mumps experience at least one complication. As well as swollen testicles, these can include inflammation of the ovaries, aseptic meningitis, acute inflammation of the brain, deafness and pancreatitis.

"The recent resurgence in the disease means that a significant proportion of 15 to 24 year-olds living in heavily populated environments are affected."

Key findings of the review include:

* Up to 50 per cent of males with mumps orchitis will experience testicular atrophy, where one or both testicles reduce in size.

* Infertility is rare, but subfertility can occur in about 13 per cent of patients, even if their testicles have not reduced in size.

* Up to half of patients can experience abnormal sperm for up to three months after recovery and 24 per cent of adults and 38 per cent of adolescents can still have abnormal sperm up to three years after recovery.

* There appears to be a direct link between high levels of testicular swelling and increased sperm abnormalities.

* Mumps orchitis, with reduced testicular size, has been suggested as a risk factor for testicular cancer, but this association appears to be weak, with an incidence of 0.5%.

"Unvaccinated males in the 15-24 year-old age group are more susceptible to virus outbreaks and have a high risk of developing mumps orchitis and long-term fertility problems" concludes Mr Davis.

"It is important that clinicians are aware of this epidemiological shift and the resurgence of mumps orchitis. They also need to ensure that male patients in this high-risk group are vaccinated and educated about the risks and complications of the virus."

Notes to editors The increasing incidence of mumps orchitis: a comprehensive review. Davis et al. BJUI. 105, 1060-1065. (April 2010). DOI: 10.1111/j.1464-410X.2009.09148.x

The pill for ovarian cysts

Ovarian endometriomas, better known as ovarian 'chocolate' cysts for the brown liquid they contain, can be easily removed by surgery. However, recurrence is common, which can cause ongoing pain and complications. A study evaluated for Faculty of 1000 suggests a simple and effective remedy – the oral contraceptive pill (OCP).

In their F1000 evaluation, Neil Johnson and Shelley Reilly from Auckland, New Zealand, highlight a trial published in Fertility and Sterility that provides evidence that the OCP can reduce the reoccurrence of endometriomas after removal by surgery. They say, "this study is perhaps the only randomized controlled trial that has evaluated the effectiveness of the use of long-term postoperative OCP treatment to prevent endometrioma recurrence."

The trial consisted of 239 patients who had just undergone surgery to remove endometriomas and who were randomized into groups: those with no prescribed treatment, those taking cyclic OCPs, and those taking continuous OCPs. Patients were followed up for two years.

Women who took OCPs had significantly fewer recurring cysts. Previous studies of the effectiveness of OCPs after laparoscopic cystectomy have produced conflicting results. But long-term treatment seems to be the key: Johnson and Reilly say, "the length of treatment appears to play an important role in the efficacy of therapy".

Johnson and Reilly suggest an immediate change to current clinical practice: "If the use of an OCP is considered to reduce the risk of recurrence of an endometrioma after laparoscopic cystectomy, treatment should be given for at least two years".

Neil Johnson, Faculty Member for Faculty of 1000 Medicine, is an Associate Professor in the Department of Obstetrics and Gynaecology, National Women's Hospital, Auckland, New Zealand

<http://f1000medicine.com/about/biography/8985030752188126>

Shelley Reilly is a medical researcher at Auckland District Health Board, Auckland, New Zealand

<http://www.healthpoint.co.nz/default,137463.sm>

The full text of the evaluation of is available free for 90 days at: <http://f1000medicine.com/article/m46pcdr1chjzlxz/id/2164956>

An abstract of the original paper by Amsterdam et al. (Long-term cyclic and continuous oral contraceptive therapy and endometrioma recurrence: a randomized controlled trial) is at: <http://www.ncbi.nlm.nih.gov/sites/entrez/18973896?dopt=Abstract&holding=f1000,f1000m,isrctn>

Judge Invalidates Human Gene Patent

By JOHN SCHWARTZ and ANDREW POLLACK

A federal judge on Monday struck down patents on two genes linked to breast and ovarian cancer. The decision, if upheld, could throw into doubt the patents covering thousands of human genes and reshape the law of intellectual property

United States District Court Judge Robert W. Sweet issued the 152-page decision, which invalidated seven patents related to the genes BRCA1 and BRCA2, whose mutations have been associated with cancer.

The American Civil Liberties Union and the Public Patent Foundation at the Benjamin N. Cardozo School of Law in New York joined with individual patients and medical organizations to challenge the patents last May:

they argued that genes, products of nature, fall outside of the realm of things that can be patented. The patents, they argued, stifle research and innovation and limit testing options.

Myriad Genetics, the company that holds the patents with the University of Utah Research Foundation, asked the court to dismiss the case, claiming that the work of isolating the DNA from the body transforms it and makes it patentable. Such patents, it said, have been granted for decades; the Supreme Court upheld patents on living organisms in 1980. In fact, many in the patent field had predicted the courts would throw out the suit.

Judge Sweet, however, ruled that the patents were “improperly granted” because they involved a “law of nature.” He said that many critics of gene patents considered the idea that isolating a gene made it patentable “a ‘lawyer’s trick’ that circumvents the prohibition on the direct patenting of the DNA in our bodies but which, in practice, reaches the same result.”

The case could have far-reaching implications. About 20 percent of human genes have been patented, and multibillion-dollar industries have been built atop the intellectual property rights that the patents grant.

“If a decision like this were upheld, it would have a pretty significant impact on the future of medicine,” said Kenneth Chahine, a visiting law professor at the University of Utah who filed an amicus brief on the side of Myriad. He said that medicine was becoming more personalized, with genetic tests used not only to diagnose diseases but to determine which medicine was best for which patient.

Mr. Chahine, who once ran a biotechnology company, said the decision could also make it harder for young companies to raise money from investors. “The industry is going to have to get more creative about how to retain exclusivity and attract capital in the face of potentially weaker patent protection,” he said.

Edward Reines, a patent lawyer who represents biotechnology firms but was not involved in the case, said loss of patent protection could diminish the incentives for genetic research.

“The genetic tools to solve the major health problems of our time have not been found yet,” said Mr. Reines, who is with the Silicon Valley office of the firm Weil, Gotshal & Manges. “These are the discoveries we want to motivate by providing incentives to all the researchers out there.”

The lawsuit also challenged the patents on First Amendment grounds, but Judge Sweet ruled that because the issues in the case could be decided within patent law, the constitutional question need not be decided.

The decision is likely to be appealed. Representatives of Myriad did not return calls seeking comment. But this month, the company’s chief executive, Peter Meldrum, told investors that “regardless of the outcome of this particular lawsuit, it will not have a material adverse effect on the company,” or its future revenues, according to the Pharmacogenomics Reporter, “or on the future revenues of our products.”

Myriad sells a test costing more than \$3,000 that looks for mutations in the two genes to determine if a woman is at a high risk of getting breast cancer and ovarian cancer. Plaintiffs in the case had said Myriad’s monopoly on the test, conferred by the gene patents, kept prices high and prevented women from getting a confirmatory test from another laboratory.

Janice Oh, a spokeswoman for the United States attorney’s office in Manhattan, which represented the Patent and Trademark Office in the case, had no comment.

One of the individual plaintiffs in the suit, Genae Girard, who has breast cancer and has been tested for ovarian cancer, applauded the decision as “a big turning point for all women in the country that may have breast cancer that runs in their family.” Chris Hansen, an A.C.L.U. staff lawyer, said: “The human genome, like the structure of blood, air or water, was discovered, not created. There is an endless amount of information on genes that begs for further discovery, and gene patents put up unacceptable barriers to the free exchange of ideas.”

Bryan Roberts, a prominent Silicon Valley venture capitalist, said the decision could push more work aimed at discovering genes and diagnostic tests to universities. “The government is going to become the funder for content discovery because it’s going to be very hard to justify it outside of academia.”

John Ball, executive vice president of the American Society for Clinical Pathology, one of the plaintiffs in the case, called the decision “a big deal.”

“It’s good for patients and patient care, it’s good for science and scientists,” he said. “It really opens up things.”

Men owe women for 'creating beer'

One of man’s great pleasures might be a pint of beer at the local – but an expert has claimed it would never have existed without the entrepreneurial skills of women.

By Nick Britten

Jane Peyton, 48, an author, said women created beer and for thousands of years it was only they who were allowed to operate breweries and drink beer. The drink is now almost exclusively marketed to men - with television characters such as Homer Simpson the epitome of the beer-loving male. Miss Peyton has conducted extensive research into the origins of beer for a new book and reports that a woman's touch was found on beer throughout the ages.

Nearly 7,000 years ago in Mesopotamia and Sumeria, so important were their skills that they were the only ones allowed to brew the drink or run any taverns. And in almost all ancient societies beer was also then considered to be a gift from a goddess, never a male God.

Between the eighth and tenth centuries AD the Vikings spread terror by rampaging through Europe, fuelled by women-made ale. Women were the exclusive brewers in Norse society and all equipment by law remained their property. And Ancient Finland also credits the creation of beer to the fairer sex, with three women, a bear's saliva and wild honey the apparent first ingredients.



Between the eighth and tenth centuries AD the Vikings spread terror by rampaging through Europe, fuelled by women-made ale Photo: AP

In England ale was traditionally made in the home by women. They were known as brewsters or ale-wives and the sale of the drink provided a valuable income for many households. It quickly became an essential staple of the diet and even royalty indulged in the tasty beverage. Queen Elizabeth I, like most people of the era, consumed it for breakfast and at other times of the day. But by the start of the late 18th century and the Industrial Revolution, new methods of making beer meant women's contribution slowly started to decline and be forgotten, until now.

Miss Peyton said: "I know men will be absolutely stunned to find this out, but they've got women to thank for beer."

Motivation by Anticipation: Expecting Rapid Feedback Enhances Performance

There are a number of factors that influence how well we do in school, including the amount of time we study and our interest in a subject. Now, according to new findings in Psychological Science, a journal of the Association for Psychological Science, how quickly we expect to receive our grades may also influence how we perform.

Psychological scientists Keri L. Kettle and Gerald Häubl of the University of Alberta in Canada wanted to investigate how the timing of expected feedback impacts individuals' performance. For this experiment, they recruited students enrolled in a class that required each student to give a 4-minute oral presentation. The presentations were rated by classmates on a scale from 0 (poor) to 10 (excellent) and the average of these ratings formed the presenter's grade for that part of the course. Students received an email 1 day, 8 days, or 15 days before their presentation and were invited to participate in this research study. Students agreeing to volunteer in the study were informed when they would receive feedback on their presentation and were asked to predict their grades. Participating students were randomly assigned to a specific amount of anticipated feedback delay, which ranged from 0 (same day) to 17 days.

The results reveal a very interesting relationship between how soon the students expected to receive their grades and their performance: Students who were told they would receive feedback quickly on their performance earned higher grades than students who expected feedback at a later time. Furthermore, when students expected to receive their grades quickly, they predicted that their performance would be worse than students who were to receive feedback later. This pattern suggests that anticipating rapid feedback may improve performance because the threat of disappointment is more prominent. As the authors note, "People do best precisely when their predictions about their own performance are least optimistic."

Although this experiment took place in a classroom, the authors conclude that these findings "have important practical implications for all individuals who are responsible for mentoring and for evaluating the performance of others."

U Alberta find could shield humans from influenza virus

A University of Alberta-led research team has discovered an influenza detector gene that could potentially prevent the transmission of the virus to humans

Edmonton A University of Alberta-led research team has discovered an influenza detector gene that could potentially prevent the transmission of the virus to humans.

Katharine Magor, a U of A associate professor of biology, has identified the genetic detector that allows ducks to live, unharmed, as the host of influenza. The duck's virus detector gene, called retinoic acid inducible gene - I, or RIG-I, enables a duck's immune system to contain the virus, which typically spreads from ducks to chickens, where it mutates and can evolve to be a human threat like the H5N1 influenza virus. The first human H5N1 cases were in Hong Kong in 1997. Eighteen people with close contact to chickens became infected and six died.

Magor's research shows chickens do not have a RIG-I gene. A healthy chicken can die within 18 hours after infection, but researchers have successfully transferred the RIG-I gene from ducks to chicken cells. The chicken's defenses against influenza were augmented and RIG-I reduced viral replication by half.

One potential application of this research could affect the worldwide poultry industry by production of an influenza-resistant chicken created by transgenesis.

The work of Katharine Magor, her U of A PhD candidate Megan Barber, and researchers from the United States (Jerry Aldridge and Robert Webster) was published March 22, in the online, early edition of Proceedings from the National Academy of Sciences.

Magnets 'can modify our morality'

Scientists have shown they can change people's moral judgements by disrupting a specific area of the brain with magnetic pulses.

They identified a region of the brain just above and behind the right ear which appears to control morality. And by using magnetic pulses to block cell activity they impaired volunteers' notion of right and wrong. The small Massachusetts Institute of Technology study appears in Proceedings of the National Academy of Sciences.

Lead researcher Dr Liane Young said: "You think of morality as being a really high-level behaviour. "To be able to apply a magnetic field to a specific brain region and change people's moral judgments is really astonishing."

The key area of the brain is a knot of nerve cells known as the right temporo-parietal junction (RTPJ). The researchers subjected 20 volunteers to a number of tests designed to assess their notions of right and wrong.

In one scenario participants were asked how acceptable it was for a man to let his girlfriend walk across a bridge he knew to be unsafe. After receiving a 500 millisecond magnetic pulse to the scalp, the volunteers delivered verdicts based on outcome rather than moral principle. If the girlfriend made it across the bridge safely, her boyfriend was not seen as having done anything wrong.

In effect, they were unable to make moral judgments that require an understanding of other people's intentions. Previous work has shown the RTPJ to be highly active when people think about the thoughts and beliefs of others.

Electric currents

The MIT team pinpointed the region in volunteers using a sophisticated functional magnetic resonance imaging (fMRI) brain scan. They then targeted the area using a technique called transcranial magnetic stimulation (TMS) to create weak electric currents that temporarily stop brain cells working normally.

In one test, volunteers were exposed to TMS for 25 minutes before reading stories involving morally questionable characters, and being asked to judge their actions. In a second experiment, volunteers were subjected to a much shorter 500 millisecond TMS burst while being asked to make a moral judgement.

In both cases, the researchers found that when the RTPJ was disrupted volunteers were more likely to judge actions solely on the basis of whether they caused harm - not whether they were morally wrong in themselves.

Morally dubious acts with a "happy" ending were often deemed acceptable.

Sarah-Jayne Blakemore, a brain expert at University College London, said the findings were insightful.

"The study suggests that this region - the RTPJ - is necessary for moral reasoning. "What is interesting is that this is a region that is very late developing - into adolescence and beyond right into the 20s. "The next step would be to look at how or whether moral development changes through childhood into adulthood."

Runaway star may have spawned the solar system

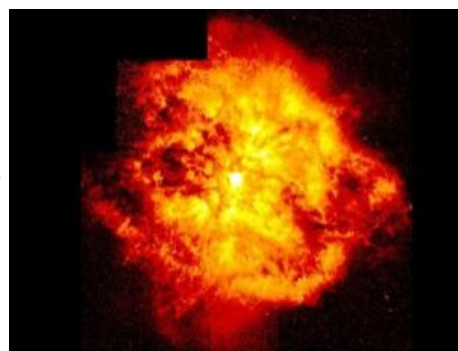
* 04:02 31 March 2010 by Rachel Courtland

The solar system may have been born inside the remains of a single star that ran away from its family, rather than from a tight-knit clan of stars. If so, it may be more unusual than previously thought.

Meteorites that contain bits of rock called calcium-aluminium-rich inclusions suggest that the solar system may have formed very quickly from the ashes of other stars. That's because the inclusions formed with the radioactive isotope aluminium-26, which is forged inside stars tens of times as massive as the sun and decays with a half-life of only 720,000 years.

Such massive stars tend to form in clusters, and they shed material in roiling winds that can cool down and seed planetary systems.

The solar system may have formed from the ashes of a massive star like WR124 (pictured), which is shedding vast amounts of material in winds (Image: Y. Grosdidier et al./WFPC2/HST/NASA)



Too hot

But Vincent Tatischeff of the National Center for Scientific Research in Orsay, France, and colleagues suspect a massive star cluster would have been so hot that most of the Al-26 would have decayed before planets could congeal. Instead, they suggest the solar system sprang from a solitary star's ashes, which could have cooled more quickly. To account for the amount of Al-26 observed in meteorites, the star would still have had to be massive, meaning it probably formed in a clutch of other stars.

At some point, it may have been flung out of its birth cluster by gravitational tussles with its siblings or the explosion of a companion. "The scenario may look complicated, but we think it is the most likely origin of the aluminium-26 in the solar system," Tatischeff says.

Ocean worlds

As it zipped through interstellar space, the star would have released Al-26 in winds, forming a shell of material around it. When the star later exploded, its remains would have slammed into this shell, creating a turbulent region with areas dense enough for the sun to form.

Tatischeff says most of the galaxy's planetary systems may not have formed as quickly as ours, since many probably arose from clusters. This makes them likely to have lower levels of Al-26, which generates heat as it decays. The cooler temperatures may have led rocky planets to take a different evolutionary path to Earth, perhaps becoming ocean worlds.

Eric Gaidos of the University of Hawaii at Manoa did preliminary work on the possibility of a runaway star parent last year, but says the single-star scenario still has trouble explaining how hot gas from the star could mix with surrounding material efficiently enough to form the solar system quickly. "We have yet to deal with the really tough nuts that have to be cracked," Gaidos says.

Journal reference: Astrophysical Journal Letters (forthcoming)

Making the blind see: Gene therapy restores vision in mice

New research in the FASEB Journal shows that nucleic acid nanoparticle platform delivery technology achieves successful gene transfer and reverses effects of retinitis pigmentosa in mice

Take a look at this: Scientists from Buffalo, Cleveland, and Oklahoma City made a huge step toward making the blind see, and they did it by using a form of gene therapy that does not involve the use of modified viruses.

In a research report published in the April 2010 print issue of The FASEB Journal (<http://www.fasebj.org>), scientists describe how they used a non-viral, synthetic nanoparticle carrier to improve and save the sight of mice with retinitis pigmentosa, an inherited disease characterized by progressive vision loss and eventual blindness.

"We hope the results of our study will be instrumental in generating a cure for the debilitating blindness associated with retinitis pigmentosa and other inherited and acquired retinal diseases," said Muna I. Naash, Ph.D., a researcher involved in the work from the Department of Cell Biology at the University of Oklahoma Health Sciences Center in Oklahoma City. "Compacted DNA nanoparticles are an exciting treatment strategy for these diseases and we look forward to exciting new developments."

To make this discovery, Naash and colleagues used groups of mice with the retinal degeneration slow (Rds) gene, which causes retinitis pigmentosa. The mice received one of three types of "treatments:" nanoparticles containing the normal copy of the Rds gene, the normal gene alone, or saline solution. After these treatments were delivered to the mice, the structure and function of the retina were analyzed by comparing them to untreated mice with retinitis pigmentosa and healthy mice with the normal Rds gene.

Researchers also measured the level and pattern of Rds gene expression, as well as functional, structural and biochemical improvements in disease symptoms. They discovered that mice receiving the nanoparticle gene therapy show significant signs of healing. These mice had structural improvement in their retinas, as well as functional vision improvements, which lasted throughout the duration of the study. The mice that received the gene alone or saline continued to lose their vision. The nanoparticles were safe and well-tolerated with no adverse effects.

"Making the blind see was once called a miracle," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "As we have expanded our understanding of evolution, genetics, and nanotechnology, chances are that "miraculous" cures will become as commonplace as those claimed by faith-healers past and present."

According to the National Institutes of Health Office of Rare Diseases Research, retinitis pigmentosa is a group of inherited eye diseases that affect the retina. Retinitis pigmentosa causes cells in the retina to die prematurely, eventually leading to vision loss. There is no cure.

Researchers Report Progress on E. Coli Test

By HENRY FOUNTAIN

It's not the pathogenic E. coli microbe itself that harms people who eat ground beef or other foods that contain it. Rather, it's the toxins that E. coli produces that do the actual damage. Proper testing of food should look for both, though, since it is possible for one to be present without the other.

That usually means two separate tests. But now scientists with the Agricultural Research Service of the United States Department of Agriculture report significant advances toward a single test that can detect both pathogenic E. coli and its toxins.

J. Mark Carter, leader of a research unit at the research service's office in Albany, Calif., said the test, described last week at the annual meeting of the American Chemical Society, uses tiny polystyrene beads that are coated with antibodies for the proteins found on the bacteria and two of the major toxins it produces. The beads are mixed with a sample of ground beef that has been further chopped up in a blender, and then separated from the sample and analyzed.

Dr. Carter said that in addition to its two-in-one nature, the test is also quicker than current E. coli tests, with results in less than 24 hours rather than about a week. In addition to ground beef, he said, it could be used on lettuce and other vegetables. More work is required, but the plan is to have a commercialized test in a few years that could be used by governments and the food industry itself.

Impaired brain connections traced to schizophrenia mutation

Like patients, engineered mice falter at working memory tasks

The strongest known recurrent genetic cause of schizophrenia impairs communications between the brain's decision-making and memory hubs, resulting in working memory deficits, according to a study in mice.

"For the first time, we have a powerful animal model that shows us how genetics affects brain circuitry, at the level of single neurons, to produce a learning and memory deficit linked to schizophrenia," explained Thomas R. Insel, M.D., director of the National Institute of Mental Health (NIMH), part of the National Institutes of Health. "This new research tool holds promise for ultimately unraveling the underlying anatomical connections and specific genes involved."

NIMH grantees Joshua Gordon, M.D., Ph.D., Joseph Gogos, M.D., Ph.D., Maria Karayiorgou, M.D., and Columbia University colleagues, report on their discovery in genetically engineered mice in the April 1, 2010 issue of the journal *Nature*. "Our findings pinpoint a specific circuit and mechanism by which a mutation produces a core feature of the disorder," said Gordon, who led the research.

Researchers have suspected such a brain connectivity disturbance in schizophrenia for more than a century, and the NIH has launched a new initiative on the brain's functional circuitry, or connectome. Although the disorder is thought to be 70 percent heritable, its genetics are dauntingly complex, except in certain rare cases, such as those traced to the mutation in question.

Prior to this study, neuroimaging studies in schizophrenia patients had found abnormal connections between the brain's prefrontal cortex, the executive hub, and the hippocampus, the memory hub, linked to impaired working memory. It was also known that a mutation in the suspect site on chromosome 22, called 22q11.2, boosts schizophrenia risk 30-fold and also causes other abnormalities). Although accounting for only a small portion of cases, this tiny missing section of genetic material, called a microdeletion, has repeatedly turned up in genetic studies of schizophrenia and is an indisputable risk factor for the illness.

Still, the mutation's link to the disturbed connectivity and working memory deficit eluded detection until now.

To explore the mutation's effects on brain circuitry, Gogos, Karayiorgou and colleagues engineered a line of mice expressing the same missing segment of genetic material as the patients. Strikingly, like their human counterparts with schizophrenia, these animals turned out to have difficulty with working memory tasks – holding information in mind from moment to moment.

Successful performance of such tasks depends on good connections in a circuit linking the prefrontal cortex and the hippocampus. To measure such functional connections, Gordon and colleagues monitored signals emitted by single neurons implanted in the two distant brain structures while mice performed a working memory task in a T-maze (see below).

The more in-sync the neurons from the two areas fired, the better the functional connections between the two structures – and the better the mice performed the task. Moreover, the better the synchrony to start with, the quicker the animals learned the task. The more synchrony improved, the better they performed.

As suspected, the mice with the chromosome 22 mutation faltered on all counts -- showing much worse synchrony, learning and performance levels than control mice.

"Our results extend beyond those in patients by showing how an undeniable genetic risk factor for schizophrenia can disrupt connectivity at the level of single neurons," explained Gordon.

The researchers plan to follow up with studies into how the mutation affects brain anatomical and molecular connections and the workings of affected genes.

The research was also funded by the Simons Foundation.

Reference: Impaired hippocampal-prefrontal synchrony in a genetic mouse model of schizophrenia. Sigurdsson T, Stark KL, Karayiorgou M, Gogos JA, Gordon JA. Nature. 2010 April 1.

More than one-quarter of elderly lack decision-making capacity at death

First large-scale study shows that those with advance directives got care they wanted, according to research published in the New England Journal of Medicine

Ann Arbor, Mich. - More than one in four elderly Americans lacked the capacity to make their own medical care decisions at the end of life, according to a study of 3,746 people to be published April 1 in the New England Journal of Medicine.

Those who had advance directives - including living wills or durable powers of attorney for healthcare - received the care they wanted most of the time, says lead author Maria Silveira, M.D., M.P.H., physician scientist at the VA Ann Arbor Healthcare System's Clinical Management Research and assistant professor of Internal Medicine at the University of Michigan.

"Prior to our study, no one knew how many elderly adults might need others to make complex medical decisions on their behalf at the end of life," says Silveira. "Our research shows that a substantial number of older adults need someone else to make decisions about whether aggressive, limited, or comfort care should be provided at the end of life. This study underscores the need to prepare oneself and one's family for the often emotional and difficult medical decisions that can arise at the end of life. It also suggests that the time spent to craft a living will and appoint a durable power of attorney for health care can be worthwhile."

Advance directives usually document patients' wishes for life-sustaining treatment in a living will, as well as their choice of a proxy decision-maker in a durable power of attorney for health care. Advance directives are sanctioned in all 50 states and can be completed for free without the aid of an attorney.

(Silveira recommends [this site](#).)

Still, "There is a lot of myth and misunderstanding about advance directives," Silveira says.

For example, many people do not understand that advance directives are used only when patients can't make medical care decisions for themselves, and they can be revoked by the patient at any time, either in writing or orally. Advance directives are frequently confused with wills and durable powers of attorney - which have no bearing on medical care decisions.

Of the subjects studied, 61 percent had advance directives. Of those, more than 90 percent requested either limited or comfort care at the end of life. Among those who needed decisions made, but couldn't make them themselves, 83% who had requested limited care and 97% who had requested comfort care, received the care that was in line with their wishes, Silveira says.

The study subjects were elderly Americans living at home or in facilities across the US who died between 2000 and 2006 and participated in the Health and Retirement Study, a national longitudinal study conducted at the University of Michigan's Institute for Social Research and funded by the National Institute on Aging.

"Folks with a living will or durable power of attorney for health care were less likely to die in a hospital or to get aggressive care -- but that is what most of them wanted," she says.

One interesting finding suggests the importance of having both a living will as well as an appointed surrogate decision-maker. The study showed that among the handful of subjects who indicated a preference for aggressive care, half did not receive it. "Given this, some might conclude that advance directives are used to deny wanted health care, but our study showed that a preference for aggressive care had a very strong association with receiving such care, when compared to those who did not state a preference for it. It's just that at the end of life, aggressive treatment is often not an option; limited care and comfort care are always an option," Silveira says.

Silveira says many patients expect their physicians to start the conversation about end of life care and advance directives, and that physicians should be supported in their attempts to do so. The recent effort to provide Medicare reimbursement for periodic end-of-life discussions was a good start, she says.

"The health care system should ensure that providers have the time, space, and reimbursement to conduct the complex and time-consuming discussions necessary to plan appropriately for the end of life. Most elderly patients want and expect this," she says.

Co-authoring the study were Kenneth M. Langa, M.D., Ph.D., professor of in the Department of Internal Medicine at the University of Michigan, core investigator with VA Ann Arbor Healthcare System's Clinical Management Research, and professor of Health Management and Policy in U-M's School of Public Health and Scott Y.H. Kim, M.D., Ph.D., associate professor of Psychiatry and an investigator in the Bioethics Program and Center for Behavioral and Decision Sciences in Medicine at the University of Michigan.

Mathematics of ancient carvings reveals lost language

* 11:24 01 April 2010 by **Kate Ravilious**

Elaborate symbols and ornate depictions of animals carved in stone by an ancient Scottish people have given up their secret – to mathematics. Statistical analysis reveals that the shapes are a forgotten written language. The method could help interpret many other enigmatic scripts – and even analyse animal communication.

Conventional statistical methods for analysing scripts calculate the entropy or "orderedness" of the symbols: Shakespeare's prose would have a higher entropy than Egyptian hieroglyphs or Morse code, for example. However, such analysis only works for datasets large enough to capture most of the vocabulary in a language.

To overcome this problem, Rob Lee of the University of Exeter, UK, and colleagues have devised a way to compare small undeciphered scripts with known texts. The team compared symbols created by the Picts – a Scottish Iron Age society that flourished from the fourth to the ninth centuries AD – with over 400 known ancient and modern language texts.

Number crunching

They standardise the texts by calculating their ratio of paired characters to single characters. They then insert this term into a two-stage calculation. The first stage measures how repetitive a script is: Pictish turned out to be much less repetitive than pictorial scripts and codes, strongly indicating that it was a written language, rather than religious imagery or heraldic arms as has been speculated in the past.

The next part of the calculation reveals the difference between words, syllables and letters. Pictish symbols that were contrasted with texts analysed at the level of whole words were found to be comparable to a modern language with a small vocabulary. "It's equivalent to the language used in the 'Janet and John' learning-to-read books," says Lee.

The meaning of the Pictish words is still a mystery, but the researchers suspect the stones are memorials to the dead. Contemporary stones carved in Old English and Latin have been found across the UK.

Unlocking other languages

Katherine Forsyth, an expert on Pictish symbols at the University of Glasgow, is delighted with the findings. "It confirms exactly what I have deduced, but uses a rigorous and context-free method to do so," she says.

Rajesh Rao of the University of Washington in Seattle is also enthusiastic. Last year he used entropy analysis to study the undeciphered script of the ancient Indus valley civilisation and concluded that it was a written language. Now he has applied the new technique to his Indus data. "[Lee and colleagues'] method predicts that the Indus symbols represent words rather than heraldic or political symbols, which is consistent with our earlier work suggesting that the Indus script represents language," he says.

Lee and his colleagues are now keen to analyse other undeciphered ancient scripts, such as the "cup and ring" marks from the northern UK and Bronze Age petroglyphs from Scandinavia.

They think the technique could also be adapted to analyse animal communication, assessing how much meaning dolphins can convey with their whistles, for example.

Journal references: Rao, Science, DOI: 10.1126/science.1170391; Lee, Proceedings of the Royal Society A, DOI: 10.1098/rspa.2010.0041

Donor Kidneys From Hepatitis C Patients Needlessly Denied To Patients With That Infection

Johns Hopkins study shows hepatitis C-positive organs pointlessly discarded

More than half of donor kidneys in the United States infected with hepatitis C are thrown away, despite the need among hepatitis C patients who may die waiting for an infection-free organ, Johns Hopkins research suggests.

In a study of national data published online in the American Journal of Transplantation, the researchers say that while outcomes are slightly worse when hepatitis C-positive patients receive hepatitis C-positive organs, the advantages of more timely transplants may outweigh the risk of waiting - perhaps more than year - for a hepatitis C-negative kidney.

Patients with hepatitis C-positive make up about 12 percent of the population with kidney failure, and those patients have an increased risk of death on dialysis compared with those without the virus, the study says.

"Nationwide, kidneys from infected donors are inappropriately thrown out and denied to patients in need," says transplant surgeon Dorry L. Segev, M.D., Ph.D., an associate professor of surgery at the Johns Hopkins University School of Medicine and the study's leader. "Many transplant centers don't use these kidneys at all,



Riders and horn blowers appear next to hunting dogs on what is called the Hilton of Cadboll stone, pictured here.

Rob Knell and Rob Lee

effectively consigning hepatitis C-positive patients to an average unnecessary wait of a year longer for an uninfected organ.”

That, he says, “means an extra year on dialysis, in which the risk of death is 10 to 15 percent.”

The use of hepatitis C-positive kidneys has been controversial in the past, owing in part to a 1 percent difference in one-year survival for patients who receive the infected kidneys and a 2 percent difference in three-year survival. Segev says this difference “is easily made up for by getting off dialysis sooner.”

Hepatitis C-positive kidneys rarely go to hepatitis C-negative patients because the organ would infect the recipient with the chronic liver disease.

In looking at data from more than 93,000 deceased kidney donors between 1995 and 2009, Segev and his colleagues found that hepatitis C-positive kidneys were two and a half times more likely to be discarded than hepatitis C-negative kidneys. Since 1995, more than 3,500 hepatitis C-positive kidneys were thrown away.

“That’s a lot of kidneys we could have transplanted into people who need them,” Segev says.

Meanwhile, he adds, some 4,800 hepatitis C patients got hepatitis C-negative kidneys. “Using hepatitis C-positive kidneys in people who are infected with the virus could help those with hepatitis C and also expand the organ supply for everyone.” One-third of the nation’s transplant centers, according to the study, did not use any hepatitis C-positive kidneys for their hepatitis C patients, while 13 percent transplanted more than half of their hepatitis C patients with hepatitis C-positive kidneys.

At The Johns Hopkins Hospital, where doctors specialize in patients with hepatitis C and kidney failure, a patient with hepatitis C could likely be successfully transplanted with a hepatitis C-positive kidney within several months of being put on the waiting list, Segev says. Recipients of hepatitis C-positive kidneys waited, on average, 395 days less than those recipients who waited for hepatitis C-negative kidneys at the same transplant center, the study shows.

Other Johns Hopkins researchers on the study include Lauren M. Kucirka, Sc.M.; Andrew L. Singer, M.D., Ph.D.; R. Loris Ros, Sc.M.; Robert A. Montgomery, M.D., Ph.D.; and Nabil N. Dagher, M.D.

For more information: <http://www.hopkinsmedicine.org/transplant/About/Segev.html>

<http://www.hopkinsmedicine.org/transplant/>

U of I scientist says slimming soybeans are on the horizon

URBANA – If you're serious about losing weight, check out recent studies done in Elvira de Mejia's University of Illinois laboratory. Her research provides insight into the way a certain type of soy protein inhibits fat accumulation and reduces inflammation.

"We found that soybeans rich in beta-conglycinins limit lipid accumulation in fat cells by inhibiting an enzyme called fatty acid synthase. What's more, we have identified the specific peptides (digested proteins) that do this, and we are now beginning to understand the mechanism behind it. This is exciting research because it could lead to the development of nutraceuticals to fight obesity," said de Mejia, a U of I associate professor of food science and human nutrition.

The study was also the first to establish the anti-inflammatory properties of soy high in this type of protein. "The peptides fight inflammation by blocking key enzymes in the body's immune response," said the scientist.

de Mejia said that soy contains, among others, two types of protein, glycinins and beta-conglycinins, and the most important factor influencing a soy cultivar's healthful effects is the proportion in which they occur. Her research shows that soy that is low in glycinins and high in beta-conglycinins is preferred for its ability to inhibit lipid accumulation and inflammation.

"Using the latest molecular marker-assisted breeding techniques, soybeans with the right composition can be tagged and later identified using a simple leaf tissue sample. This would make it possible to create high-yielding cultivars that contained the 'slimming' trait for soybean farmers to grow in their fields," she said.

How did de Mejia discover that certain soybeans had this slimming effect? She had learned from her previous research that administration of soy protein caused weight loss in laboratory rats, but she wanted to know exactly why it happened.

She incubated human fat cells in the lab, treated them with soy hydrolysates from 15 soy genotypes containing varying amounts of beta-conglycinin, and then measured the amount of fat that accumulated.

"As we increased the concentration of beta-conglycinin, we saw more inhibition of lipids and less accumulation of fat.

Further testing showed that this occurred because fatty acid synthase, an enzyme responsible for synthesizing lipids, had been suppressed. "We also found that fat cells exposed to digests made from the 'slimming' soybeans increased the synthesis of adiponectin, a hormone that enhances insulin sensitivity and fat metabolism," she said.

She then compared the activity of beta-conglycinins with glycinins and found that hydrolysates from beta-conglycinins inhibited almost 50 percent of lipid accumulation in the fat cells. Glycinins did not inhibit lipid accumulation at all, she said.

In a separate study, her team identified specific soy peptides that inhibit fatty acid synthase, and they were able to learn exactly how it happens. de Mejia and her colleagues are now taking their research a step further by performing human trials with soy milk that is high in beta-conglycinins.

"For years we've known that soy protein is a good source of essential amino acids. Soy helps us maintain muscle mass, and its peptides make people feel full so they don't eat as much," she said.

"Now it appears that products made from soybeans selected for this particular protein profile may also help limit fat accumulation. Food manufacturers will be able to create soy products targeted at consumers who are trying to maintain their ideal weight," she said.

The first study appeared in a recent issue of Molecular Nutrition and Food Research. Cristina Martinez-Villaluenga and Vermont P. Dia of the University of Illinois, Mark Berhow of the Agricultural Research Service, and Neal A. Bringe of The Monsanto Company are co-authors.

It was supported by Monsanto, whose geneticists provided the 15 soy genotypes; the USDA Cooperative State Research, Education and Extension Service (CSREES); and a Marie Curie International Outgoing Fellowship for Career Development. The study that identifies the specific peptides and the mechanism by which they inhibit fatty acid synthase appears in FEBS Journal 277:1481, 2010. Co-authors are the U of I's Cristina Martinez-Villaluenga, Sanjeewa G. Rupasinghe, and Mary A. Schuler. Funding was provided by the USDA CSREES Future Foods Illinois initiative; the Illinois Soybean Association; and a Marie Curie fellowship.

A drug that extends life span prevents Alzheimer's deficits Rapamycin proves mettle in second model of memory-robbing disease

San Antonio - If research results continue to be repeated and are turned into clinical trials, a drug already approved for some uses could be marshaled - sooner than we expect - to prevent Alzheimer's disease in humans and improve health to the end of life.

A few weeks after a report that rapamycin, a drug that extends lifespan in mice and that is currently used in transplant patients, curbed the effects of Alzheimer's disease in mice, a second group is announcing similar results in an entirely different mouse model of early Alzheimer's.

Both reports are from The University of Texas Health Science Center at San Antonio, where the rapamycin studies are conducted in the Sam and Ann Barshop Institute for Longevity and Aging Studies and in basic science departments.

The second report, released April 1 by the journal PLoS ONE, published by the Public Library of Science, showed that administration of rapamycin improved learning and memory in a strain of mice engineered to develop Alzheimer's. The improvements in learning and memory were detected in a water maze activity test that is designed to measure learning and spatial memory. The improvements in learning and memory correlated with lower damage in brain tissue.

Less sticky

"Rapamycin treatment lowered levels of amyloid-beta-42, a major toxic species of molecules in Alzheimer's disease," said Veronica Galvan, Ph.D., assistant professor from the Barshop Institute and the Department of Physiology. "These molecules, which stick to each other, are suspected to play a key role in the early memory failure of Alzheimer's."

This strain of mice has been engineered to have defects in the genes that make amyloid precursor protein, ultimately resulting in the abnormal accumulation of amyloid-beta-42 that dampens synaptic connections. Synapses are junctions where neurons communicate with each other, providing the essential "wiring" for normal function of the brain. Without this communication, neurons die, leading to the memory losses seen in Alzheimer's.

Longer life for mice

In July 2009, Barshop Institute researchers and colleagues at two other institutions reported that microencapsulated rapamycin extended the life span of mice, possibly by delaying aging. A bacterial product first isolated from soil of Easter Island, rapamycin is approved by the U.S. Food & Drug Administration to prevent organ rejection in transplant patients. Rapamycin is the first pharmacologic intervention shown to extend life in an animal model of aging.

If rapamycin treatment indeed delays aging in mice, are age-associated diseases, such as Alzheimer's, delayed or blocked? The new study, authored by Spilman et al, sought to answer this question. In the study, the same rapamycin-supplemented diet as in the life span study was fed to groups of the Alzheimer's-susceptible mice and their normal littermates. A non-rapamycin diet was fed to control groups. Rapamycin feeding began at

4 months of age, when the susceptible mice show high amyloid-beta-42 levels and synaptic dysfunction, but do not yet have amyloid beta plaques or spatial memory impairments.

Get out of the water

After 13 weeks of treatment, all groups were trained in the water maze exercise to see how quickly they could learn to exit the water via a hidden platform. Doing so requires the use of spatial cues, such as patterned posters or photos, positioned all around the water tank. The Alzheimer's model mice that were fed the control diet predictably showed significant losses in learning and memory and reduced performance.

"Strikingly, the Alzheimer's mice treated with rapamycin displayed improved performance on the maze, even reaching levels that were indistinguishable from their normal littermates," Dr. Galvan said. "Levels of amyloid-beta-42 were also reduced in these mice after treatment, and we are seeing preserved numbers of synaptic elements in the brain areas of Alzheimer's disease mice that are ravaged by the disease process."

Intriguingly, differences in resistance to swimming in the middle of the pool (a measure of anxiety) and in floating (a measure of hopelessness) were not observed among groups. "This suggests that improved performance in rapamycin-treated, Alzheimer's-susceptible mice is a result of effects on purely cognitive processes but is not due to effects related to non-cognitive components of behavior, such as helplessness and anxiety," Dr. Galvan said.

Changing a toxic process

"The fact that we are seeing identical results in two vastly different mouse models of Alzheimer's disease," Dr. Galvan added, in reference to the recent study by Caccamo et al, "provides robust evidence that rapamycin treatment is effective and is acting by changing a basic pathogenic process of Alzheimer's that is common to both mouse models. This suggests that it may be an effective treatment for Alzheimer's in humans, who also have very diverse genetic makeup and life histories."

Grants from the Alzheimer's Association and the National Institute on Aging supported the study. Co-authors are Drs. Patricia Spilman, Natalia Podlutskaya, Matthew J. Hart, Jayanta Debnath, Olivia Gorostiza, Dale Bredesen, Arlan G. Richardson, Randy Strong and Veronica Galvan. Collaborating institutions are the UT Health Science Center San Antonio (Barshop Institute, departments of Physiology, Pharmacology, Cellular and Structural Biology, and Molecular Medicine); the South Texas Veterans Health Care System (Geriatric Research, Education and Clinical Center and Research Service); the University of California, San Francisco (Department of Pathology); and the Buck Institute for Age Research, Novato, Calif.

'Pig sushi' diabetes trial brings xenotransplant hope

* 17:01 01 April 2010 by **Wendy Zukerman**

Four more people with diabetes will soon be implanted with high doses of living pig cells coated in seaweed, bringing the prospect of widespread animal-to-human transplants a step closer.

Several people in New Zealand and Russia with type 1 diabetes have already received the "pig sushi", known as Diabecell, and now New Zealand company Living Cell Technologies (LCT) has received approval from the country's health authorities to begin phase II human trials on the implants.

Type 1 diabetes occurs when insulin-producing cells in the pancreas called islets are destroyed. People with the disease must have daily insulin injections to normalise their blood glucose levels.

But this causes blood glucose levels to yo-yo, which can lead to cardiovascular and nervous system complications, shortening the lifespan of sufferers by a third, according to Bob Elliott, LCT's medical director.

Seaweed diffusion

LCT's treatment uses islet cells taken from pigs to replace the cells missing from a person with diabetes. The pig islets are surgically implanted into a patient's abdomen, from where they secrete insulin throughout the body.

To avoid immune rejection, the pig cells are coated in alginate, a substance found in seaweed that prevents immune-system cells from touching – and so recognising and attacking - the alien islets. "So immunosuppressant drugs aren't needed after implantation," says Elliott. However, the alginate allows nutrients and glucose to diffuse into the islets, and insulin to diffuse out, so the cells can do their job.

In the earlier phase I trials, four people with type 1 diabetes who suffered from "hypoglycaemic unawareness" – in other words, they didn't notice when their blood sugar levels became dangerously low – were implanted with a few of the cells. "In one patient, the implants reduced their daily insulin dose by 25 per cent, and hypoglycaemic unawareness disappeared," says Elliott. The other three are being monitored, and Elliott says "results look very satisfying".

Research is further ahead in Russia, where LCT began trials of Diabecell in 2007. Five patients have since been given higher doses and are successfully responding.

Cold pigs

According to Elliott, there are not enough human islet cells available to treat the 20 to 30 million people who suffer from diabetes type 1 worldwide, so porcine islets are the best alternative.

To minimise the risk of transmitting porcine diseases into humans, LCT uses cells from pigs of Auckland Island in the Southern Ocean south of New Zealand. "They have lived in isolation for 200 years and are remarkably free of any form of organism that can infect humans," says Elliott.

LCT's trial is the most promising research in the area, says Peter Cowan from St Vincent's University Hospital in Melbourne, Australia, who also researches pig islets for diabetes treatment, but was not involved in this work. But, he says, the results "are quite preliminary, and demonstration of longer-term function of the islet implants will be critical", he says.

LCT implanted similar capsules in a patient in 1996: although those pig cells are still alive, few continue to produce insulin.

How your brain remembers the future

IT'S like remembering the future. Our brain generates predictions of likely visual inputs so it can focus on dealing with the unexpected.

Predictable sights trigger less brain activity than unfamiliar stimuli, bolstering the view that the brain is not merely reactive, but generates predictions based on the recent past. "The brain expects to see things and really just wants to confirm it now and again," says Lars Muckli at the University of Glasgow, UK.

He and Arjen Alink at the Max Planck Institute for Brain Research in Frankfurt, Germany, asked 12 volunteers to focus on a cross on a screen, above and below which bars flashed on and off to create the illusion of movement.

To test a predictable stimulus, a third bar would appear in a position timed to fit in with the illusion of smooth movement. For the unpredictable stimulus it would appear out of sync. fMRI scans showed that the unpredictable stimulus increased the activity in parts of the brain which deal with the earliest stages of visual processing (Journal of Neuroscience, vol 30, p 2960).

The finding supports the "Bayesian brain" theory, which sees the brain as making predictions about the world which it updates when new information comes in.

Most women unaware of risk for debilitating fractures

Landmark international study of more than 60,000 women highlights need for public education about osteoporosis risk factors and treatment

WORCESTER, Mass.— Underscoring what researchers call a serious international public health concern, results from the Global Longitudinal Study of Osteoporosis in Women (GLOW) showed that among women at an elevated level of risk for osteoporosis-associated fractures, there is a failure to perceive the implications of having important risk factors. For example, among postmenopausal women from 10 countries in Europe, North America and Australia diagnosed with osteoporosis, a condition putting them at high risk for fractures, only 43% thought their risk of a fracture was higher than that of other women their age. Additionally, only one in three (33%) women in GLOW who reported two or more major risk factors for fracture perceived themselves as being at higher risk for fracture than their age-matched peers.

This latest study from GLOW, which is based at the Center for Outcomes Research at the University of Massachusetts Medical School, was published today in the journal *Osteoporosis International* and included more than 60,000 postmenopausal women in 10 countries.

"We've found that many women aren't making the connection between their risk factors and the serious consequences of fractures," said the lead author of the paper, Ethel Siris, MD, GLOW investigator and Director of the Toni Stabile Osteoporosis Center of the Columbia University Medical Center, New York-Presbyterian Hospital. "Without a clear understanding of their risks, women cannot begin to protect themselves from fracture."

One in two women will suffer an osteoporosis-related fracture after age 50; these fractures often carry with them chronic pain, reduced mobility, loss of independence, and especially in the case of hip fracture, an increased risk of death. Because the likelihood of fractures increases substantially with older age, fracture numbers are projected to rise as the population ages.

Osteoporosis-related fractures are an international public health problem; in addition to the human suffering associated with these fractures, they are also the source of enormous health care costs.

Improved education of both physicians and postmenopausal women about osteoporosis risk factors is urgently needed, according to the study authors. Osteoporosis causes bones to become fragile and therefore more likely to break. If left untreated, the disease can progress painlessly until a fracture occurs.

Several risk factors for fractures have been identified and should be considered by physicians treating women age 55 and over:

- * older age
- * low weight
- * parental hip fracture
- * personal history of fracture (clavicle, arm, wrist, spine, rib, hip, pelvis, upper leg, lower leg, ankle) since age 45
- * two or more falls in the past year
- * current use of cortisone or prednisone (steroids often prescribed for a number of medical conditions)
- * rheumatoid arthritis
- * cigarette smoking
- * consumption of three or more alcoholic beverages daily.

Other risk factors include a variety of medical conditions and medications. Although tools for diagnosis and risk assessment, including bone density testing and the World Health Organization FRAX fracture risk assessment tool, are widely available, the connection between identified risk factors and serious fracture outcomes is not being made by a majority of women who are at the highest risk. Since many fractures can be prevented by appropriate treatment, it is important that elevated risk be recognized.

"We hope the insight we obtain from GLOW will help physicians and patients work together to both identify those at risk for fracture and to enhance understanding of the meaning of that risk," said Dr. Siris. "Education is critical if we are to reduce the burden of fractures worldwide."

Study Details

GLOW is a prospective, international cohort study of women 55 years of age and older who visited their primary care physician during the 2 years prior to enrollment in the study. Over 60,000 women were recruited by more than 700 primary care physicians in 17 cities in 10 countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, United Kingdom and United States.) GLOW is gathering information on osteoporosis risk factors, treatments, patient behaviors, and fracture outcomes over a 5-year period. Self-perceived risk of fracture was assessed using a five-point scale ranging from "much lower" to "much higher" risk than other women of the same age.

GLOW in Worcester, Massachusetts

Of the 28,000 US women enrolled in GLOW, 5091 were from Worcester, Massachusetts. One fifth (20%) of these women reported an osteoporosis diagnosis, 23% had a previous fracture, 16% were low weight, 38% reported recent falls, and 17% a parental hip fracture. Despite the high prevalence of risk factors, only 35% of women with two or more major risk factors perceived themselves to be at higher risk of a fracture than their peers. This failure by women to appreciate their personal risk of fracture presents a barrier to them receiving appropriate management and safe and effective treatments.

Sponsors GLOW is supported by a grant from The Alliance for Better Bone Health (formerly sanofi-aventis and P&G Pharmaceuticals, now sanofi-aventis and Warner Chilcott) and is being directed by The Center for Outcomes Research, University of Massachusetts Medical School.

Thyroid condition increases stroke risk in young adults

DALLAS - Young adults with overactive thyroid face a 44 percent increased risk of stroke compared to those with normal thyroid function, according to a study reported in Stroke: Journal of the American Heart Association.

"Strokes of undetermined cause account for between one-third and one-fourth of all ischemic strokes in young people," said Heng-Ching Lin, Ph.D., senior author of the study and professor at the School of Health Care Administration, College of Medicine, Taipei Medical University in Taipei, Taiwan. "To the best of our knowledge, hyperthyroidism has never been considered as a potential risk factor for stroke in the 18 to 44 age group."

Hyperthyroidism, also known as overactive thyroid, is a common endocrine disorder that affects an estimated 0.5 percent (1 in 200 people) to 2 percent (1 in 50 people) of the world's population, including a significant group of young adults, Lin said. The condition causes overproduction of thyroid hormone, which speeds up the metabolism and causes symptoms such as sweating, weight loss, diarrhea and nervousness.

For the study, researchers used data on 3,176 young adults diagnosed with hyperthyroidism between Jan. 1, 1998 and Dec. 31, 2001, and 25,408 comparison patients free of thyroid disease who were treated under Taiwan's national, single-payer healthcare system. The patients' average age was 32.

The researchers tracked each patient's data for five years to identify those who developed ischemic stroke, the most common type of stroke caused by blocked arteries in or leading to the brain. During those five years,

198 of the 28,584 patients developed ischemic stroke (0.7 percent), including 31 (1 percent) of the hyperthyroidism patients and 167 (0.6 percent) of the comparison group, Lin said.

After adjusting for factors including patient age, gender, income, level of urbanization, high blood pressure, diabetes, an irregular heart rhythm called atrial fibrillation (AF), high cholesterol, coronary heart disease and whether they were taking medication to treat heart rhythm problems, the risk of having a stroke during the five-year follow-up period was 44 percent higher for patients with hyperthyroidism than for those without it.

The medical records used in the study are a subset of a large database collected by Taiwan's national health insurance program, in which 98 percent of the population participated as of 2007.

"Hyperthyroidism may be associated with various syndromes or conditions linked to cerebrovascular disease in young adults," Lin said. "However, only case reports or case series were found in the literature, and the causal relationships could not be established."

For example, an association is well known between hyperthyroidism and AF in adults over age 60. AF occurs when the heart beats erratically and ineffectively, and AF can lead to both stroke and sudden cardiac death. There has been a notable absence of data related to the risk of stroke in younger individuals with hyperthyroidism, he said.

"Our study shows an association between hyperthyroidism and the risk of subsequent ischemic stroke in young adults," Lin said. "A more thorough evaluation in future studies may help elucidate the causes of stroke in this age group. Our results indicate a need for thyroid function testing and detection of hyperthyroidism in surveys to identify the causes of ischemic stroke in young people."

Other authors include lead author Jau-Jiaun Sheu, M.D., M.P.H.; and Jiunn-Horng Kang, M.D., M.Sc. and Hsiu-Chen Lin, M.D.