http://medicalxpress.com/news/2011-12-athletes-wrong.html

Athletes warming up wrong: study

Static stretching warm ups are being overused by athletes even though they can be counter-productive, according to Victoria University research.

Medical Xpress - James Zois from Victoria University's School of Sport & Exercise Science said too many athletes were using static stretching such as calf, quad and hip flex stretches just before competing even though it has been shown to reduce power.

"It's an epidemic: I see it at almost every AFL club, tennis match or international soccer event were athletes are stretching on the sidelines just prior to playing," he said. "People just aren't getting the message."

Mr. Zois' research showed static stretching decreased jumping performance by almost 8 per cent, while a more dynamic warm-up increased participants' vertical jump by 3 per cent. Dynamic warm-ups included range of motion activities like high-knee raises, leg swings and run-throughs or change of direction tasks.

Mr. Zois said the study proved that, from a power point of view, static stretching was worse than no warm up at all. "It's called a warm-up because its aim is to increase the metabolic processes, heart rate, muscle temperature and oxygen delivery to working muscles," he said. "If you do anything passive, like static stretching, you actually reverse those processes and so are actually doing the opposite of a warm up."

With an almost 11 per cent difference between static and dynamic stretching, Mr. Zois said athletes could not afford to ignore the facts. "Too many athletes still use the counterproductive technique of static stretching during the warm-up", he said. He said there was definitely a place for static stretching, particularly for those with chronic injuries or muscle stiffness concerns, but that it should not be a part of a normal athlete's warm-up regime inside an hour of performance.

Mr. Zois has been working with the Collingwood Football Club to improve warm-up techniques and is currently Tennis Victoria's strength and conditioning performance manager. *Provided by Victoria University*

http://www.eurekalert.org/pub_releases/2011-12/nu-npo121911.php

New predictor of heart attack or stroke

Blood pressure change at middle age more accurately predicts a heart attack or stroke

CHICAGO - A hike in your blood pressure during middle age significantly raises the risk of having a heart attack or a stroke during your lifetime, according to new Northwestern Medicine research. The study offers a new understanding on the importance of maintaining low blood pressure early in middle age to prevent heart disease later in life. Men and women who developed high blood pressure in middle age or who started out with high blood pressure had an estimated 30 percent increased risk of having a heart attack or stroke compared to those who kept their blood pressure low.

Previous estimates of a person's risk of cardiovascular disease were based on a single blood pressure measurement. The higher the blood pressure reading, the greater the risk. The new Northwestern Medicine study expands on that by showing a more accurate predictor is a change in blood pressure from age 41 to 55.

The study is published in Circulation: Journal of the American Heart Association.

"We found the longer we can prevent hypertension or postpone it, the lower the risk for cardiovascular disease," said lead author Norrina Allen, assistant professor of preventive medicine at Northwestern University Feinberg School of Medicine. "Even for people with normal blood pressure, we want to make sure they keep it at that level, and it doesn't start increasing over time."

"There hasn't been as much of a focus on keeping it low when people are in their 40's and 50's," Allen added. "That's before a lot of people start focusing on cardiovascular disease risk factors. We've shown it's vital to start early." People that maintain or reduce their blood pressure to normal levels by age 55 have the lowest lifetime risk for a heart attack or a stroke.

The study used data from 61,585 participants in the Cardiovascular Lifetime Risk Pooling Project. Starting with baseline blood pressure readings at age 41, researchers measured blood pressure again at age 55, then followed the patients until the occurrence of a first heart attack or stroke, death or age 95.

Men who developed high blood pressure in middle age or who started out with high blood pressure had a 70 percent risk of having a heart attack or stroke compared to a 41 percent risk for men who maintained low blood pressure or whose blood pressure decreased during the time period. Women who developed high blood pressure had almost a 50 percent risk of a heart attack or stroke compared to a 22 percent risk for those who kept their blood pressure low or saw a decrease.

Men generally have a 55 percent risk of cardiovascular disease in their lifetimes; women have a 40 percent risk.

"Our research suggests people can take preventive steps to keep their blood pressure low early on to reduce their chances of a heart attack or stroke," said Donald M. Lloyd-Jones, MD, study co-author, chair of

preventive medicine at Northwestern's Feinberg School and a cardiologist at Northwestern Memorial Hospital. "Maintaining a healthy diet, combined with exercise and weight control, can help reduce blood pressure levels and, consequently, your risk for cardiovascular disease later in life."

http://www.eurekalert.org/pub_releases/2011-12/bmj-hbl121611.php

High bodily levels of nickel and selenium may lower pancreatic cancer risk

High bodily levels of the trace elements nickel and selenium may lower the risk of developing the most common type of pancreatic cancer, finds research published online in Gut.

Similarly, high levels of lead, arsenic, and cadmium could boost the likelihood of developing the disease, the study shows. The researchers assessed 12 trace element levels in the toenails of 118 patients with exocrine pancreatic cancer - the most common form of the disease - and just under 400 hospital patients without cancer.

Nails, and particularly toenails, are considered reliable indicators of trace element levels, rather than dietary assessment, because they capture intake/exposure from other sources over the long term.

Analysis of the nail content showed that levels of certain trace elements were significantly higher or lower among the cancer patients than among patients in the comparison group. The higher or lower the level, the greater or lesser was the risk of having the disease. Patients with the highest levels of arsenic and cadmium in their nails were between two and 3.5 times more likely to have pancreatic cancer than those with the lowest levels. And those with the highest levels of lead were more than 6 times as likely to have the disease.

On the other hand, those with the highest levels of nickel and selenium were between 33% and 95% less likely to have the disease compared with those with the lowest levels. These findings held true even after taking account of other known risk factors, such as diabetes, overweight, and smoking.

Smoking is thought to account for around a third of all cases of pancreatic cancer. Tobacco contains trace metals, including cadmium, which is a known cancer causing agent, and has been associated with an increased risk of lung, kidney, and prostate cancers. High levels of selenium, on the other hand, have been associated with conferring protection against certain cancers, and previous research indicates that selenium may counter the harmful effects of cadmium, arsenic, and lead.

The authors point out that despite decades of research, the causes of pancreatic cancer remain largely unknown: "Our results support an increased risk of pancreatic cancer associated with higher levels of cadmium, arsenic, and lead, as well as an inverse association with higher levels of selenium and nickel," they conclude.

"These novel findings, if replicated in independent studies, would point to an important role of trace elements in pancreatic carcinogenesis."

http://www.newscientist.com/article/dn21300-twist-in-the-tail-of-eukaryotic-origins.html

Twist in the tail of eukaryotic origins

Complex life may have had parasitic origins. New evidence suggests that the relatives of the mitochondria within our cells once had a tail, like many parasitic bacteria.

15:18 19 December 2011 by Wendy Zukerman

Life on Earth is packaged into three domains: the simple bacteria, the archaea, and the complex eukaryotes that make up most of the life we see with the naked eye. The first eukaryotes appeared around 2 billion years ago. One popular theory suggests they did so after an immobile bacterium was ingested by an archaeon. The bacterium somehow escaped being digested and instead formed a symbiotic relationship with its consumer. As that relationship blossomed, the engulfed bacteria evolved into mitochondria – the energy producers in our cells.

Different picture

Nathan Lo at the University of Sydney in Australia and Claudio Bandi at the University of Milan, Italy, and colleagues think it is time to view this serendipitous encounter in a different light. They say that a few bacteria within the Rickettsiales – the closest genetic match to mitochondria – carry genes for a flagellum, a whip-like tail that some bacteria use to propel themselves.

That suggests that the bacteria might once have been mobile, like many parasitic bacteria. "Our results indicate that the mitochondrial ancestor may have acted as a parasite rather than prey," says Lo.

The team focused on Midichloria mitochondrii, a relatively little-known member of the Rickettsiales. Although the Rickettsiales do not boast a flagellum, the Midichloria genome contained 26 genes that help to build one in other bacteria. "We thought, that's strange," says Lo. "Where the hell did these genes come from?"

Open relationships

Bacteria take an open approach to sharing genetic information, so it's possible that Midichloria picked up the genes from a distant relative that does carry a flagellum. To make sure that wasn't the case, the team, led by Davide Sassera, also of the University of Milan, built an evolutionary tree incorporating Midichloria and a number of unrelated bacteria, using just the information in the flagella genes.

If Midichloria had obtained these genes from an unrelated bacteria, the two would have appeared to share a close evolutionary history. In fact, the tree placed Midichloria exactly where the team expected the Rickettsiales to be, confirming that the flagella genes must have been an ancient feature of this group. "Midichloria has hung on to these genes and everyone else in the group has lost them," says Lo.

If the original mitochondrion also had a tail, it may have invaded an archaeon as a parasite – inadvertently creating the first eukaryote in the process, Lo adds. "We are changing the story."

Predator, prey, parasite

"The authors have made a compelling case for flagella being present in the lineage leading to mitochondria," says Anthony Poole of the University of Canterbury in Christchurch, New Zealand. "We need to think more broadly than a passive predator-prey scenario."

Nick Lane at University College London agrees that the ancestral mitochondrion may have had a tail, but he is not convinced that it was a parasite. "Parasitic relationships don't benefit the host cell," he says.

Lo defends his position, however. "Many symbiotic relationships start as parasitism," he says. "They give up fighting each other and then work together."

Journal reference: Molecular Biology and Evolution, DOI: 10.1093/molbev/msr159

http://nyti.ms/sBpjfJ

Really? The Claim: Symptoms of Heart Disease Can Show Up in the Eyes

THE FACTS Is heart disease in the eyes? For some people, it just might be.

By ANAHAD O'CONNOR

Studies have shown that higher levels of lipids, or fats, in the blood can cause some people to develop raised yellow patches of skin around the eyelids, known as xanthelasma. Generally the spots are considered a benign cosmetic issue. Though they affect people of all ages, they are most common in middle age and later. Last year an Italian researcher reported that he spotted clear signs of xanthelasma around Mona Lisa's left eye.

But in a study this year in the journal BMJ, Danish scientists decided to look at whether these yellow patches could be an indication of underlying cardiovascular disease, tied to high cholesterol. In the study, the researchers followed nearly 13,000 adults over age 30 who were taking part in the Copenhagen City Heart Study.

People who developed the spots, it turned out, were more likely to have a heart attack or die of heart disease, regardless of other risk factors, like obesity and cholesterol levels. Over all, men who had xanthelasma had a 12 percent higher risk of heart disease, compared with those who did not, and women who developed the condition had an 8 percent rise in risk.

The nature of the link is not entirely clear. But an editorial with the study suggested that in people with no other overt signs of heart disease, an examination that includes a close inspection of the eyes could help identify those at greater risk.

THE BOTTOM LINE Research suggests that in some people, small yellow patches around the eyes could be a harbinger of heart disease.

http://nyti.ms/uo4T1D

Studies Suggest an Acetaminophen-Asthma Link

THE HYPOTHESIS Acetaminophen increases the risk of childhood asthma.

By CHRISTIE ASCHWANDEN

THE INVESTIGATOR Dr. John T. McBride, Akron

The sharp worldwide increase in childhood asthma over the past 30 years has long perplexed researchers, who have considered explanations as varied as improved hygiene and immunizations. Over the last decade, however, a new idea has emerged.

The asthma epidemic accelerated in the 1980s, some researchers have noted, about the same time that aspirin was linked to Reye's syndrome in children. Doctors stopped giving aspirin to children with fevers, opting instead for acetaminophen. In a paper published in The Annals of Allergy and Asthma Immunology in 1998, Dr. Arthur Varner, then a fellow in the immunology training program at the University of Wisconsin School of Medicine, argued that the switch to acetaminophen might have fueled the increase in asthma.

Since then, more than 20 studies have produced results in support of his theory, including a large analysis of data on more than 200,000 children that found an increased risk of asthma among children who had taken acetaminophen. In November, Dr. John T. McBride, a pediatrician at Akron Children's Hospital in Ohio, published a paper in the journal Pediatrics arguing that the evidence for a link between acetaminophen and asthma is now strong enough for doctors to recommend that infants and children who have asthma (or are at risk for the disease) avoid acetaminophen.

Dr. McBride based his assertion on several lines of evidence. In addition to the timing of the asthma epidemic, he said, there is now a plausible explanation for how acetaminophen might provoke or worsen asthma, a chronic inflammatory condition of the lungs. Even a single dose of acetaminophen can reduce the body's levels of glutathione, a peptide that helps repair oxidative damage that can drive inflammation in the airways, researchers have found.

"Almost every study that's looked for it has found a dose-response relationship between acetaminophen use and asthma," Dr. McBride said. "The association is incredibly consistent across age, geography and culture."

A statistical link between acetaminophen and asthma has turned up in studies of infants, children and adults. Studies have also found an increased risk of asthma in children whose mothers who took acetaminophen during pregnancy.

For instance, a study published in The Lancet in 2008 examined information collected on more than 205,000 children from 31 countries as part of the International Study of Asthma and Allergies in Childhood, known as the Isaac study. The 2008 analysis found that children who had taken acetaminophen for a fever during the first year of life had a 50 percent greater risk of developing asthma symptoms, compared with children who had not taken the drug. The risk rose with increasing use — children who had taken acetaminophen at least once a month had a threefold increase in the risk of asthma symptoms.

A study published by British researchers in 2000 using data from the Isaac study found that the prevalence of asthma increased in lock step with sales of acetaminophen in the 36 countries examined. The more acetaminophen used in a country, the greater that country's prevalence of asthma.

A meta-analysis published in 2009 calculated that children who had taken acetaminophen in the past year had nearly double the risk of wheezing compared with those who had not taken the drug. "We know that acetaminophen can cause increased bronchial constriction and wheezing," said Mahyar Etminan, a pharmacoepidemiologist at the University of British Columbia and lead author of the study.

Still, Dr. Etminan believes it is not yet clear that acetaminophen itself is responsible for the increasing prevalence of asthma. "Children who take acetaminophen are usually getting it for fever control, and they get fevers because they have viral infections, which on their own are associated with developing asthma later in life," Dr. Etminan said. "It's hard to tease out whether it's the drug or the viral infection."

Another potential problem, Mr. Etminan said, is that many of the studies required parents to accurately recall how much acetaminophen they gave their children, and how often. Parents whose children have asthma are likely to scrutinize the events that preceded an attack, he said, and thus may be more likely than other parents to recall giving their children the drug.

So far, only one randomized controlled trial has investigated the link. Researchers at Boston University School of Medicine randomly assigned 1,879 children with asthma to take either acetaminophen or ibuprofen if they developed a fever. The results, published in 2002, showed that children who took acetaminophen to treat a fever were more than twice as likely to seek a doctor's care later for asthma symptoms as those who took ibuprofen.

Other trials are in the works. Dr. Richard Beasley, a professor of medicine at the Medical Research Institute of New Zealand, is just completing a 12-week randomized controlled trial of acetaminophen to see if the drug provokes or worsens asthma in adults. The results of that trial will be completed next year. Dr. Beasley said the highest priority now should be rigorous trials to test whether acetaminophen use in infancy increases the risk of developing asthma.

"I cannot say with 100 percent certainty that acetaminophen makes asthma worse, but I can say that if I had a child with asthma, I would give him or her ibuprofen for the time being," Dr. McBride said. "I think the burden of proof is now to show that it's safe."

Not all experts agree. "At this time I just don't feel you can recommend one over the other," said Dr. Stanley Szefler, head of pediatric clinical pharmacology at National Jewish Health in Denver. "They both have advantages and disadvantages."

Aspirin and other nonsteroidal anti-inflammatory drugs, including ibuprofen, are known to provoke asthma attacks in some people, Dr. Beasley noted. He suggested a middle course for parents: Simply use acetaminophen (also known as paracetamol) more sparingly. "We should be reserving paracetamol for very high fevers or for major pain relief," he said. "We know that paracetamol is used much more widely than that — when a child is a bit irritable or teething or having an immunization."

Acetaminophen has been shown to reduce the antibody response to immunizations, so the drug should not be given to children in advance of a vaccination, Dr. Beasley also noted.

Dr. Szefler and his colleagues are working on a study looking at early interventions for asthma that will also track asthma patterns in children who take either acetaminophen or ibuprofen for fevers. The data will not answer all the questions, Dr. Szefler said, but they should provide more guidance for parents and pediatricians.

Dr. McBride, for one, is not waiting for results. "If studies prove that acetaminophen makes asthma worse," he said, "I can't imagine telling my patients that I knew about this five years ago, but I wasn't sure so I didn't mention it."

This article has been revised to reflect the following correction:

Correction: December 22, 2011

An article on Tuesday about studies linking childhood asthma to use of acetaminophen, using information provided by a researcher, described glutathione, a compound in the body that helps repair oxidative damage, incorrectly. It is a peptide, not an enzyme.

http://www.bbc.co.uk/news/magazine-16165605

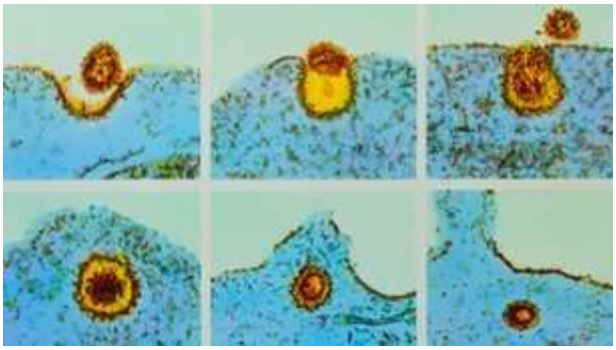
Is a cure for the common cold on the way?

In the northern hemisphere, cold and flu season is upon us. But the coughing, wheezing and spluttering masses that hit the streets each winter could, some scientists hope, soon be a thing of the past.

By Stephanie Hegarty BBC World Service

The reason for this optimistic thought is the progress being made towards the creation of a drug known as an antiviral.

Just as antibiotics kill many different types of bacteria, antivirals could kill multiple viruses, from the ubiquitous cold and flu to the life-threatening hepatitis virus and HIV. They could even prove crucial in the case of viral epidemics like Sars and bird flu. Existing antiviral drugs are tailored to specific diseases - HIV, hepatitis and certain types of flu for example. Vaccinations are also very virus-specific and have to be redeveloped at great cost as a virus evolves.



Viruses have special tags on their outer layer that allow them to break through the cell wall

But Todd Rider, a research scientist at the Massachusetts Institute of Technology, is developing an antiviral drug called Draco, which has proven successful against all 15 viruses to which it has been applied in lab trials with human tissue and mice. These include the common cold, H1N1 or swine flu, a polio virus, dengue fever and the notorious and fatal Ebola virus.

To produce it, Mr Rider took an unusual approach, "wiring together" two natural proteins - one that detects virus entry, and another that acts as a suicide switch that kills the infected cell. "I studied both biology and engineering back in the dark ages and really wanted to combine those studies," he says. "Everyone in both departments thought I was crazy."

The dream of a broad-based antiviral drug has for years been a holy grail for microbiologists. Recent developments in biotechnology - especially the ability of computers to analyse reams of information on DNA and the genetic make-up of viruses - has allowed for great leaps in scientific understanding of how these micro-organisms work. This has brought a few researchers closer to the goal of a broad-based antiviral, targeting the problem in several different ways.

Last year, a breakthrough study at Cambridge University showed that cells have an internal system which fights and kills viruses. It was previously thought that once a virus succeeded in entering a cell, infection was inevitable.

Dr Leo James, the author of this study, is now working on creating antiviral drugs that can latch on to a virus and destroy it inside the cell.

At Mount Sinai Medical School in New York, Professor Peter Palese has developed an antiviral drug that has so far proven very successful against influenza, though less so against other viruses.

And in a laboratory at the other side of the US, Dr Benhur Lee stumbled across a drug that seemed to be effective against several viruses including various pox viruses and Ebola. He soon

How Draco works

Natural *proteins in an infected cell detect the presence of a virus.*
These *proteins are sensitive to double stranded RNA, a genetic molecule unique to and present in nearly all viruses.*
Todd Rider *has taken one of these natural proteins and bound it to another natural protein - also present in all cells - that triggers cell suicide.*
To *help the new protein penetrate a cell, he added a feature that imitates part of the HIV virus, borrowing that virus' ability to break into cells.*
Once *administered, the drug travels to every cell in the body but it will only activate in infected cells.*
In *a matter of hours, the RNA-sensing part of the drug detects the virus and activates the cell suicide part. When the host cell dies, so does the virus.*

realised it only worked against viruses that shared a distinct characteristic, a greasy outer membrane or lipid envelope.

Dr James maintains some scepticism about Mr Rider's study. "It is potentially very exciting but because the results are so unusual and because it was published in an unusual journal it needs to be proven by others," he says.

PLoS One, the online journal which published the paper encourages ideas that challenge established thinking.

Draco appears to have a greater range than its rivals, but it will be several years before Draco can be tested on humans. First the drug will have to go through several rounds of testing on larger mammals.

Cold facts

The *common cold is caused primarily by the rhinovirus and coronavirus, while flu / influenza is a more severe illness caused by the orthomyxoviridae family of viruses - because both are prevalent at the same time of year, they are often confused*

In *the northern hemisphere flu season runs from November to March, in southern latitudes, it is from May until September*

Influenza *comes from an Italian expression, influenza di freddo, which means "influence of the cold"*

Cold *and flu are transmitted faster at colder air temperatures and in low humidity*

"Translating from the lab to people is really quite hard," says immunologist Hugh Pennington, Professor Emeritus at Aberdeen University. Viruses and human cells become closely linked on infection, as a result there are many possible side-effects of a drug like this.

In the 1950s, scientists thought they had come up with a similar broad-spectrum antiviral wonder drug, interferon. The drug causes an infected cell to secrete a warning signal to other cells, allowing them to build up their natural defences. However, it also triggers the immune system to send white blood cells to the infection, which can cause inflammation of the area, fever, aches and pains.

"Interferons are fantastic drugs," says Wendy Barclay, chair of influenza virology at Imperial College London. "They are still used today, to treat hepatitis C virus. But if you had a mild virus infection like a common cold you would not want to take interferon to deal with it because it would make you feel horrible, even worse than the cold was making you feel. "The problem with using that same approach today to develop a broad-spectrum antiviral is always the worry that something in your strategy is going to trigger that same response."

Like interferon, Draco is a protein and has the potential to provoke an immune response. This could be especially problematic when the drug is administered a second time. But no immune response has been observed in mice so far.

For the average human, who suffers through a cold up to four times a year, antivirals could be the answer to days of misery - and businesses could save weeks of lost work hours. But for those on the front line of healthcare, it could mean much more. A broad-based antiviral could obliterate the threat of a global pandemic and mitigate health scares such as that caused by the Sars virus in 2002 or bird flu in 2009.

"No-one can say when the next pandemic will occur, it may be next year or it may be in 100 years' time," says Hugh Pennington. "We're still in the niggling worry scenario even when we are very optimistic… If we had a wonder drug like Draco might be, we could sleep much easier at night."

Find out more about Todd Rider's work and the search for a broad-based antiviral on Discovery from the BBC World Service. ***Listen to the programme here****.*

http://www.eurekalert.org/pub_releases/2011-12/bmj-ccl121911.php

Could cod liver oil help combat tuberculosis?

Cod liver oil and tuberculosis

A review of a historical study from 1848 reveals that cod liver oil was an effective treatment for tuberculosis, says Professor Sir Malcolm Green in the Christmas issue published on bmj.com today.

In the study, carried out by physicians at the Hospital for Consumption, Chelsea (now the Royal Brompton Hospital), 542 patients with consumption (tuberculosis) received standard treatment with cod liver oil. These patients were compared with 535 'control' patients who received standard treatment alone (without cod liver oil).

While improvement rates were similar in the two groups, the disease was stabilised in 18% of the patients given cod liver oil, compared with only 6% of those in the control group. Deterioration or death occurred in 33% of patients given standard treatment alone, but in only 19% of those given cod liver oil, a reduction of 14%.

Professor Green says that some children are still given cod liver oil today and perhaps this relates back to the late 19th and early 20th centuries when cod liver oil was widely used to treat and prevent tuberculosis.

He adds that the steady fall in tuberculosis deaths in the late 19th and early 20th centuries is often attributed to better living conditions. While a reduction in overcrowded living might have reduced transmission, Green believes improved nutrition was probably as important. "It could well be that the widespread use of cod liver oil encouraged by doctors played a significant part," he writes.

Cod liver oil is a rich source of Vitamin D, which we now know is important in fighting infections, as well as preventing conditions such as rickets, says the author.

He says: "A role for vitamin D in combating tuberculosis gives a rational basis for sunshine therapy, which was widely practised for patients in sanatoriums before chemotherapy became available, as vitamin D is synthesised in the skin when exposed to the sun. Patients were put out on their beds to lie in the sun in summer and winter, and many were sent to Switzerland and other sunny countries for treatment." He adds that today many patients who develop TB in the UK are found to be Vitamin D deficient.

Green concludes that since tuberculosis is still a common infection, accounting for millions of deaths annually across the world, there may yet be a role for vitamin D supplements in combating this terrible killer.

http://medicalxpress.com/news/2011-12-breast-cancer-heart-disease-common.html

Breast cancer and heart disease may have common roots

Women who are at risk for breast cancer may also be at greater risk for heart disease, new research has found.

The majority of women with hereditary breast and ovarian cancer have a mutated form of the BRCA1 or BRCA2 genes, which normally suppress the growth of breast and ovarian tumours.

Dr. Subodh Verma, a cardiac surgeon at St. Michael's Hospital, said his research team was surprised to discover the genes also regulate heart function. Following a heart attack, mice with the mutated BRCA1 gene had a three-to-five times higher rate of death. This was largely due to the development of profound heart failure, possibly because their heart attacks were twice as severe as those in mice who did not have the mutated gene.

A similar two-fold increase in heart failure was observed when mice with a mutated BRCA1 or BRAC2 gene were treated with doxorubicin, one of the most common chemotherapy drugs for patients with breast cancer. In addition to studies in mice, the authors also verified this observation in human tissues. The researchers believe that the mutated BRCA1/2 prevents DNA repair in muscle cells that is essential to recovery after a heart attack.

Their findings were published in the journals Nature Communications and Journal of Biological Chemistry.

"Our findings suggest that individuals who are at risk of breast cancer may also be at a previously unrecognized risk of heart disease," Dr. Verma said. "More importantly, we now understand that breast cancer and heart disease - the two leading causes of death for Canadian women - have a common biological basis, a common soil."

Dr. Verma emphasized that these findings may have important implications for patients. Knowing that the BRCA1/2 gene is essential to DNA repair may lead to future treatments for anyone with heart disease, a leading cause of death worldwide. Women who carry this mutated gene now know they may also be at a higher risk for developing heart disease in addition to the risk of developing cancer.

Dr. Christine Brezden-Masley, an oncologist at St. Michael's and a co-author of the paper, said that while physicians knew doxorubicin was associated with heart failure, the new research shows women with the mutated BRCA1/2 gene are particularly sensitive to its toxicity. "What this means is that when a patient has the mutated gene, I now have to think about how much doxorubicin I'm going to give them or whether we should consider an alternate therapy," Dr. Brezden-Masley said. *Provided by St. Michael's Hospital*

http://www.eurekalert.org/pub_releases/2011-12/lm-pfa122111.php

Positive feedback and tumorigenesis

A vicious circle that promotes cell proliferation

Cancer cells are essentially immortal. The acquisition of an unlimited capacity to divide – the process of immortalization - is a central event in the genesis of tumors. Normally, cells are subject to stringent mechanisms which control their proliferation. Together these ensure that pre-malignant cells are induced to enter a senescent, non-dividing state or to undergo apoptosis, i.e. commit suicide. A research team led by Professor Heiko Hermeking and Dr. Antje Menssen from LMU's Institute of Pathology has now discovered how the regulatory protein c-MYC subverts these controls, thus facilitating the growth of tumors. High levels of c-MYC, which are present in most tumor cells, activate SIRT1, an enzyme that inhibits both senescence and apoptosis. The new results show that the two proteins actually form a positive feedback loop, in that SIRT1 also promotes the activity of c-MYC. Normal cells avoid this vicious circle because they keep the gene that codes for c-MYC turned off, unless they receive growth-promoting signals. In tumor cells, this mechanism no longer functions and the cells can proliferate unchecked. Their latest findings have implications for cancer treatment, as Menssen explains: "Our results indicate that tumor types in which c-MYC plays a crucial role, such as lymphomas and colon or breast cancers, should be especially susceptible to pharmacological inhibitors that

interrupt the feedback loop. In particular, combinations of drugs that interact with different components of the loop could provide a new route to effective therapies of these malignancies." (PNAS 19.-23.12)

The c-MYC protein is involved in the control of many basic biological functions, including cell growth and division. It is therefore vital for processes that require cell proliferation, such as embryonic development and the generation of all the cell types in the blood. Overproduction of c-MYC, on the other hand, can have lethal consequences for the organism. Continuous synthesis of c-MYC is a prominent feature of immortalized cells, which divide in an uncontrolled fashion and thus facilitate the formation of tumors. Normally, multiple mechanisms serve to regulate the expression of the gene for c-MYC, and keep the level of the protein present in cells within appropriate limits. In essence, the gene is activated only when a cell is instructed to do so by specific growth-promoting signals. If this failsafe mechanism is disabled, a second internal system switches in. This back-up circuit ensures that increased concentrations of c-MYC cause premature cell senescence (which makes cells unresponsive to growth signals) and induce programmed cell death. However, in tumor cells, these safeguards no longer function – and in some tumors and cell types it has emerged that c-MYC itself is responsible for knocking them out. "How c-MYC achieves this has remained largely unclear," says Hermeking. In order to clarify the mechanisms involved, the researchers focused on the enzyme SIRT1 as a possible accomplice of c-MYC. As Hermeking explains, "SIRT1 seemed to us a likely candidate because a related enzyme has been shown to play a role in extending the lifespan of cells in lower organisms. In human cells, SIRT1 is known to inhibit a regulator that promotes senescence and programmed cell death."

The hunch turned out to be correct, since the team, which included molecular biologists from Aachen University and the Karolinska Institute in Stockholm, was able to show that c-MYC actually enhances SIRT1 function in a number of different ways. First, it activates NAMPT (nicotinamide phosphoribosyltransferase), which is responsible for the synthesis of a molecule required for the action of SIRT1. Secondly, c-MYC represses an inhibitor of SIRT1, so releasing a further brake on its function. Finally, SIRT1 itself potentiates these effects by reducing the rate of degradation of c-MYC. The end result is a positive feedback loop which drives the continuous accumulation of both SIRT1 and c-MYC in the cell.

The c-MYC protein is synthesized in large amounts in most tumors. Furthermore, in certain cancers, such as lymphomas and cancers of the colon and the breast, c-MYC is known to play a causative role in the origin of the primary tumor. In these cases, mutations in the c-MYC gene itself, or in genes that regulate its expression, result in constant production of the c-MYC protein. The new findings are thus of particular relevance for the development of new treatment options for these types of cancer, since one would expect them to be highly sensitive to direct inhibition of SIRT1 or NAMPT. Interestingly, several studies in recent years have revealed that levels of NAMPT are also increased in many tumors. Indeed, a chemical inhibitor of NAMPT is already undergoing clinical trials. "Our study strongly suggests that the feedback loop initiated by excess c-MYC drives the overproduction of NAMPT. A combination of drugs that would allow us to inhibit the actions of both SIRT1 and NAMPT might therefore have a synergistic effect and could open up new therapeutic possibilities," Menssen points out.

In addition, the new findings raise questions regarding the allegedly positive effect of a daily glass of red wine on lifespan. The putative health benefits of this regime have been attributed in part to the activation of SIRT1 by the compound resveratrol, which is found in red wine. Indeed, commercial development of pharmacological SIRT1 activators such as resveratrol is already underway – in the hope that they will slow the aging process and block the development of obesity and diabetes. In this context, Hermeking advises caution: "In the light of our results, these agents should only be used after further extensive study."

The project was supported by a Habilitation Fellowship (funded by the Exzellence Initiative at LMU) to Dr. Antje Menssen, and by the Deutsche Krebshilfe e.V. and the Max-Planck-Society. (göd)

Publication: *The c-MYC oncoprotein, the NAMPT enzyme, the SIRT1 inhibitor DBC1, and the SIRT1 deacetylase form a positive feedback loop. A. Menssen, P. Hydbring, K. Kapelle, J. Vervoorts, J. Diebold, B. Lüscher, L.- G. Larsson, H. Hermeking. PNAS Early Edition 19.-23.12.2011 doi: 10.1073/pnas.1105304109*

http://news.discovery.com/earth/dinosaur-penguin-antarctica-titanosaur-bone-111220.html

Biggest Beast Once Roamed Antarctica

Argentinean researchers uncovered the remains of a titanosaur indicating it roamed the continent.

Talk about a titanic discovery!

The sauropod family includes some of the largest terrestrial vertebrates that ever existed -- giant, lumbering beasts weighing tens or even hundreds of tons. And they lived everywhere but Antarctica, paleontologists thought -- until now.

Argentinean researchers have just uncovered the Antarctic remains of a titanosaur, a plant-eating, sauropod dinosaur that remains one of the largest creatures to ever plod the surface of the planet.

Despite the enormous size of the creatures, the evidence was remarkably small: Just a section of vertebrae barely 7.5 inches long believed to have come from the middle third of the dinosaur's tail.

"These sauropod dinosaur remains from Antarctica improves our current knowledge of the dinosaurian faunas during the Late Cretaceous on this continent," said Ignacio Alejandro Cerda from Argentinan science foundation CONICET, who was part of the team that discovered the remains of the "lithostrotian titanosaur." The giant beast lumbered around approximately 70 million years ago, according to a report in the Daily Mail.

***Titanosaurs are a genus of sauropods, some of the largest animals to have ever existed. Brachiosaurus (Giraffatitan) brancai* by John Conway**

The specific size and morphology of the specimen, including its distinctive ball and socket articulations, lead the authors to identify it as an advanced titanosaur.

Other important dinosaur discoveries have been made in Antarctica in the last two decades -- principally in the James Ross Basin where this bit of bone was found, the scientists noted. These titanosaurs originated during the Early Cretaceous and were the predominant group of sauropod dinosaurs until the extinction of all non-bird beasts at the end of the Cretaceous. Although they were one of the most widespread and successful species of sauropod dinosaurs, their origin and dispersion are not completely understood.

Their research has just been published online in Springer's journal, Naturwissenschaften - The Science of Nature

http://www.nytimes.com/2011/12/20/science/dura-europos-a-melting-pot-at-the-intersection-of-empires.html

A Melting Pot at the Intersection of Empires for Five Centuries

In its time and place, the ancient city of Dura-Europos had much in common with today's most cosmopolitan urban landscapes.

By JOHN NOBLE WILFORD

Religious, linguistic and cultural diversity characterized much of the city's life for more than 500 years, starting at the outset of the third century B.C. in what is now Syria.

Greek, Aramaic, Latin, Parthian, Middle Persian and Hebrew - all of these languages were used concurrently throughout the society, according to inscriptions and graffiti uncovered by archaeologists. A temple altar epitomizes the multiculturalism: The inscription is in Greek, and a man with a Latin name and a Greek-titled office in the Roman army is shown presenting an offering to Iarhibol, a god of the migrants from the old Syrian caravan city of Palmyra.

New Yorkers would have felt at home in the grid pattern of streets, where merchants lived, scribes wrote and Jews worshiped in the same block, not far from a Christian house-church as well as shrines to Greek and Palmyrene deities. Scholars said the different religious groups seemed to maintain their distinct identities.

An exhibition of prized and quotidian artifacts from Dura-Europos, "Edge of Empires: Pagans, Jews, and Christians at Roman Dura-Europos," is on view through Jan. 8 at New York University's Institute for the Study of the Ancient World. The objects - notably art from antiquity's best-preserved synagogue, and evocative photographs of the buried city's excavations - are on loan from the Yale University Art Gallery. "As a city of extraordinary cultural diversity," said Jennifer Y. Chi, an archaeologist and the exhibition's chief curator, "Dura-Europos has great resonance for the modern world, where multiculturalism shapes the very nature and quality of daily life."

Macedonian successors to Alexander the Great founded Dura-Europos on a plateau high above the Euphrates River. The precipitous drop to the river and deep ravines made the city virtually invulnerable on three sides; stone fortifications faced the desert to the west. "It was beautifully made by nature as a fortress

town," said Glen W. Bowersock, an authority on the late antiquity period at the Institute for Advanced Study in Princeton, N.J.

There the city stood at the intersection of empires for five centuries. The Greeks named it Europos, after the hometown of its founders, and built it around an eight-block agora, the political and commercial center typical of any Greek city. When the stone wall was erected, "Dura," the Assyrian term for a fortified city, was added.

Parthians from the Caspian Sea region took over in the late second century B.C. Romans seized it as the eastern outpost of their empire in A.D. 165, but about 100 years later, the Sasanians from Persia laid siege to the city and destroyed it. Dura-Europos was never rebuilt. Its ruins were soon buried under desert sands, to be discovered in 1920 by British soldiers digging a trench. By the late 1930s archaeologists, including a Yale team led by Michael Rostovtzeff, exposed at least a quarter of the city. The excavations opened scholars' eyes to the art and architecture of a thriving multiethnic city of perhaps 10,000 people.

As it happened, the soldiers dug into wall paintings in what turned out to be the Temple of the Palmyrene Gods, or Temple of Bel, the first of several spectacular finds.

The discoveries of the synagogue and the Christian place of worship during the Roman period brought international attention to the excavations. Although more recent digs have more than doubled the area examined, the exhibition focuses on the earlier findings and the years the city was a Roman military base.

The synagogue, built on the western edge of the city after the Roman conquest, was an impressive building, the high walls of its main hall painted with biblical scenes: the infancy of Moses, the Exodus, the sacrifice of Elijah and more than 50 other events. All the paintings are seen in the digital slide show at the exhibition, and 10 painted tiles from the ceiling are on display for the first time as a group. (The most complete reconstruction of the synagogue is in the Damascus Museum.)

The elaborate decorations were a surprise to some scholars, for the paintings offered proof that figural representation in a Jewish religious setting was not anathema at this time in history, despite the Mosaic commandment against graven images.

The building that is said to be the earliest surviving Christian "house of the church" was much less impressive, for good reason. At the time, the religion was officially banned in the Roman empire (it was 325 before Emperor Constantine endorsed Christianity), and the faithful met in secret, often in private houses. On the outside, the house-church in Dura-Europos looked like other residences on the block. Inside, paintings from the baptistery illustrated the miracles of Jesus and the procession of women in the baptism ritual.

The Roman military culture also contributed to the city's diversity. Troops were recruited from all parts of the empire, a polyglot mix from northern Europe to the Mediterranean and beyond. Several Celtic bronze belt ornaments and horse-harness pieces in the show call attention to international influences. Uncovered from the ruins was a shrine to the god Mithras, a deity favored by soldiers.

At the entrance to one of the galleries stands a Roman military shield, or scutum, a semicylindrical piece made of wood and rawhide that a soldier held in front of him for head-to-toe protection. Nothing olive drab about this military gear, handsomely painted in high imperial style.

Through the centuries, one culture after another left its imprint on Dura-Europos. As Dr. Bowersock pointed out, even if Romans issued military orders in Latin, the clerks and shopkeepers spoke Aramaic, and many people in the street kept their native tongues, the principal language of government and culture remained the Greek of its founders.

"Edge of Empires" is at the Institute for the Study of the Ancient World, 15 East 84th Street, Manhattan, through Jan. 8. Closed Mondays, and Christmas and New Year's Day. Admission is free.

http://www.sciencedaily.com/releases/2011/12/111221105643.htm

New Material Cools Under Pressure

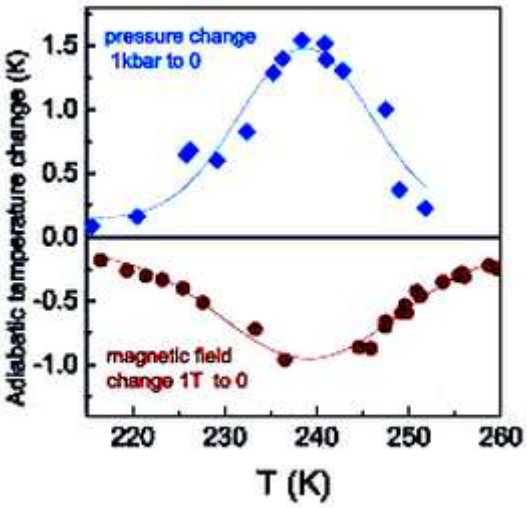
A team from the University of Barcelona has identified a new material that exhibits an inverse barocaloric effect at room temperature, which means that it cools when pressure is applied

ScienceDaily - Research led by a team from the University of Barcelona, published in the online version of the journal Nature Communications, has identified a new material that exhibits an inverse barocaloric effect at room temperature, which means that it cools when pressure is applied, unlike most other materials. The study, carried out within the framework of Barcelona Knowledge Campus (BKC), also included work by researchers from the Polytechnic University of Catalonia. BarcelonaTech (UPC), the University of Duisburg-Essen (Germany) and the Indian Association for the Cultivation of Science.

The barocaloric effect refers to the change in temperature produced in a material by the application of hydrostatic pressure. Most objects heat up when compressed and cool down when decompressed, but some solids display the opposite behaviour: their temperature decreases when they are compressed and increases

when they are decompressed. Lluís Mañosa, UB professor, explains: "This highly unusual behaviour is what we have termed the inverse barocaloric effect. In our study we have found a material which exhibits a substantial change at moderate pressures: its temperature drops by 1ºC for each additional 1 kbar of pressure."

During the study, the Group on Characterization of Materials at the Polytechnic University of Catalonia. BarcelonaTech (UPC) carried out a characterization of the processes to which the solid material was submitted, at different temperatures and pressures, using a custom system developed by the team.



The material developed during the study is an intermetallic compound of the magnetocaloric metals lanthanum, iron, silicon and cobalt (La-Fe-Si-Co), which change temperature when an external magnetic field is applied. This group of materials is considered to be the most promising for novel refrigeration systems. According to Mañosa, "in the material we studied, the temperature change brought about by moderate pressures is of sufficient magnitude to be considered for use in environmentally respectful refrigeration systems. In addition, the fact that it responds to two types of external stimulus -- magnetic fields and pressure -- would allow for the design of devices that apply these stimuli simultaneously to obtain higher levels of performance."

The inverse barocaloric effect is created by a phase transition in the material below a given temperature, which leads to changes in its structural and magnetic properties. It has recently been suggested that materials displaying this behaviour could also be used in novel energy harvesting systems.

http://medicalxpress.com/news/2011-12-french-maggots-wounds-faster-surgery.html

French study suggests maggots may clean wounds faster than surgery

A new study has shown that at least for some types of wounds, maggots may be the preferential form of treatment

Medical Xpress - For thousands of years, people have used maggots to clean out wounds, particularly in battlefield situations when there were few other options. Use of maggots (fly larvae) virtually disappeared in the modern world though once antibiotics arrived on the scene, but that may change as a new study conducted by a team in France has shown that at least for some types of wounds, maggots may be the preferential form of treatment.

The team, made up of doctors and researchers from various facilities in France, conducted a study with elderly male volunteers who had lower leg wounds or skin ulcers that weren't healing well, and as they describe in their study published in Archives of Dermatology, the patients that were treated with maggots, fared better, at least in the first week, than did those treated with conventional surgical procedures.

In order to reproduce, flies lay their eggs in the carcasses of dead animals. The eggs develop into maggots which eventually grow into adults by eating the meat in which they exist. To accomplish this feat they secrete a substance into the dead tissue that helps to break it down first. The maggots then simply eat the result. When introduced into injured human flesh, the maggots perform the same trick, eating dead flesh while leaving healthy flesh alone, though not necessarily in the same fashion. In the wild, as anyone that has stumbled upon the carcass of a dead animal and found it literally crawling with the small rice looking larvae knows, it's a truly stomach retching sight. In a medical environment, on the other hand it can be a truly innocuous experience.

Image: National Institutes of Health

In the study, the team split up a group of 119 men into two groups of close to 50 each; one group received conventional surgery to repair their wound, while the other received maggot therapy. Both were kept in the hospital for two weeks and both were blindfolded during treatment.

In the surgical procedure, a scalpel is used to cut away dead flesh, along with some that is not dead. The maggot procedure is done by pressing a bag that has sterile maggots in it against a wound which has first been covered by a thin film to protect against infection. Thus, the maggots are not free to crawl around inside of the patient.

Afterwards, in looking at the results, the team found that those patients that had received maggot therapy, for the most part, showed better results at the end of the first week. After that, there was no discernible difference in the two procedures. In this context, better results meant there was less slough (dead matter) in the wound

(54.5% vs 66.5%) and more apparent healing. The team noted that roughly half of the people in both groups reported a crawling-around feeling in the wound, and most agreed the pain involved was minimal.

This one study suggests that more research needs to be done regarding the use of maggots in healing wounds, because despite the ick factor; people should have access to the best possible treatment. Thus far, little has been done though. In the United States, for example, despite the fact that the FDA gave approval for use of maggot therapy back in 2004, little testing, research or actual procedures have been carried out and some patients, such as those with diabetes or those that cannot abide anesthesia, have likely suffered for it.

More information: Maggot Therapy for Wound Debridement, Arch Dermatol. Published online December 19, 2011. doi:10.1001/archdermatol.2011.1895

Abstract

Objective *To study the efficacy of bagged larvae on wound debridement compared with conventional treatment.*

Design *Randomized, multicenter, controlled, prospective phase 3 trial with blinded assessment of outcome measures by a single observer.*

Setting *Two hospital referral centers in Caen and Lyon, France.*

Patients *Random sampling of 119 patients with a nonhealing, sloughy wound 40 cm2 or smaller, less than 2 cm deep, and an ankle brachial index of 0.8 or higher.*

Intervention *During a 2-week hospital stay, patients received either maggot debridement therapy (MDT) or conventional treatment. At discharge, conventional dressings were applied and a follow-up visit occurred at day 30.*

Main Outcome Measure *Percentage of slough in wounds at day 15.*

Results There was a significant difference between groups at day 8 (54.5% in the MDT group and 66.5% in the control group) (P = .04). The mean percentage of slough at day 15 was 55.4% in the MDT group and 53.8% in the control group (P = .78).

Conclusions *Although MDT shows no significant benefit at day 15 compared with conventional treatment, debridement by MDT is significantly faster and occurs during the first week of treatment. Because there is no benefit in continuing the treatment after 1 week, another type of dressing should be used after 2 or 3 applications of MDT.*

Trial Registration *clinicaltrials.gov Identifier: NCT01211236*

http://medicalxpress.com/news/2011-12-abnormality-auditory-underlies-dyslexia.html

Listen up: Abnormality in auditory processing underlies dyslexia

New research finds that a specific abnormality in the processing of auditory signals accounts for the main symptoms of dyslexia

People with dyslexia often struggle with the ability to accurately decode and identify what they read. Although disrupted processing of speech sounds has been implicated in the underlying pathology of dyslexia, the basis of this disruption and how it interferes with reading comprehension has not been fully explained. Now, new research published by Cell Press in the December 22 issue of the journal Neuron finds that a specific abnormality in the processing of auditory signals accounts for the main symptoms of dyslexia.

"It is widely agreed that for a majority of dyslexic children, the main cause is related to a deficit in the processing of speech sounds," explains senior study author, Dr. Anne-Lise Giraud and Franck Ramus from the Ecole Normale Supérieure in Paris, France. "It is also well established that there are three main symptoms of this deficit: difficulty paying attention to individual speech sounds, a limited ability to repeat a list of pseudowords or numbers, and a slow performance when asked to name a series of pictures, colors, or numbers as quickly as possible. However, the underlying basis of these symptoms has not been elucidated."

Dr. Giraud and colleagues examined whether an abnormality in the early steps of auditory processing in the brain, called "sampling," is linked with dyslexia by focusing on the idea that an anomaly in the initial processing of phonemes, the smallest units of sound that can be used to make a word, might have a direct impact on the processing of speech.

The researchers found that typical brain processing of auditory rhythms associated with phonemes was disrupted in the left auditory cortex of dyslexics and that this deficit correlated with measures of speech sound processing. Further, dyslexics exhibited an enhanced response to high-frequency rhythms that indirectly interfered with verbal memory. It is possible that this "oversampling" might result in a distortion of the representation of speech sounds.

"Our results suggest that the left auditory cortex of dyslexic people may be less responsive to modulations at very specific frequencies that are optimal for analysis of speech sounds and overly responsive to higher frequencies, which is potentially detrimental to their verbal short-term memory abilities," concludes Dr. Giraud. "Taken together, our data suggest that the auditory cortex of dyslexic individuals is less fine-tuned to the specific needs of speech processing." *Provided by Cell Press*

http://medicalxpress.com/news/2011-12-bigger-brain-memory.html

Why bigger is better when it comes to our brain and memory

New research reveals characteristics of the human hippocampus that allow scientists to use anatomical brain scans to form predictions about an individual's recollection ability

The hippocampus is an important brain structure for recollection memory, the type of memory we use for detailed reliving of past events. Now, new research published by Cell Press in the December 22 issue of the journal Neuron reveals characteristics of the human hippocampus that allow scientists to use anatomical brain scans to form predictions about an individual's recollection ability. The new research helps to explain why this relationship has been hard to find in the past and provides evidence for a possible underlying mechanism.

The hippocampus, a deep brain structure named for its curving seahorse shape, can be divided into anterior and posterior portions. Although research has generally linked smaller hippocampi with worse recollection in neuropsychological patients and during aging, this relationship has not held up among healthy young adults. "There is some evidence that extensive spatial memory acquisition leads to enlargement of the posterior hippocampus and a decrease in the anterior hippocampus," explains lead study author, Dr. Jordan Poppenk who conducted the study at Baycrest's Rotman Research Institute. "This suggested to us that the crucial predictor of individual differences in recollection ability might not be the overall size of the hippocampus but the separate contributions of the posterior and anterior segments of the hippocampus."

Dr. Poppenk and coauthor Dr. Morris Moscovitch analyzed high-resolution magnetic resonance imaging brain scans of healthy adults who had participated in recollection memory tests. Better recollection was associated with a larger posterior hippocampus and a smaller anterior hippocampus. The overall size of the hippocampus did not predict recollection, as larger posterior hippocampi were offset by smaller anterior hippocampi. The researchers went on to show that the link between the posterior hippocampus and recollection depended on interactions with other parts of the brain between the times that memories were learned and retrieved, particularly regions involved in perception which form the basis of recollected experience.

"Our results show for the first time that the size of the posterior hippocampus, especially when expressed as a ratio to the size of the anterior hippocampus, reliably predicts recollection in healthy adults. This finding explains the longstanding failure to correlate the overall size of the hippocampus with memory," concludes Dr. Poppenk. "We also provide evidence that it is the functional connections, possibly related to memory consolidation, between the posterior hippocampus and other parts of the brain that may underlie enhanced memory recollection." *Provided by Cell Press*

http://bit.ly/uAOVA6

A drug that activates only your father's version of a gene may treat neural disorder

Imprinted genes are expressed from either the maternal or paternal allele. When this process goes wrong, it can lead to diseases. Researchers have identified a possible way to treat imprinting errors

By Diana Gitig | Published 4 days ago

Anyone who's passed basic biology knows that we get one copy of a gene from our mother, a second from our father. But few people realize that not all of these genes end up being treated equally. Imprinted genes are expressed from only the maternal or paternal allele, rather than both. And, when this process goes wrong, it can actually lead to diseases. Now, researchers have identified a possible way to treat imprinting errors.

In the brain, Ube3a is an imprinted gene; only the maternal allele is expressed, even if it is mutated and the paternal allele is normal. This is the case in Angelman syndrome, a severe neurodevelopmental disorder caused by mutation or deletion of the maternal allele of Ube3a. Ube3a is imprinted only in the brain, though; in other tissues, the paternal allele is expressed along with the maternal one.

This led Benjamin Philpot and his colleagues at UNC Chapel Hill to wonder: wouldn't it be great if we could get the normal, paternal version of Ube3a to work in the brain—to unsilence it? Maybe this could help kids with Angelman syndrome.

To find a drug that might allow the paternal copy of Ube3a to be expressed, they first made mice in which only the paternal copy of the gene was linked to the gene for yellow fluorescent protein. They then isolated cortical neurons from these mice and exposed the neurons to a variety of chemicals. If any of these chemicals caused the cells to glow yellow, that meant that they allowed expression of the paternal UBE-3A-yellow fluorescent protein hybrid.

The scientists screened 2,306 different compounds, four times each. Most of the compounds have already been approved for use in humans, so if the researchers found anything promising, clinical trials would be expedited. They concentrated on agents known to be active in the central nervous system and those that are

known to interfere in epigenetic regulation (like the methylation often used in imprinting). Unfortunately, none of these activated the paternal UBE-3A-yellow fluorescent protein hybrid.

But there was one compound that unsilenced the gene: topotecan, a drug that is part of a class called topoisomerase inhibitors. Topoisomerases are enzymes that alleviate the stress on a DNA double helix that occurs when the two strands are pulled apart, as they are when a gene is expressed.

Once topotecan was identified, the researchers went on to show that other topoisomerase-inhibiting drugs, both those structurally similar to topotecan and those with different structures, could unsilence paternal Ube3a. They then injected topotecan into mouse brains to demonstrate that it could work in vivo, and not just in tissue culture dishes. They found that paternal Ube3a expression persisted in spinal cord neurons for up to 12 weeks after drug treatment; this long lasting effect is significant because genetic imprinting is thought to be established during specific points in embryonic development and then maintained for life.

Paternal Ube3a is normally silenced by what's called an antisense transcript—a piece of RNA that covers up the gene to prevent its expression. (This antisense transcript is not made from the maternal chromosome.) Topotecan worked on the paternal chromosome, dampening antisense transcription there.

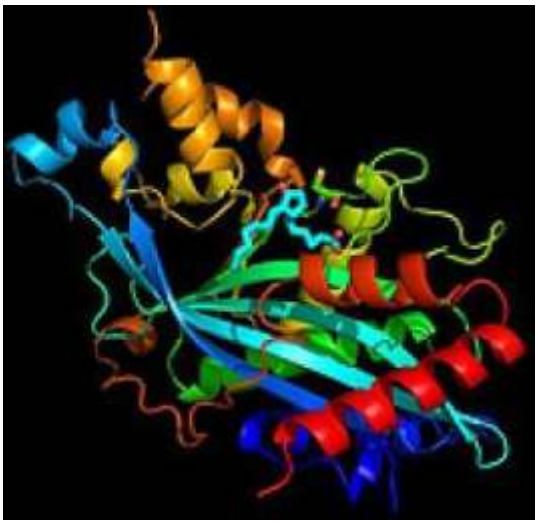
Inherited neurological disabilities have been extremely difficult to treat. In Angelman's syndrome, the brain architecture seems normal at birth, so it is possible that the restoration of normal gene expression could correct some of the pathologies. Topotecan is approved for use in people with cancer, and it has been shown to be well tolerated in children. Hopefully, it could be therapeutically valuable for those with Angelman's syndrome; it has definitely been valuable in showing how a dormant but functional gene can be reactivated.

Nature, 2011. DOI: 10.1038/nature10726, 10.1038/nature10784 (About DOIs).

http://www.eurekalert.org/pub_releases/2011-12/ps-fom122211.php

Fish oil may hold key to leukemia cure

A compound produced from fish oil that appears to target leukemia stem cells could lead to a cure for the disease, according to Penn State researchers.



The compound - delta-12-protaglandin J3, or D12-PGJ3 - targeted and killed the stem cells of chronic myelogenous leukemia, or CML, in mice, said Sandeep Prabhu, associate professor of immunology and molecular toxicology in the Department of Veterinary and Medical Sciences. The compound is produced from EPA - Eicosapentaenoic Acid - an Omega-3 fatty acid found in fish and in fish oil, he said.

"Research in the past on fatty acids has shown the health benefits of fatty acids on cardiovascular system and brain development, particularly in infants, but we have shown that some metabolites of Omega-3 have the ability to selectively kill the leukemia-causing stem cells in mice," said Prabhu. "The important thing is that the mice were completely cured of leukemia with no relapse."

The compound shown above is D12-PGJ2, which closely resembles delta-12-protaglandin J3, or D12-PGJ3, a compound that targeted and killed the stem cells of chronic myelogenous leukemia, or CML, in mice during experiments conducted by Penn State researchers. According to the American Cancer Society, about 5,150 new cases of CML are reported annually and approximately 270 people die from the disease each year. **Sandeep Prabhu**

The researchers, who released their findings in the current issue of Blood, said the compound kills cancer-causing stem cells in the mice's spleen and bone marrow. Specifically, it activates a gene -- p53 -- in the leukemia stem cell that programs the cell's own death. "p53 is a tumor suppressor gene that regulates the response to DNA damage and maintains genomic stability," Prabhu said.

Killing the stem cells in leukemia, a cancer of the white blood cells, is important because stem cells can divide and produce more cancer cells, as well as create more stem cells, Prabhu said.

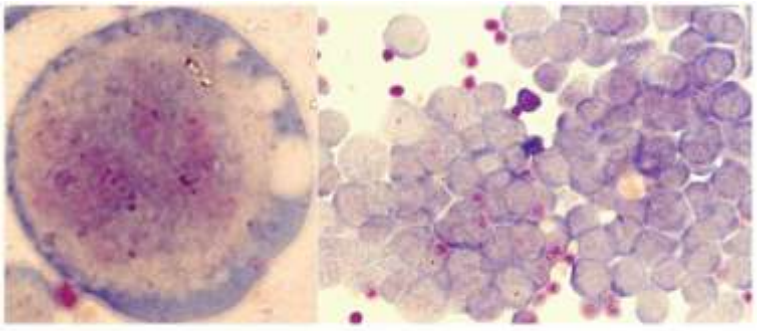
The current therapy for CML extends the patient's life by keeping the number of leukemia cells low, but the drugs fail to completely cure the disease because they do not target leukemia stem cells, said Robert Paulson, associate professor of veterinary and biomedical sciences, who co-directed this research with Prabhu.

"The patients must take the drugs continuously," said Paulson. "If they stop, the disease relapses because the leukemia stem cells are resistant to the drugs."

Current treatments are unable to kill the leukemia stem cells, Paulson noted. "These stem cells can hide from the treatment, and a small population of stem cells give rise to more leukemia cells," said Paulson. "So, targeting the stem cells is essential if you want to cure leukemia."

During the experiments, the researchers injected each mouse with about 600 nanograms of D12-PGJ3 each day for a week. Tests showed that the mice were completely cured of the disease. The blood count was normal, and the spleen returned to normal size. The disease did not relapse.

In previous experiments, the compound also killed the stem cells of Friend Virus-induced leukemia, an experimental model for human leukemia.



Leukemia cells **Credit: Robert Paulson**

The researchers focused on D12-PGJ3 because it killed the leukemia stem cells, but had the least number of side effects. The researchers currently are working to determine whether the compound can be used to treat the terminal stage of CML, referred to as Blast Crisis. There are currently no drugs available that can treat the disease when it progresses to this stage.

The researchers, who applied for a patent, are also preparing to test the compound in human trials.

http://www.eurekalert.org/pub_releases/2011-12/uocp-rcm122211.php

Researcher contends multiple sclerosis is not a disease of the immune system

An article argues that multiple sclerosis is not actually a disease of the immune system, instead MS is caused by faulty lipid metabolism similar to coronary atherosclerosis than to other autoimmune diseases

An article to be published Friday (Dec. 23) in the December 2011 issue of The Quarterly Review of Biology argues that multiple sclerosis, long viewed as primarily an autoimmune disease, is not actually a disease of the immune system. Dr. Angelique Corthals, a forensic anthropologist and professor at the John Jay College of Criminal Justice in New York, suggests instead that MS is caused by faulty lipid metabolism, in many ways more similar to coronary atherosclerosis (hardening of the arteries) than to other autoimmune diseases.

Framing MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals says. She believes this new framework could help guide researchers toward new treatments and ultimately a cure for the disease.

Multiple sclerosis affects at least 1.3 million people worldwide. Its main characteristic is inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage. Medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease. Genes, diet, pathogens, and vitamin D deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory, frustrating researchers in their search for effective treatment.

"Each time a genetic risk factor has shown a significant increase in MS risk in one population, it has been found to be unimportant in another," Corthals said. "Pathogens like Epstein-Barr virus have been implicated, but there's no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of autoimmunity simply hasn't led to any unifying conclusions about the etiology of the disease."

However, understanding MS as metabolic rather than an autoimmune begins to bring the disease and its causes into focus.

THE LIPID HYPOTHESIS

Corthals believes that the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids (fats and similar compounds) throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors (PPARs), causes a toxic byproduct of "bad" cholesterol called oxidized LDL to form plaques on the affected tissue. The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring. This is essentially the same mechanism involved in atherosclerosis, in which PPAR failure causes plaque accumulation, immune response, and scarring in coronary arteries.

"When lipid metabolism fails in the arteries, you get atherosclerosis," Corthals explains. "When it happens in the central nervous system, you get MS. But the underlying etiology is the same."

A major risk factor for disruption of lipid homeostasis is having high LDL cholesterol. So if PPARs are at the root of MS, it would explain why cases of the disease have been on the rise in recent decades. "In general

people around the world are increasing their intake of sugars and animal fats, which often leads to high LDL cholesterol," Corthals said. "So we would expect to see higher rates of disease related to lipid metabolism—like heart disease and, in this case, MS." This also explains why statin drugs, which are used to treat high cholesterol, have shown promise as an MS treatment.

The lipid hypothesis also sheds light on the link between MS and vitamin D deficiency. Vitamin D helps to lower LDL cholesterol, so it makes sense that a lack of vitamin D increases the likelihood of the disease - especially in the context of a diet high in fats and carbohydrates.

Corthals's framework also explains why MS is more prevalent in women.

"Men and women metabolize fats differently," Corthals said. "In men, PPAR problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role. Disruption of lipid metabolism in women is more likely to affect the production of myelin and the central nervous system. In this way, MS is to women what atherosclerosis is to men, while excluding neither sex from developing the other disease."

In addition to high cholesterol, there are several other risk factors for reduced PPAR function, including pathogens like Epstein-Barr virus, trauma that requires massive cell repair, and certain genetic profiles. In many cases, Corthals says, having just one of these risk factors isn't enough to trigger a collapse of lipid metabolism. But more than one risk factor could cause problems. For example, a genetically weakened PPAR system on its own might not cause disease, but combining that with a pathogen or with a poor diet can cause disease. This helps to explain why different MS triggers seem to be important for some people and populations but not others.

"In the context of autoimmunity, the various risk factors for MS are frustratingly incoherent," Corthals said. "But in the context of lipid metabolism, they make perfect sense."

Much more research is necessary to fully understand the role of PPARs in MS, but Corthals hopes that this new understanding of the disease could eventually lead to new treatments and prevention measures.

"This new framework makes a cure for MS closer than ever," Corthals said.

Angelique Corthals, "Multiple Sclerosis (MS) is not a disease of the immune system," The Quarterly Review of Biology 86:4 (December 2011).

http://www.bbc.co.uk/news/world-asia-16297811

Kim Jong-il death: 'Nature mourns' N Korea leader

Strange natural phenomena have been witnessed in North Korea since the death of the country's leader Kim Jong-il, the state news agency KCNA reports.

Ice cracked on a famous lake "so loud, it seemed to shake the Heavens and the Earth", and a mysterious glow was seen on a revered mountain top, KCNA said. The personality cult surrounding North Korea's founding father and son bestows near-divine status on them. Meanwhile, South Korean intelligence has questioned how Mr Kim died.

Citing US satellite photos, the country's national intelligence service director Won Sei-hoon said there was no sign that the special train, on which Mr Kim is reported to have died while on a visit on Saturday, had ever left Pyongyang over the weekend. South Korea's president says Seoul is trying to show no hostility towards Pyongyang. Lee Myung-bak said a return to stability in the communist state was in the interests of the region.

Seoul is also sending its top nuclear negotiator to Beijing for talks on the situation in its northern neighbour.

In North Korea, state media continue to report mass grieving following Mr Kim's death, reportedly from a heart attack.

'Message in rock'

The 69-year-old had led North Korea since the death of his father in 1994 and an elaborate personality cult, involving multiple stories of alleged miracles or astonishing deeds, has been built up around him.

Even nature is mourning, the state-run Korean Central News Agency reported on Thursday. A snowstorm hit as Mr Kim died and ice on the volcanic Chon lake near his reported birthplace at Mount Paektu cracked, it said.

Following the storm's sudden end at dawn on Tuesday, a message carved in rock - "Mount Paektu, holy mountain of revolution. Kim Jong-il" - glowed brightly, it said. It remained there until sunset.

On the same say, a Manchurian crane also apparently adopted a posture of grief at a statue of the late leader's father in the northern city of Hamhung. "Even the crane seemed to mourn the demise of Kim Jong-il, born of Heaven, after flying down there at dead of cold night, unable to forget him," KCNA reported officials as saying.

On Wednesday state media said more than five million people had already turned out to pay their respects to Kim Jong-il. State media have called on North Koreans to unite behind his designated heir, youngest son Kim Jong-un, who is being called the "Great Successor".

Observers fear that because the transfer of power from father to son had not been formalised before Mr Kim's death, it could trigger instability. Regional neighbours are keenly watching events in the internationally-isolated nuclear-armed state.

'Flexibility'

South Korea, which remains technically at war with its northern neighbour following the 1950-1953 Korean War, put its military on a state of alert after Mr Kim's death was announced. But it has also scrapped a plan to turn on controversial Christmas lights on the border that anger North Korea, and offered "sympathies" over the death.

"The measures we have taken so far are basically aimed at showing North Korea we are not hostile toward the North," Yonhap news agency quoted the president as saying on Thursday. "An early stabilisation of North Korea's system is in the interests of neighbouring countries," he said. "On future relations with North Korea, there is room for exercising as much flexibility as possible. We will discuss the matter with all political parties."

Ties between the two Koreas have been very tense in recent months, following the sinking of a South Korean warship in March 2010 and the shelling of a border island in November 2010. North Korea denies a role in the first incident and says Seoul provoked the second.

Relations have also been hit by Mr Lee's refusal to offer aid to Pyongyang without progress on the nuclear issue. South Korea's nuclear envoy, Lim Sung-nam, is heading to Beijing to discuss how stalled six-nation talks aimed at denuclearising North Korea should be tackled in the wake of Mr Kim's death. South Korean media have also accused Beijing of failing to communicate with Seoul since the announcement came.

http://news.discovery.com/human/pill-coatings-chemicals-hormones-111222.html

Drug Coatings Can Contain Problematic Chemicals

Potentially harmful chemicals show up in a wide variety of drugs and supplements, especially ones with time-release coatings.

By Emily Sohn

A large number of common drugs and supplements contain chemicals called phthalates, which are often found in plastics, found a new study. These chemicals have been linked to a variety of hormonal and reproductive problems in both rats and people. Scientists can't yet say how levels of phthalates in pills might translate into health risks. But for now, pregnant women and children might want to be cautious, said scientists behind the work, especially those who take regular doses of medicine for chronic conditions.

It may be impossible to completely avoid phthalates in medicines, though, because not all phthalate-containing drugs mention inactive ingredients on their packaging. And researchers don't want people to stop taking the pills they need. Instead, the new work points to the need for both further research and possible action by regulating agencies.

"Since medications are an important component of health care, I would not ask the consumer to make these decisions," said Russ Hauser, a reproductive physiologist at the Harvard School of Public Health and one of the authors of the new study. "This decision about whether phthalates should be used in medications should be made at the federal level by the F.D.A."

Phthalates describe a class of chemicals that have a wide range of industrial uses. As ingredients in plastics, they provide flexibility and resilience. In coatings on capsules and pills, they can help regulate the release of drugs over time or the delivery of active ingredients to specific areas in the digestive tract where it is most useful for them to be absorbed.

In previous research, scientists have detected high levels of phthalate breakdown products in the urine of patients taking coated medicines for a variety of conditions, including cystic fibrosis and chronic inflammation of the digestive tract.

To get a sense of how widespread these chemicals are in a broader set of pharmaceutical products, the researchers started with about 450 drugs that are listed as not safe to crush or chew because of their special coatings. Next, they scanned newsletters for information about new drugs, said Kathy Kelley, a co-author and research pharmacist at Boston Unviersity's Slone Epidemiology Center.

To cast an even wider net, they did Internet searches. They trolled the aisles of pharmacies looking for phthalates on ingredient lists. And they contacted manufacturers in cases where that information was not readily available.

Because the FDA does not require companies to disclose the use of phthalates if the chemicals are used in recipes for drug delivery systems that are trade secrets, the researchers also looked through patents for mentions of the chemicals.

In total, the search included between 500 and 1,000 supplements and drugs, both prescription and over-the-counter. Of those, the team reported in Environmental Health Perspectives, more than 100 contained two forms of phthalates that have been shown to have deleterious health effects in studies on animals and human infants.

Called dibutyl phthalate (DBP) and diethyl phthalate (DEP), these chemicals affect the reproductive tracts of developing males, leading to hormonal, fertility and reproductive problems, said Shanna Swan, a reproductive epidemiologist at the Mount Sinai School of Medicine in New York. Among other studies, she has found that preschool boys who had been exposed to the highest levels of DBP in the womb were least likely to choose typically male toys.

In the new study, which only included a fraction of the many thousands of drugs on the market, phthalates showed up in all kinds of products, including blood pressure medications, laxatives, anti-inflammatories, antibiotics, muscle relaxers, dietary supplements and lots of acid-reducers. The chemicals were most common in drugs that had either timed-release or targeted-release properties.

It's too early to know what the health risks are, but pregnant women are the biggest source of concern, Swan said, especially if they take coated medicines for long-term issues. A drug called Asacol, which is prescribed for ulcerative colitis, is known to have particularly high levels of phthalates, for example, and phthalate-free alternatives for that medicine are available.

"I would recommend that pregnant women who take regular medication for a chronic condition try and avoid phthalate-containing medications," Swan said. "These only add to the phthalate burden they are receiving from other sources, such as food, personal care products, and household products."

For anyone who wants to avoid phthalates, Kelly suggested, read labels for inactive ingredients. You can also keep an eye out for delivery systems that are most likely to use phthalates, such as "delayed-release," "controlled-release," "time-release," "targeted-release," and "enteric coatings." Without a direct reference to phthalates, though, it can be impossible to know whether the chemicals are present or how much might be there.

http://www.scientificamerican.com/article.cfm?id=prozac-extinguishes-anxiety-rejuvenating-brain

Fearless Youth: Prozac Extinguishes Anxiety by Rejuvenating the Brain

New research shows that the antidepressant reduces fear in adult mice by increasing brain plasticity

By Ferris Jabr | December 22, 2011 | 19

Once adult lab mice learn to associate a particular stimulus - a sound, a flash of light - with the pain of an electric shock, they don't easily forget it, even when researchers stop the shocks. But a new study in the December 23 issue of Science shows that the antidepressant Prozac (fluoxetine) gives mice the youthful brain plasticity they need to learn that a once-threatening stimulus is now benign. The research may help explain why a combination of therapy and antidepressants is more effective at treating depression, anxiety and post-traumatic stress disorder (PTSD) than either drugs or therapy alone. Antidepressants may prime the adult brain to rewire faulty circuits during therapy.

Nina Karpova, Eero Castrén and their colleagues at the University of Helsinki's Neuroscience Center created and extinguished fearful behaviors in mice. First, Castrén placed mice in a cage and repeatedly played a tone just before electrically shocking their feet. Soon the animals froze in fear whenever they heard the tone, at which point Castrén put them through "extinction training." He moved the mice to a different cage and played the same tone again. This time there was no electric shock.

Researchers have previously shown that young mice less than three weeks old quickly learn that the tone is no longer a herald of danger and stop freezing in fear. But adult mice are harder to put at ease. Even if the adults become less fearful during extinction training, their relaxation is not permanent - a week later the tone turns them into statues again.

In Castrén's study, adult mice that took fluoxetine while they went through extinction training behaved much like young mice - they lost their fear much faster than mice that were not taking the drug, and their anxiety did not return. In contrast, mice that were given fluoxetine but never went through extinction training remained anxious.

Castrén makes an analogy between these findings and the consensus that antidepressants in combination with therapy are almost always more effective than either antidepressants or therapy alone. Scientists know what most antidepressants do at the molecular level—they change the amounts of neurotransmitters in the spaces between neurons, for instance—but how these changes treat depression remains an open question. Research has not supported the idea that antidepressants treat depression simply by correcting chemical imbalances in the brain. More recently, researchers have hypothesized that depression kills neurons whereas antidepressants like Prozac encourage new neural growth in the brain. Castrén's study suggests Prozac returns

regions of the brain to an immature state in which neurons make or break more connections with one another than is typical of the adult brain. In other words, Prozac increases brain plasticity.

Castrén looked for characteristic electrical and molecular signs of plasticity in the brains of mice that received fluoxetine and in those that did not. Specifically, Castrén looked in the amygdala at neural circuits responsible for fear responses. He found that fluoxetine increased levels of a cell-adhesion molecule associated with young neurons and decreased the levels of a transporter protein associated with adult neurons. He also found greater changes in membrane potential in neurons from the brains of mice that had learned to relax. These neurons were also better at synchronizing their communication through a process called long-term potentiation, which is crucial for learning and memory.

"We know that a combination of antidepressant treatment and cognitive behavioral therapy has better effects than either of these treatments alone, but the neurobiological basis is not known," Castrén says. "We show a possible mechanism is bringing the network into a more immature and plastic state."

http://www.physorg.com/news/2011-12-quadrantids-beautiful-jan.html

Quadrantids Will Create Brief, Beautiful Show on Jan. 4

The 2012 Quadrantids, a little-known meteor shower named after an extinct constellation, will present an excellent chance for hardy souls to start the year off with some late-night meteor watching.

PhysOrg.com - Peaking in the wee morning hours of Jan. 4, the Quadrantids have a maximum rate of about 100 per hour, varying between 60-200. The waxing gibbous moon will set around 3 a.m. local time, leaving about two hours of excellent meteor observing before dawn. It's a good thing, too, because unlike the more famous Perseid and Geminid meteor showers, the Quadrantids only last a few hours - it's the morning of Jan. 4, or nothing.

Like the Geminids, the Quadrantids originate from an asteroid, called 2003 EH1. Dynamical studies suggest that this body could very well be a piece of a comet which broke apart several centuries ago, and that the meteors you will see before dawn on Jan. 4 are the small debris from this fragmentation. After hundreds of years orbiting the sun, they will enter our atmosphere at 90,000 mph, burning up 50 miles above Earth's surface -- a fiery end to a long journey!

The Quadrantids derive their name from the constellation of Quadrans Muralis (mural quadrant), which was created by the French astronomer Jerome Lalande in 1795. Located between the constellations of Bootes and Draco, Quadrans represents an early astronomical instrument used to observe and plot stars. Even though the constellation is no longer recognized by astronomers, it was around long enough to give the meteor shower -- first seen in 1825 -- its name.

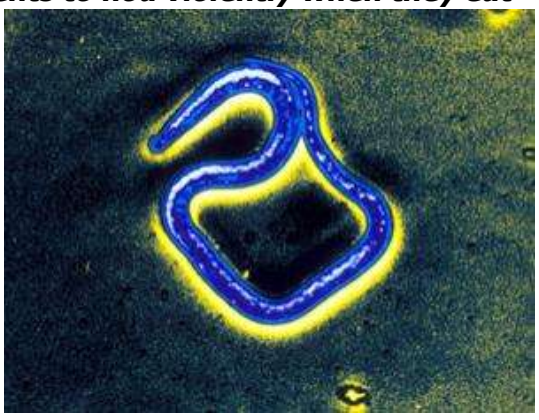
Given the location of the radiant - northern tip of Bootes the Herdsman - only northern hemisphere observers will be able to see Quadrantids. *Provided by JPL/NASA*

http://bit.ly/rTW20K

Mysterious nodding syndrome spreading through Uganda

Large areas of northern Uganda are experiencing an outbreak of nodding syndrome, a mysterious disease that causes young children and adolescents to nod violently when they eat food.

10:30 23 December 2011 by Curtis Abraham, Uganda



Worm in the frame **(Image: Joubert/Phanie/Rex Features)**

The disease, which may be an unusual form of epilepsy, could be linked to the parasitic worm responsible for river blindness, a condition that affects some 18 million people, most of them in Africa.

The current outbreaks are concentrated in the districts of Kitgum, Pader and Gulu. In Pader alone, 66 children and teenagers have died. More than 1000 cases were diagnosed between August and mid-December.

Onchocerca volvulus, a nematode worm that causes river blindness, is known to infest all three affected districts. Nearly all the children with nodding syndrome are thought to live near permanent rivers, another hint of a connection with river blindness.

The link is not clear cut, though. "We know that [Onchocerca volvulus] is involved in some way, but it is a little puzzling because [the worm] is fairly common in areas that do not have nodding disease," says Scott

Dowell, who researches paediatric infectious diseases and is lead investigator into nodding syndrome with the US Centers for Disease Control and Prevention.

There is no known cure for nodding syndrome, so Uganda's Ministry of Health has begun using anticonvulsants such as sodium valproate to treat its signs and symptoms. Meanwhile the disease is continuing to spread, say Janet Oola, Pader's health officer, and Sam William Oyet, the district's medical entomology officer.

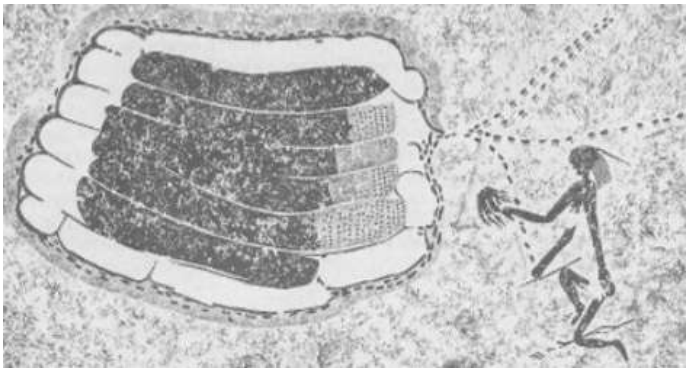
It has now reached the Ugandan district of Yumbe, which borders the Republic of South Sudan – and cases have also been reported in the southern region of the world's newest country. Since gaining independence from the rest of Sudan in July, South Sudan has remained on track to eradicate one of humanity's oldest diseases – guinea worm. It is unclear, though, whether foreign aid for the new country could help prevent the spread of nodding syndrome.

http://blogs.smithsonianmag.com/hominids/2011/12/humans-the-honey-hunters/

Humans, the Honey Hunters

To fuel their added brain power, hominids probably introduced new energy-rich foods to their diet. Researchers have pointed to meat and underground tubers as critical foods that allowed for this brain expansion. But another crucial food may have been honey.

Anthropologists have suggested early Homo was a meat-and-potatoes kind of hominid. Starting roughly 2.5 million years ago, early species of Homo were the first hominids to have brains bigger than an ape's. But brains are expensive, metabolically speaking. To fuel their added brain power, these hominids probably introduced new energy-rich foods to their diet. Researchers have long pointed to meat as the critical food that allowed for this initial brain expansion; after all, stone tools useful for hunting and butchering appear in the archaeological record at this time. More recently, the significance of underground tubers has been highlighted. But another crucial food may have been honey. Alyssa Crittenden, a behavioral ecologist and nutritional anthropologist at the University of Nevada, Las Vegas, makes the case for the sweet liquid's importance in the journal Food and Foodways.



This ancient rock painting from Zimbabwe depicts a person smoking out a beehive. **Image © the International Bee Research Association, www.ibra.org.uk**

Honey has several qualities that make it a super food, Crittenden points out. It's very energy dense, about 80 to 95 percent sugar, and it's a good source of the glucose needed to nurture brain development. Wild honey also contains traces of bee larvae, adding fat, protein, vitamins and minerals. And on top of that, it's easy to digest. The nutritional benefits of honey are clear, but there is no concrete evidence in the fossil record of hominids eating honey; honey consumption doesn't leave behind the kind of scraps that can fossilize the way that hunting and butchering does. So Crittenden relies on some indirect clues to bolster her argument.

First, the significance of honey to human evolution may be inferred from the fact that the sugary liquid is an important dietary staple for people around the world. In Paraguay, for example, the Ache believe honey is the second most important food in their diet, after game meat; honey can provide an Ache with more than 1,100 calories per day. Honey can constitute 80 percent of the calories consumed by the Efe pygmy people of the Congo and 15 percent of the diet of the Hadza of Tanzania. Furthermore, people go to great lengths to get honey. The Hadza often follow honeyguide birds to hives of stinging bees. The honey hunters then burn brush near the entrance of the beehive to smoke out the bees, who become confused and disarmed by the smoke. In Nepal, honey collectors climb bamboo ladders positioned on cliff faces to access nests tucked away in crevices. Ancient art verifies that honey consumption is not a recent phenomenon. Rock art depicting honeycombs, swarms of bees and honey collecting date to as many as 40,000 years ago. Such art has been found in Africa, Europe, Asia and Australia.

Our primate cousins are another line of evidence. A variety of monkeys and apes eat honey today. Baboons and macaques, for example, use their hands and mouths to harvest honey from the nests of stingless bees. Orangutans, gorillas and chimpanzees also like honey and bee larvae, often using sticks to extract the food from hives. If these primates are able to procure honey, Crittenden says, "it is highly likely that early hominids were at least as capable of honey collection." Like modern apes, australopithecines may have used sticks to retrieve honey. Honey may have become a larger component of the diet with the invention of stone tools, which would have allowed our ancestors to more easily open beehives, Crittenden says. "Their success rates would have

skyrocketed." Later, exactly when is debatable, mastering fire may have allowed hominids to smoke out stinging bees, as modern people do, making it even easier to collect honey.

Although Crittenden thinks honey was a critical food that allowed for brain expansion, she acknowledges it wasn't the only food. Our ancestors were omnivores, she says. Meat, tubers, honey - and perhaps other foods - all helped hominids evolve their most notable feature.

http://www.sciencenews.org/view/generic/id/337088/title/Network_analysis_predicts_drug_side_effects

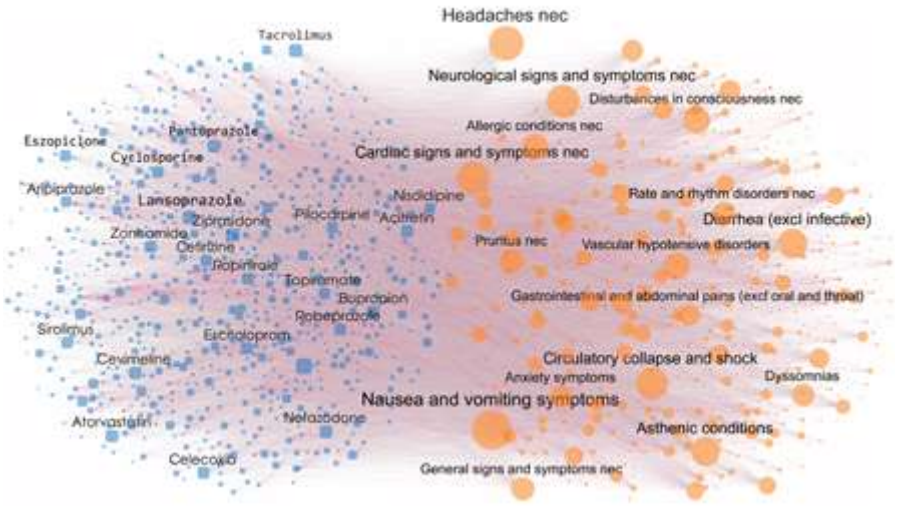
Network analysis predicts drug side effects

Technique can foresee adverse events before medications hit the market

By Rachel Ehrenberg

Using a new mathematical approach, scientists have predicted drug side effects that typically aren't discovered until thousands of people have taken a medication. The technique is especially good at foreseeing side effects that show up after days or months of taking a drug, suggesting that a similar approach could help make drugs safer before they come to market and may even save lives.

Researchers started with a 2005 catalog of existing medications and their known side effects, such as heart attacks or sleeping problems. After linking drugs and their side effects into a network, they instructed a computer to predict likely new connections between drugs and side effects. The program was able to predict 42 percent of the drug–side effect relationships that were later found in patients, the researchers report in the Dec. 21 Science Translational Medicine.



After linking drugs (on the left) to their known side effects (on the right) in a network, researchers trained a computer to predict new connections, an approach that might make drugs safer before they hit the market. **Cami et al/Science Translational Medicine 2011**

"Adverse drug events are very important and understudied," says Russ Altman, a biomedical informatics specialist at Stanford University who wasn't involved with the work. Before a drug ever gets to market it undergoes toxicology testing and clinical trials to establish that it is effective but not dangerous. These trials are often extensive enough to prove that the drug works, but not big enough to say anything meaningful about side effects, says Altman. So, many side effects aren't discovered until after the drug is on the market.

"You routinely find a whole bunch of annoying ones and every now and then there's a showstopper," Altman says. Such interactions lead to 770,000 injuries and deaths each year.

To clear some of the haze surrounding side effects, scientists from Harvard Medical School and Children's Hospital Boston created a network linking 809 medications to 852 side effects that were known as of 2005. The team also added information to their network on chemical properties, such as the drug's melting point and molecular weight, and where the drug does its stuff in the body. Using these data and relationships alone, the computer predicted side effects that were reported in later years, such as the seizure drug zonisamide causing suicidal thoughts in some people and the antibiotic norfloxacin's link to ruptured tendons. It also linked the controversial diabetes drug Avandia (rosiglitazone) to heart attacks, a connection that is supported by some research.

The team tried adding additional information about drugs, such as data describing molecular structure. But the network diagram of the known relationships between drugs and side effects alone had more predictive power and fewer false positives than methods that added the additional information, the team reports.

"We were pleasantly surprised," says team member Ben Reis, who directs the predictive medicine group at Children's Hospital Boston. "The network encodes a lot of information from other worlds. Perhaps that's why it did so well."

There were some side effects for which the model performed less well, such as skin problems, notes mathematician Aurel Cami of Harvard Medical School and Children's Hospital Boston.

This first round established that network math, typically used for assessing social relationships or how a disease spreads, can uncover important drug reactions. Now Reis and Cami are investigating what kinds of data work best and trying to tackle drug-drug interactions that can also be dangerous and are rarely studied in clinical trials.

"We're moving from a paradigm of detection - where it takes sick people to know something is wrong - to prediction," says Reis.

http://www.physorg.com/news/2011-12-year-old-puzzle-superstring-theory-supercomputer.html

A 40-year-old puzzle of superstring theory solved by supercomputer

Three researchers have for the first time revealed the way our universe was born with 3 spatial dimensions from 10-dimensional superstring theory in which spacetime has 9 spatial directions and 1 temporal direction

A group of three researchers from KEK, Shizuoka University and Osaka University has for the first time revealed the way our universe was born with 3 spatial dimensions from 10-dimensional superstring theory in which spacetime has 9 spatial directions and 1 temporal direction. This result was obtained by numerical simulation on a supercomputer.

According to Big Bang cosmology, the universe originated in an explosion from an invisibly tiny point. This theory is strongly supported by observation of the cosmic microwave background and the relative abundance of elements. However, a situation in which the whole universe is a tiny point exceeds the reach of Einstein's general theory of relativity, and for that reason it has not been possible to clarify how the universe actually originated.

In superstring theory, which is considered to be the "theory of everything", all the elementary particles are represented as various oscillation modes of very tiny strings. Among those oscillation modes, there is one that corresponds to a particle that mediates gravity, and thus the general theory of relativity can be naturally extended to the scale of elementary particles. Therefore, it is expected that superstring theory allows the investigation of the birth of the universe. However, actual calculation has been intractable because the interaction between strings is strong, so all investigation thus far has been restricted to discussing various models or scenarios.

Superstring theory predicts a space with 9 dimensions, which poses the big puzzle of how this can be consistent with the 3-dimensional space that we live in.

A group of 3 researchers, Jun Nishimura (associate professor at KEK), Asato Tsuchiya (associate professor at Shizuoka University) and Sang-Woo Kim (project researcher at Osaka University) has succeeded in simulating the birth of the universe, using a supercomputer for calculations based on superstring theory. This showed that the universe had 9 spatial dimensions at the beginning, but only 3 of these underwent expansion at some point in time. This work will be published soon in Physical Review Letters.

In this study, the team established a method for calculating large matrices (in the IKKT matrix model), which represent the interactions of strings, and calculated how the 9-dimensional space changes with time. In the figure, the spatial extents in 9 directions are plotted against time.

If one goes far enough back in time, space is indeed extended in 9 directions, but then at some point only 3 of those directions start to expand rapidly. This result demonstrates, for the first time, that the 3-dimensional space that we are living in indeed emerges from the 9-dimensional space that superstring theory predicts.

This calculation was carried out on the supercomputer Hitachi SR16000 (theoretical performance: 90.3 TFLOPS) at the Yukawa Institute for Theoretical Physics of Kyoto University.

It is almost 40 years since superstring theory was proposed as the theory of everything, extending the general theory of relativity to the scale of elementary particles. However, its validity and its usefulness remained unclear due to the difficulty of performing actual calculations. The newly obtained solution to the space-time dimensionality puzzle strongly supports the validity of the theory.

Furthermore, the establishment of a new method to analyze superstring theory using computers opens up the possibility of applying this theory to various problems. For instance, it should now be possible to provide a theoretical understanding of the inflation that is believed to have taken place in the early universe, and also the accelerating expansion of the universe, whose discovery earned the Nobel Prize in Physics this year. It is expected that superstring theory will develop further and play an important role in solving such puzzles in particle physics as the existence of the dark matter that is suggested by cosmological observations, and the Higgs particle, which is expected to be discovered by LHC experiments. *Provided by KEK*

http://www.eurekalert.org/pub_releases/2011-12/idm-dte122311.php

Discovered the existence of neutrophils in the spleen

These neutrophils are there without there being any infection and play an immunoregulating role

Barcelona - For the first time, it has been discovered that neutrophils exist in the spleen without there being an infection. This important finding made by the research group on the Biology of B Cells of IMIM (Hospital del Mar Research Institute) in collaboration with researchers from Mount Sinai in New York, has also made it possible to determine that these neutrophils have an immunoregulating role.

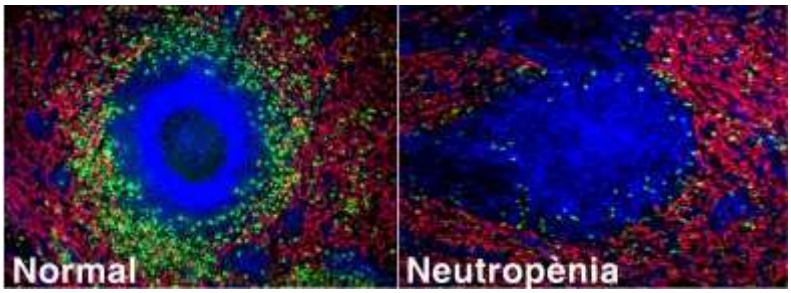


Image of B lymphocytes (in blue) surrounded by neutrophils (in green) and endothelial cells (in red) of a human spleen. The image on the left side corresponds to a normal spleen and on the right side to a spleen of a patient with neutropenia, where the presence of neutrophils is much lower. **IMIM (Hospital del Mar Research Institute)**

Neutrophils are the so-called cleaning cells, since they are the first cells to migrate to a place with an infection and inflammation to destroy the pathogens. Until now, scientific literature had considered neutrophils essentially as lowly qualified soldiers that simply limited the expansion of an infection, as a first action to pave the way for other cells of the immune system in charge of eradicating the infection permanently.

"This study has revealed that neutrophils are found in the spleen without there being an infection, contributing totally new knowledge in the field of biology" explains Andrea Cerutti, the coordinator of the research group on the Biology of B Cells of IMIM, a professor at ICREA and the last signatory of the article.

Researchers noticed that the existence of neutrophils in the spleen started when the fetus is developing, even when there is no infectious process involved; this was not known in scientific literature. The study was expanded to people of different ages and other mammals. Detecting the presence of neutrophils in the spleen suggested that these played a different role in the spleen to the one usually given to them.

The neutrophils in the spleen are located around B lymphocytes to help their activation and offer a first rapid response when there are pathogens. "through several different experimental approaches we have proven that neutrophils in the spleen acquire the ability to interact with B cells or B lymphocytes, inducing the production of antibodies, a role that lymphocytes circulating in blood are not able to do" states Irene Puga, researcher of the IMIM and a signatory of this article.

This finding improves the understanding of the mechanisms with which our immune system protects us against an infection, an essential requirement to better control all pathologies linked to it. Also, when faced with certain diseases, such as neutropenia (or a numeric deficiency of neutrophils), it will become necessary to study not only the deficiency of neturophils, but also how this affects the production of antibodies.

This work opens the door to therapies which are geared at, and more affective against, different pathogens, for example, to develop vaccines to increase the capacity of neutrophils in the spleen so as to have an incidence on the production of antibodies by type B lymphocytes.

This study has been made possible thanks to the simples gathered mainly in different Catalan hospitals such as Hospital del Mar, Hospital Clínic, Hospital de la Vall d'Hebron and Hospital Sant Joan de Déu, together with other centres in the USA and Europe.

Reference article

"B–helper neutrophils stimulate immunoglobulin diversification and production in the marginal zone of the spleen" Irene Puga, Montserrat Cols, Carolina Barra, Bing He, Linda Cassis, Maurizio Gentile, Laura Comerma, Alejo Chorny, Meimei Shan, Weifeng Xu, Giuliana Magri, Daniel M.Knowles, Wayne Tam, April Chiu, James B Bussel, Sergi Serrano, José Antonio Lorente,Beatriz Bellosillo, Josep Lloreta, Nuria Juanpere, Francesc Alameda, Teresa Baró, Cristina Díaz de Heredia, Núria Torán, Albert Català, Montserrat Torrebadell, Claudia Fortuny,Victoria Cusi, Carmen Carreras, George A. Diaz, J. Magarian Blander, Claire-Michèle Farber, Guido Silvestri, Charlotte Cunningham-Rundles, Michaela Calvillo, Carlo Dufour, Lucia Dora Notarangelo, Vassilios Lougaris, Alessandro Plebani, Jean-Laurent Casanova, Stephanie C. Ganal, Andreas Diefenbach, Juan Ignacio Aróstegui, Manel Juan, Jordi Yagüe, Nizar Mahlaoui, Jean Donadieu, Kang Chen & Andrea Cerutti. Nature Immunology 2011