Angiotensin receptor blockers are lower incidence, progression of Alzheimer's disease

Boston, MA—Researchers at Boston University School of Medicine (BUSM) have, for the first time, found that angiotensin receptor blockers (ARBs)—a particular class of anti-hypertensive medicines—are associated with a striking decrease in the occurrence and progression of dementia. Data from this study will be presented this weekend (July 27) at the 2008 International Conference on Alzheimer's disease in Chicago.

Using data from the Decision Support System Database of the U.S. Department of Health System Veterans Affairs (with information on more than 5 million people), researchers looked at records from patients using ARBs, and compared them with subjects who had a similar health status, but were taking different medications. They found patients taking ARBs had about a 35-40 percent lower chance of getting Alzheimer's disease or dementia.

The researchers also examined patients who were already suffering from Alzheimer's disease or dementia, and found those subjects had up to a 45 percent lower chance of developing delirium, being admitted to nursing homes or dying. Patients who appeared to benefit particularly well from use of ARBs were those who had experienced strokes before or during the course of their illness.

According to the researchers these results suggest that ARBs might protect against developing Alzheimer's disease and dementia. "For those who already have dementia, use of ARBs might delay deterioration of brain function and help keep patients out of nursing homes," said lead presenter Benjamin Wolozin, MD, PhD, a professor of pharmacology at BUSM. "The study is particularly interesting because we compared the effects of ARBs to other medications used for treating blood pressure or cardiovascular disease. This suggests that ARBs are more effective than other blood pressure and cardiovascular medications for preventing Alzheimer's disease or dementia," he added.

Although the researchers are unsure why ARBs might be so beneficial, they believe one possibility suggested by prior studies on animal models is that ARBs help prevent nerve cell injury from blood vessel damage or help promote nerve cell recovery after blood vessel damage. Damage to blood vessels is thought to reduce brain capacity and promote dementia, so reducing this damage might prevent the occurrence or progression of dementia.

This study was funded by the Retirement Research Foundation and from the Casten Foundation.

Hip bone density helps predict breast cancer risk

Measuring a woman's bone mineral density can provide additional information that may help more accurately determine a woman's risk of developing breast cancer. That is the conclusion of a new study published in the September 1, 2008 issue of CANCER, a peer-reviewed journal of the American Cancer Society. The study's results suggest that incorporating bone mineral density tests with current risk assessments might significantly improve physicians' ability to predict breast cancer risk in older, postmenopausal women.

Bone mineral density testing is done to diagnose osteoporosis and help assess the risk of fractures. Low bone mineral density is linked to higher risk of fractures, while normal density is linked to lower risk of fractures. It is possible that over a woman's lifetime, hormonal and other factors that lead to higher bone mineral density (and lower risk of fractures) can also lead to higher risk of breast cancer. Studies have found an association between higher bone mineral density and higher breast cancer risk, and bone mineral density tests have been proposed as a potential addition to breast cancer risk models. This study, supported by Eli Lilly & Company, is the first to investigate the relationships among bone mineral density, traditional breast cancer risk assessment tool results, and breast cancer incidence among the same group of postmenopausal women.

To investigate these relationships, Dr. Zhao Chen of the University of Arizona Mel and Enid Zuckerman College of Public Health and her colleagues studied approximately 10,000 post-menopausal women (average age 63) taking part in the Women's Health Initiative, a study conducted in 40 clinical centers throughout the United States and supported by the National Heart, Lung and Blood Institute of the National Institutes of Health. The researchers assessed the women's initial bone mineral density level as well as their score on the Gail risk model, a well known and commonly used tool that estimates five year and lifetime risk of invasive breast cancer for women 35 years of age or older. They then followed the women for an average of approximately 8 years, noting which women developed breast cancer.

As expected, the study found that women with a high Gail score had a 35 percent increased risk of developing breast cancer compared to women with a lower Gail score. But the study also found a 25 percent increase in the risk of developing the disease with each unit increase in total hip bone mineral density t-score. While the two scores were independent of each other, women who had the highest scores on both assessments had a much higher risk in breast cancer.

The findings suggest that adding bone mineral density to currently used risk assessment tools may significantly improve the prediction of breast cancer risk. "Future studies should investigate whether

incorporating bone mineral density and Gail score with other risk factors, such as breast density, can further improve the identification of women at high risk for developing breast cancer," the authors wrote. This study also suggests that bone mineral density is a potential alternative for predicting breast cancer risk in postmenopausal women if Gail score is not available. Additional studies are needed to determine if the results from this investigation are applicable to a broader group of women, including minorities. The findings do not change the use of bone mineral density testing to diagnose osteoporosis or the need to treat osteoporosis in order to reduce the risk of fractures.

***Article**: "Hip bone density predicts breast cancer risk independently of Gail score - results from the Women's Health Initiative." Zhao Chen, Leslie Arendell, Mikel Aickin, Jane Cauley, Cora E. Lewis, and Rowan Chlebowski. CANCER; Published Online: July 28, 2008 (DOI:10.1002/cncr.23674); Print Issue Date: September 1, 2008.*

Prostate cancer patients undergoing hormone therapy may experience cognitive effects

A recent review of the literature has found that hormone deprivation therapy, a commonly used treatment for prostate cancer, may have subtle adverse effects on cognition in patients-- such as in the ability to recall and concentrate. Published in the September 1, 2008 issue of CANCER, a peer-reviewed journal of the American Cancer Society, the study indicates that clinicians and patients should be aware of these potential effects and watch closely for their appearance.

For years, hormone deprivation therapy, also known as androgen depletion therapy, has been used as an effective treatment for prostate cancer because hormones such as testosterone drive the growth of prostate cancer cells. The most common way to achieve androgen depletion is through chemical castration with drugs such as leuprolide and goserelin. Androgen depletion therapy has traditionally been reserved for advanced cases of prostate cancer, but increasing numbers of men with earlier stages of the disease are also undergoing the treatment.

Prostate cancer patients who are prescribed these drugs often stay on them for the duration of their life, and researchers have been documenting the potential adverse effects associated with their use. Men may experience hot flashes, osteoporosis, anemia, fatigue, loss of libido, erectile dysfunction, risk of diabetes, risk of cardiovascular disease, emotional distress, and other effects. Research also indicates that androgen depletion may impact cognitive functioning, which can affect a patient's decision-making skills and quality of life.

Unfortunately, only a handful of relatively small studies have investigated the impact of androgen depletion on cognitive functioning, and some of these studies have reported contradictory results. Dr. Christian Nelson, a psychologist at Memorial Sloan-Kettering Cancer Center in New York City and his colleagues recently conducted the first review of these studies and summarized their overall results.

After performing a systematic literature search of studies in animals and humans, Dr. Nelson's team found that testosterone and its derivatives may impact cognition via several mechanisms in the brain. For example, testosterone can modulate brain chemicals called neurotransmitters and stimulate the connections between neurons. Also, studies that have examined the impact of androgen depletion therapy in prostate cancer patients indicate that between 47% and 69% of men being treated decline in at least one cognitive area, most commonly in processes dependent on spatial ability and in high-order capacities such as the ability to multi-task.

The findings indicate that larger, more thorough studies that include brain imaging techniques are needed to better understand the nature and extent of the cognitive effects of androgen depletion.

In addition, researchers are exploring the effectiveness of using androgen depletion therapy in men with rising levels of prostate specific antigen, a potential precursor to prostate cancer. The authors concluded that "as the use of androgen depletion therapy increases, clinicians should become aware of this relationship [with cognitive decline], and inform and monitor patients for this possible side effect of treatment."

***Article**: "The cognitive effects of hormone therapy in men with prostate cancer: a review." Christian J. Nelson, Jennifer S. Lee, Maria C. Gamboa, and Andrew J. Roth. CANCER; Published Online: July 28, 2008 (DOI: 10.1002/cncr.23658); Print Issue Date: September 1, 2008.*

Erectile dysfunction drugs allowed more chemotherapy to reach brain tumors in laboratory study

The drugs blocked an enzyme and opened blood vessels to tumors but not normal brain

LOS ANGELES (July 28, 2008) – In a study using laboratory animals, researchers found that medications commonly prescribed for erectile dysfunction opened a mechanism called the blood-brain tumor barrier and increased delivery of cancer-fighting drugs to malignant brain tumors.

The experiments were conducted at Cedars-Sinai Medical Center's Maxine Dunitz Neurosurgical Institute and published in Brain Research.

Viagra (sildenafil) and Levitra (vardenafil) are known as PDE5 inhibitors because they block an enzyme, phosphodiesterase5, which interrupts a series of biochemical events that cause the decreased blood flow of

erectile dysfunction. This laboratory rat study, published online ahead of print in the journal, found that similar biochemical interactions in the small vessels of the brain play a major role in the blood-brain tumor barrier, which impedes delivery of anti-tumor drugs into brain tumors. PDE5 inhibitors were found to open the barrier and increase drug transport in this early animal study.

Although the normal blood-brain barrier, which regulates access to the brain from the bloodstream, shares many characteristics with the blood-brain tumor barrier, the signaling mechanism blocked by PDE5 inhibitors is unique to the blood-brain tumor barrier. This allows the PDE5 inhibitors to selectively increase drug transport to malignant brain tumors without affecting normal brain tissue. According to the researchers, these findings may have significant implications in improving drug delivery to brain tumors in patients.

"This is the first study to show that oral administration of PDE5 inhibitors increases the rate of transport of compounds across the blood-brain tumor barrier and improves the effectiveness of the anti-tumor drug adriamycin in the treatment of brain tumors in a rat model. We chose adriamycin for this study because it is one of the most effective drugs against brain tumor cell lines in the laboratory but it has very little effect in animals and humans because it is unable to cross the blood-brain tumor barrier. The combination of vardenafil and adriamycin resulted in longer survival and smaller tumor size," said neurosurgeon Keith L. Black, M.D., chairman of the Department of Neurosurgery at Cedars-Sinai Medical Center and director of the Maxine Dunitz Neurosurgical Institute.

Black, the article's first and corresponding author, has been recognized for his earlier groundbreaking work to break through the blood-brain tumor barrier with natural and synthetic bradykinin, a peptide that temporarily opens the barrier and increases anti-cancer drug delivery into certain tumors by more than 1,000 percent. In 2000, he received the Javits Neuroscience Investigator Award from the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, for his blood-brain barrier research.

In the current studies, the blood-brain tumor barrier-opening effects of PDE5 lasted considerably longer than those of bradykinin and allowed greater transport across the barrier into tumor tissues. Because vardenafil was found to be more effective than sildenafil in increasing blood-brain tumor barrier permeability and transport, vardenafil was used in a survival study of 29 tumor-bearing rats. Those treated with saline (control) survived 32 days on average while those treated with vardenafil alone survived about 35 days and those treated with adriamycin alone survived about 42 days. When vardenafil was combined with adriamycin, rats survived an average 53 days.

Although the researchers exposed the laboratory animals to doses of sildenafil and vardenafil that are comparable to the dose range approved for erectile dysfunction in humans, there were no detectable side effects in the rats, and neither drug increased transport of tracers into normal brain tissue.

Funding for the studies was provided by the National Institute of Neurological Disorders and Stroke (the Javits Award), the Maxine Dunitz Neurosurgical Institute and the Ruth and Lawrence Harvey Chair in Neuroscience, held by Black.
***Citation**: Brain Research, "PDE5 Inhibitors Enhance Tumor Permeability and Efficacy of Chemotherapy in a Rat Brain Tumor Model," available online ahead of print.*

Snapshot of past climate reveals no ice in Antarctica millions of years ago

A snapshot of New Zealand's climate 40 million years ago reveals a greenhouse Earth, with warmer seas and little or no ice in Antarctica, according to research published this week in the journal Geology

A snapshot of New Zealand's climate 40 million years ago reveals a greenhouse Earth, with warmer seas and little or no ice in Antarctica, according to research published this week in the journal Geology.

The study suggests that Antarctica at that time was yet to develop extensive ice sheets. Back then, New Zealand was about 1100 km further south, at the same latitude as the southern tip of South America – so was closer to Antarctica – but the researchers found that the water temperature was 23-25°C at the sea surface and 11-13°C at the bottom.

"This is too warm to be the Antarctic water we know today," said Dr Catherine (Cat) Burgess from Cardiff University's School of Earth and Ocean Sciences, and lead-author of the paper. "And the seawater chemistry shows there was little or no ice on the planet."

These new insights come from the chemical analysis of exceptionally well preserved fossils of marine micro-organisms called foraminifers, discovered in marine rocks from New Zealand. The researchers tested the calcium carbonate shells from these fossils, which were found in 40 million-year-old sediments on a cliff face at Hampden Beach, South Island.

"Because the fossils are so well preserved, they provide more accurate temperature records." added Dr Burgess. "Our findings demonstrate that the water temperature these creatures lived in was much warmer than previous records have shown."

"Although we did not measure carbon dioxide, several studies suggest that greenhouse gases forty million years ago were similar to those levels that are forecast for the end of this century and beyond.

Our work provides another piece of evidence that, in a time period with relatively high carbon dioxide levels, temperatures were higher and ice sheets were much smaller and likely to have been completely absent."

The rock sequence from the cliff face covers a time span of 70,000 years and shows cyclical temperature variations with a period of about 18,000 years. The temperature oscillation is likely to be related to the Earth's orbital patterns.

The research was funded by the Natural Environment Research Council, the Netherlands Organisation for Scientific Research (NOW) and GNS Science, New Zealand.

Notes for editors *1. "Middle Eocene climate cyclicity in the Southern Pacific: Implications for global ice volume" is published in the August issue of Geology. (vol.36, no.8, p.651-654; doi:10.1130/G24762A.1)*

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Wild orangutans treat pain with natural anti-inflammatory

* 11:21 28 July 2008
* NewScientist.com news service
*** Matt Walker**

Wild orangutans have been spotted using naturally occurring anti-inflammatory drugs.

Four individuals have been seen rubbing a soothing balm onto their limbs, the first known examples of orangutans self medicating. Great apes have never before been seen using drugs in this way. Remarkably though, local people use the same balm, administering it in a similar way to treat aches and pains.

Primatologist Helen Morrogh-Bernard, of the University of Cambridge, UK, made the discovery while studying Bornean orangutans (Pongo pygmaeus) in the Sabangau Peat Swamp Forest in Central Kalimantan, Indonesia.

In 2005, she witnessed an adult female pick a handful of leaves from a plant and then chew them, mixing the leaves with her saliva to produce a green-white lather. The female then scooped up some of the lather with her right hand and applied it up and down the back of her left arm, from the base of the shoulder to the wrist, just as a person would apply sunscreen.

"She was concentrating on her arm only and was methodical in the way she was applying the soapy foam," says Morrogh-Bernard. "I knew this must be some form of self-medication."

After using the leaves, the orangutan dropped them, allowing Morrogh-Bernard and her assistant to find out what they were. The leaves belong to a genus called Commelina, a group of plants that orangutans do not eat as part of their normal diet. However, local indigenous people know the plant well, grinding it into a balm and applying it to their skin to treat muscular pain, sore bones and swellings.

Chimpanzees and gorillas are thought to self medicate, mainly by swallowing rough leaves or chewed plant pith to help flush out intestinal parasites. A few monkey species and one species of lemur are known to rub concoctions, such as tobacco, onion or garlic onto their fur to repel insects or parasites. But wild great apes have never before been seen rubbing ointments onto their fur.

Morrogh-Bernard, who has since seen three other orangutans using the plant in the same way, says the finding "links apes and humans directly".

The apes may not have learnt how to apply the anti-inflammatory ointment from local people, she says, but perhaps ancestors of the indigenous population learnt about the drug from the apes.

Journal Reference*: International Journal of Primatology (DOI:10.1007/s10764-008-9266-5)*

Blue light helps flies feel the force

A PROTEIN that detects blue light also helps fruit flies tune into the Earth's magnetic field. Sensing this weak field is crucial for the homing and migration abilities of many animals.

Researchers suspected that proteins known as cryptochromes detect magnetic fields, perhaps by making charged molecules - called free radicals - when they're struck by blue light. The number of free radicals formed may depend on the strength of the field, indicating the creature's latitude. But evidence from migratory warblers and salamanders has so far only hinted at this connection.

Now a team led by Robert Gegear and Steven Reppert of the University of Massachusetts in Worcester, has shown that fruit flies must have these proteins in order to perceive a magnetic field. The team built a T-shaped maze, on one side of which was a field roughly 10 times as strong as Earth's. Once flies had learned to associate the magnet with a sugar treat, they drifted towards the magnetised side even when no sugar was there. Flies with an inactive version of cryptochrome could not tell one side from the other.

While the experiment does not prove that other animals use the same proteins to navigate, the fruit flies could help researchers explain how the proteins work - and perhaps find out how migratory animals such as birds and butterflies make their way home.

Hypnosis shown to reduce symptoms of dementia

A scientist at the University of Liverpool has found that hypnosis can slow down the impacts of dementia and improve quality of life for those living with the condition.

Forensic psychologist, Dr Simon Duff, investigated the effects of hypnosis on people living with dementia and compared the treatment to mainstream health-care methods. He also looked at how hypnosis compared to a type of group therapy in which participants were encouraged to discuss news and current affairs.

They found that people living with dementia who had received hypnosis therapy showed an improvement in concentration, memory and socialisation compared to the other two treatment groups. Relaxation, motivation and daily living activities also improved with the use of hypnosis.

Dr Duff said: "Over a nine month period of weekly sessions, it became clear that the participants attending the discussion group remained the same throughout. The group who received 'treatment as usual' showed a small decline over the assessment period, yet those having regular hypnosis sessions showed real improvement across all of the areas that we looked at.

"Participants who are aware of the onset of dementia may become depressed and anxious at their gradual loss of cognitive ability and so hypnosis – which is a tool for relaxation – can really help the mind concentrate on positive activity like socialisation."

Further research will now take place to establish whether hypnosis maintains its effects on dementia as the illness progresses, over longer periods of time.

Dr Dan Nightingale, co-author of the research and leading dementia consultant at the Abacus Clinic in Newark, added: "Evidence to date has shown that we can enhance the quality of life for people living with dementia through the correct use of hypnosis. We have now developed a course for clinicians who wish to incorporate hypnosis into health care plans."

Compound that helps rice grow reduces nerve, vascular damage from diabetes

Toni Baker - 2008 July 28

You may want to soak your brown rice.

Researchers have found that a compound that helps rice seed grow, springs back into action when brown rice is placed in water overnight before cooking, significantly reducing the nerve and vascular damage that often result from diabetes.

"You have to let it grow, germinate a little bit," says Dr. Robert K. Yu, director of the Institute of Molecular Medicine and Genetics and Institute of Neuroscience at the Medical College of Georgia. "Some of the active ingredients generated as a result of the germination process are beneficial to you."

Germinated brown rice's ability to help diabetics lower their blood sugar has been shown but how it works remained unknown. New research, published online in the Journal of Lipid Research, shows the growth factor acylated steryl glucosides or ASG, helps normalize blood sugar and enzymes that are out-of-whack in diabetes.

"The advantage of knowing this key ingredient and its structure is we can now make a ton of it; you don't have to rely on rice to produce it or eating rice to get this beneficial effect," says Dr. Yu, the paper's corresponding author.

Studies were done in animal models of type 1 diabetes with two different blood sugar levels that reflect patients' varying blood sugars. They were fed diets of white, brown or pre-germinated brown rice. Unlike white rice, less-processed brown rice still has some of the germ or growth structure that, after about 24 hours in water, resumes activity. Scientists watched as the resurrected ASG, a growth factor and lipid, helped normalize metabolism.

"When blood sugar levels increase, the metabolic balance changes," says Dr. Seigo Usuki, neurobiologist in the MCG School of Medicine and the paper's first author. "Part of the way we know this growth factor works is by increasing levels of good enzymes that are decreased in diabetes."

Dr. Usuki is talking about enzymes such as ATPase, which help maintain nerve membranes so they can conduct electricity and communicate. Decrease of ATPase is a hallmark of the nerve damage that accompanies diabetes. Also reduced in diabetes is homocysteine-thiolactonase, or HTase, an enzyme that decreases levels of homocysteine, a known risk factor for vascular disease. The liver produces a low level of homocysteine but that level is elevated in diabetes while the enzyme that controls it decreases. Unchecked, homocysteine makes oxidative stress compounds that injure and kill cells. HTase is one way HDL, the so-called "good cholesterol," helps protect blood vessels from disease. A regular diet of pre-germinated brown rice diet helps get both back to a healthier level.

Fancl Hatsuga Genmai Co., Ltd., in Yokohama, Japan, which funded the studies and supplied the pre-germinated rice, already is working with Dr. Usuki on a supplement that can provide consumers who prefer not to soak – or eat – rice with the benefits of ASG.

The MCG research team reported in December 2007 in Nutrition & Metabolism that pre-germinated brown rice was better at protecting nerves from diabetes than un-soaked brown or white rice. They showed a then-unidentified lipid helped protect the nerve membrane and increase activity of HTase and the good cholesterol. Germination also is known to increase levels of the neurotransmitter GABA, which is believed to have many beneficial health effects such as lowering blood pressure, improving cognition and lowering blood glucose levels. However the MCG scientists have shown the lipid has a more powerful impact on HTase activity.

The germ layer activated by soaking brown rice contains many vitamins and minerals in addition to the bioactive ingredient that would be beneficial to everyone, Dr. Yu says. The roughage of the rice grain also is helpful.

Alleviating the Fear of Falling

Ritalin could prevent fatal falls, a TAU study finds

Getting old isn't just about body aches and pains. As we get older, our risk of falling greatly increases. Old bones don't heal like young ones, and for senior citizens, falls are a leading cause of death.

But researchers at Tel Aviv University provide hopeful news from an unexpected source. Ritalin, used for managing Attention Deficit Disorder in hyperactive children, may have therapeutic benefits for seniors too. Older people who take methylphenidate (the generic name for Ritalin) may improve their cognitive abilities and their gait, cutting the risk for serious falls. This surprising finding was made by Prof. Jeffrey M. Hausdorff, a lecturer at the Sackler School of Medicine at Tel Aviv University, and his colleagues, and reported in the Journal of the American Geriatrics Society.

TAU's researchers are the first to investigate the power of Ritalin to prevent falling in the elderly. After only one dose of Ritalin, seniors walked with a steadier gait and performed better on a standard screening test for fall risk, Prof. Hausdorff found.

"Our study suggests that it may be possible to reduce the risk of falls in older adults by treating cognitive deficits associated with aging and disease," Prof. Hausdorff said. "This is consistent with a growing body of literature which has demonstrated that walking is not a simple, automated task, as it was once believed," he explains. "We've taken this idea a step further and shown that you can capitalize on this dependence on cognitive function and use it to reduce the risk of falls."

Sidestepping a Fatal Fall

Knowing how to improve cognitive functioning could lead to fewer falls -- and fewer related deaths -- among America's senior population. "Some have estimated that more than 50 percent of seniors who break a hip from a fall will die within the year," says Prof. Hausdorff. This is partly due to a vicious cycle fueled by a fear of falling and subsequent inactivity, causing elderly patients to spiral into further decline.

In the recent study, Prof. Hausdorff gave Ritalin to 26 healthy seniors who resided in independent living arrangements. They were assessed for fall risk before taking a single dose of Ritalin or placebo administered in a double blind fashion. The subjects were then asked to perform the "Timed Up and Go" test, during which they were asked to stand up from a chair, walk at a normal pace for about ten feet and then turn around, walk back and sit down. The longer it takes to accomplish the task, the greater the fall risk.

Therapeutic Value for Parkinson's Patients

Those who took Ritalin performed the test quicker and had less variability in their "stride time," a common sign of instability, researchers found. Preliminary research on patients with Parkinson's disease also shows that Ritalin may help decrease the risk of falling even in the face of this common neurodegenerative disease.

While the notion of treating fall risk with a pill is "an intriguing concept," says Prof. Hausdorff, it is not likely to be a silver bullet solution, and it is still too early to recommend Ritalin on a wide scale basis. Additional studies are planned to more fully assess clinical utility, but it's likely that, for example, the drug would not be suitable for people who have certain types of heart disease.

Doctor's Orders: Get off the Couch, Strengthen Bones and the Brain

What can seniors do to prevent a potentially catastrophic fall now? "Remain active, that's been well-established," says Prof. Hausdorff. "Our findings indicate that it's also important to look at falls and relate them to one's cognitive functioning. It's important to strengthen your muscles, but seniors need to strengthen their minds as well."

Prof. Hausdorff is currently the Director of the Laboratory for the Analysis of Gait and Neurodynamics in the Neurology Department of the Tel-Aviv Sourasky Medical Center (Ichilov Hospital) and also lectures at Harvard Medical School.

How molecules out of balance lead to human multiple myeloma and other cancers

An international team of scientists has identified processes that are heavily implicated in human multiple myeloma and other B cell cancers, moving us closer to developing quick tests and readouts that could help in the tailored treatment of patients.

B cells, the white blood cells that produce antibodies, form a key part of our 'immune response'. To remain healthy, we need to maintain the right number of B cells, not too many and not too few. This in turn relies on an intricate interplay of molecules within our bodies, and inside our B cells.

Professor Fabienne Mackay, Professor Klaus Rajewsky and Dr Marc Schmidt-Supprian, from Sydney's Garvan Institute of Medical Research, Harvard Medical School and Germany's Max Planck Institute of Biochemistry respectively, have identified two processes that appear to influence B cell driven cancers. Their findings are published online this week in the international journal Proceedings of the National Academy of Sciences (US).

"We already know that the over-expression or mutation of molecules known as NIK and TRAF3 in B cells is associated with human multiple myeloma," said Professor Mackay. "Our collaborative research uncovered two distinct processes involving these molecules that help explain why."

The first process involves NIK, an enzyme that acts closely with BAFF, the substance that regulates the number of B cells in our bodies. Work done previously by Professor Mackay on BAFF showed that levels correlate with B cell hyperplasia (expansion) and cancer. The current study shows that if we have too much NIK in our systems, then our B cells will also expand, and we will be prone to cancer.

The second process, associated with the first, involves TRAF3, the molecule that negatively regulates NIK.

Professor Mackay explained that in a healthy person, NIK and TRAF3 work together, helping to maintain the right number of B cells for survival. "But when there are mutations in either molecule, they become uncoupled. In other words, TRAF 3 no longer represses the action of NIK when necessary."

"The important thing to note is that when you uncouple NIK from TRAF3 action, its levels are not necessarily going to go up, but its function is going to be changed. This can lead to B cell hyperplasia and cancer."

"Our paper is saying 'be careful'! Sometimes you can find a patient without high expression of NIK, so you think NIK is not implicated, where it might be."

"In the very near future, we will have the capacity to do blood tests and test for specific gene mutations in patients. Once you identify a mutation, you can bypass the action of that gene, with targeted medications."

"Both NIK and TRAF3 are molecules, so can potentially be targeted by pharmaceuticals. We anticipate that new treatments for cancers may emerge from our findings."

'Chicken and chips' theory of Pacific migration

A new study of DNA from ancient and modern chickens has shed light on the controversy about the extent of pre-historic Polynesian contact with the Americas.

The study questions recent claims that chickens were first introduced into South America by Polynesians, before the arrival of Spanish chickens in the 15th century following Christopher Columbus.

It is published this week in the Proceedings of the National Academy of Sciences USA (July 28) by an international research group, including scientists from the University of Adelaide's Australian Centre for Ancient DNA (ACAD).

ACAD Director Professor Alan Cooper says there has been considerable debate about the existence and degree of contact between Polynesians and South Americans, with the presence of the sweet potato throughout the Pacific often used as evidence of early trading contacts.

"Similarly, Polynesians are known to have spread chickens across the Pacific at least as far as Easter Island, but were not thought to have introduced them to South America," he says.

A recent study claimed to have found the first direct evidence of a genetic link between ancient Polynesian and apparently pre-Columbian chickens from archaeological sites in Chile, supporting the idea that there was extensive contact between Polynesia and South America and that chicken and `chips' had been traded in opposite directions.

The current work challenges this conclusion however, by generating DNA data from 41 native Chilean chicken specimens, and comparing these with over 1000 modern domestic chickens from around the world, and the previously published DNA from Polynesian and Chilean chicken bones.

"The results showed that the ancient Polynesian and Chilean chickens possessed a genetic sequence that is the most common in the world today, the so-called `KFC' gene" Professor Cooper says.

"This sequence would undoubtedly have been common in the early Spanish chickens, and therefore provides no evidence of Polynesian contact. So while we can say the KFC chicken was popular amongst early Polynesian voyagers, we certainly can't use it as evidence for trade with South America."

The researchers did find a highly unusual DNA sequence in the ancient Easter Island chickens, which originate from Indonesia or the Philippines, but this apparently did not get passed on to South America.

"This is important because Easter Island is commonly thought of as a major jumping off point for Polynesian contact with South America," says team member and ACAD PhD student Nicolas Rawlence.

According to project leader Dr Jaime Gongora from the University of Sydney, many people in South America like to believe they are descendants of Polynesians. "This study does not disprove this idea, but we have found no evidence to support pre-historic contact."

Hey fever! The surprise benefit of allergies

Long-suffering victims of allergies such as asthma and hay fever might enjoy a surprise benefit, according to research led by the University of New South Wales (UNSW).

In a paper presented at an international symposium in Sydney, the researchers show that people with one of these atopic diseases are up to 25 percent less likely to get the most common type of Non-Hodgkin Lymphoma (NHL).

The InterLymph Symposium is co-hosted by the Leukaemia Foundation, the Cancer Institute NSW, UNSW and the National Centre in HIV Epidemiology and Clinical Research.

The more atopic diseases the individual has, the less likely they are to succumb to NHL. If an individual has three of these conditions, they are 40 percent less likely to get NHL.

Having had asthma and hay fever for a long time, also appears to be of greater benefit.

The result is significant given that the incidence of NHL in developed countries has escalated dramatically in the past 50 years. It is three times more prevalent now than it was in 1950, making it the sixth most common cause of cancer death in Australia, yet the cause of most cases remains unknown.

"This was a surprise result," said the lead author, Dr Claire Vajdic. "The only known strong risk factors for NHL are immune deficiency and certain infections. This occurs in people with uncontrolled HIV infection, and those who have had a solid organ transplant.

"So we thought other forms of immune dysregulation such as atopic diseases – including hayfever, asthma and food allergies – might relate to the development of lymphoma. It was therefore intuitive to think that these conditions would increase the risk, but in fact, they do the reverse," she said.

The research found that risk was reduced in B-cell NHL only. This is the most common type of NHL.

"While the relevant biological mechanisms are not yet known, the pooled data indicate that chronic and multiple atopic conditions impart the greatest reduction in risk," said Dr Vajdic. "Investigation of the genetic and environmental factors underlying atopy and the apparent inverse effect of atopy on NHL risk will inform our understanding of the complex biological pathways that may be involved."

The research involved a pooled analysis of data from 13 case-control studies involving 13,535 NHL cases and 16,388 control participants, funded by the Leukaemia Foundation.

Boozy tree shrews avoid fermented fruit hangovers

* 22:00 28 July 2008
* NewScientist.com news service
*** Jeff Hecht**

We have distant cousins who regularly guzzle alcoholic floral nectar without regretting it the morning after.

Pen-tailed tree shrews, which are related to the ancestors of primates, eat giant flower clusters of the stemless bertam palm in the rainforests of Malaysia.

Sugars in the palm's floral nectar ferment in the warm, moist environment, producing alcohol in concentrations up to a beer-like 3.8% with a mean concentration of about 0.6%.

As the nectar is an essential part of the shrews' diet, their taste for alcohol may help us understand the evolutionary forces that drive humans to drink, argues Frank Wiens of the University of Bayreuth, Germany, who carried out the study.

Mammalian pollinators

The alcohol content of the nectar is no accident. The flower structure fosters fermentation, apparently to attract mammalian pollinators.

The tree shrews do not seem to get drunk, although they consume enough alcohol to be intoxicated about a third of the time if they had a human-like metabolism. Their fur reveals the key to their sobriety – a metabolic byproduct called ethyl glucuronide (EtG).

Tree shrews seem to convert much of the alcohol they consume into EtG, which ends up in their fur. The compound is seen at levels normally found only in severely alcoholic humans although humans convert only a little alcohol into EtG.

'Beautiful example'

"It's a beautiful example of the natural biology of alcohol consumption, which people have totally neglected in alcohol research," says Robert Dudley of the University of California at Berkeley.

Dudley has previously suggested that our taste for alcohol may be an "evolutionary hangover" from our fruit-eating primate ancestors, who developed a taste for fermented fruit.

Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0801628105)

New study finds healthy children of Alzheimer patients show early brain changes

Medical College of Wisconsin researchers in Milwaukee have reported that children of Alzheimer's patients who are carriers of a genetic risk factor for Alzheimer's disease have neurological changes that are detectable long before clinical symptoms may appear.

Functional MRI brain imaging revealed that these symptomless carriers of the APOE-4 gene demonstrated significantly reduced functional brain connectivity between the hippocampus and the posterior cingulated cortex, two important brain structures for memory processing. These structures are relevant for information acquisition, filtering and sorting.

The study, conducted at Froedtert Hospital, was led by Shi Jiang Li, Ph.D., professor of biophysics, and was presented at the Alzheimer's Association International Conference on Alzheimer's disease in Chicago, July 29th

"Just as if cancer could be detected when there were only a few cells, decades before it was evident, the advantage of identifying those at great risk for having Alzheimer's would be of tremendous value in development of interventional therapies," says Dr. Li.

The researchers studied 28 neurologically-normal subjects, between ages 45 and 65. Twelve carried the APOE-4 gene and 16 did not. The two groups showed no significant difference in age, educational level, or neuropsychological performances. All subjects received fMRI scans. For each subject, functional connectivity between the two brain structures was measured in a resting state.

Results showed that functional connectivity in the non APOE-4 carriers was approximately 65 percent better than that of the carriers.

Other members of the research team were Piero Antuono, M.D., professor of neurology, and Zhilin Wu, Ph.D., Chunming Xie, Ph.D., and Jennifer L. Jones, M.S., research associates in the departments of biophysics and neurology.

1/5 of British adult survivors of childhood cancer smoke despite hazards

One-fifth of British adult survivors of childhood cancers are current smokers, and nearly a third have been regular smokers at some point in their lives, according to a study in the July 29 online issue of the Journal of the National Cancer Institute.

Adult survivors of childhood cancer are at increased risk of developing cardiovascular disease, lung problems, and second malignancies, relative to the general public. These increased risks are due to long-term effects of the original cancer and its treatment, as well as to genetic conditions that predispose the survivors to multiple cancers. Smoking would be an additional source of risk for this population.

To learn what fraction of adult survivors are current smokers or have smoked regularly in the past, Clare Frobisher, Ph.D., of the University of Birmingham, UK, and colleagues sent surveys to all those who could be contacted from among 14,836 eligible survivors of childhood cancer in the National Registry of Childhood Tumors. To be eligible for the study, survivors had to have been diagnosed with their primary cancer between 1940 and 1991 and be aged 16 years or older at the time of the survey. Of those survivors, 10,326 returned completed study questionnaires and were included in the current analysis.

Of the respondents, 20 percent were current regular smokers and 29.8 percent were regular smokers at some time in their life prior to the completion of the survey. When the researchers analyzed the responses by tumor site, they found that survivors of central nervous system cancers or heritable retinoblastoma were least likely to smoke, while survivors of Wilms tumor, Hodgkin lymphoma, or soft tissue sarcomas were most likely to report being a regular current smoker. Individuals who had been treated with radiation or chemotherapy were less likely to smoke than those who had not received that type of therapy. Also, those who did not have regular hospital follow-up appointments were more likely to smoke than those who did.

The rate of current smoking in the survivors was approximately half of the rate in the general British population. The socioeconomic factors that are associated with an increased risk of smoking in the general public, though, are the same as those in the adult survivor group, including manual occupations compared with managerial or professional work, lower educational attainment, and being widowed, divorced, or separated.

The relatively high rate of smoking in survivors of Wilms tumor, Hodgkin lymphoma, and soft tissue sarcomas is concerning because previous research suggests that these survivors are at a particularly high risk for second malignancies.

The researchers conclude that although the rate of smoking in adult survivors of childhood cancer is lower than in the general public, further efforts are needed to reduce the smoking prevalence in this group. In general, any program of clinical follow-up for survivors of childhood cancer should include advice on the health risks of smoking, the authors assert. "Smoking cessation interventions would be more appropriate for the [British Childhood Cancer Survivor Study] cohort than smoking prevention interventions because a high proportion of the survivors were older than the age at which most individuals initiate smoking (i.e., ≤20 years of age)," the authors write.

In an accompanying editorial, Karen Emmons, Ph.D., of the Dana-Farber Cancer Institute and Harvard School of Public Health in Boston notes that the new findings are remarkably similar to data from the U.S. Childhood Cancer Survivor Study, in which 17 percent of adult survivors reported being current smokers and 28 percent reported being ever smokers. The good news is that the rates are lower than the general public. The bad news, according to Emmons, is that for the survivors who do smoke, the habit is likely to exacerbate the already negative long-term effects of cancer treatment.

More needs to be done to reduce the rate of smoking in adult cancer survivors, Emmons writes, noting that fewer than half of the survivorship programs in the U.S. currently offer smoking cessation services. Beyond just treating this issue specifically, however, Emmons argues that broader efforts are needed to improve the socioeconomic pressures and social disadvantages that encourage smoking and reduce public health. "It is time to think well beyond our disciplinary boundaries and implement inter¬ventions that we know are efficacious, such as provider-delivered counseling and pharmacotherapy, and seek solutions for the social conditions that serve as a trajectory for a lifetime of smoking," she writes.

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New research challenges notion that dinosaur soft tissues still survive

Paleontologists in 2005 hailed research that apparently showed that soft, pliable tissues had been recovered from dissolved dinosaur bones, a major finding that would substantially widen the known range of preserved biomolecules.

But new research challenges that finding and suggests that the supposed recovered dinosaur tissue is in reality biofilm – or slime.

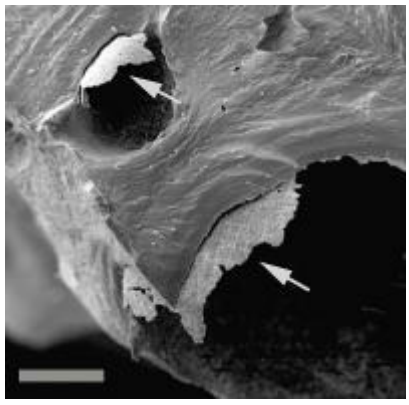
"I believed that preserved soft tissues had been found, but I had to change my opinion," said Thomas Kaye, an associate researcher at the Burke Museum of Natural History and Culture at the University of Washington. "You have to go where the science leads, and the science leads me to believe that this is bacterial biofilm."

The original research, published in Science magazine, claimed the discovery of blood vessels and what appeared to be entire cells inside fossil bone of a Tyrannosaurus rex. The scientists had dissolved the bone in acid, leaving behind the blood vessel- and cell-like structures.

But in a paper published July 30 in PloS ONE, a journal of the open-access Public Library of Science, Kaye and his co-authors contend that what was really inside the T. rex bone was slimy biofilm created by bacteria that coated the voids once occupied by blood vessels and cells.

He likens the phenomenon to what would happen if you left a pail of rainwater sitting in your backyard. After a couple of weeks you would be able to feel the slime that had formed on the inner walls of the bucket.

"If you could dissolve the bucket away, you'd find soft, squishy material in the shape of the bucket, and that's the slime," Kaye said. "The same is true for dinosaur bones. If you dissolve away the bone, what's left is biofilm in the shape of vascular canals."



Arrows on this electron microscope image indicate biofilms, or slime, peeling away from the walls of vascular canals in dinosaur bone.

Co-authors of the new paper are Gary Gaugler of Microtechnics Inc. of Granite Bay, Calif., and Zbigniew Sawlowicz of Jagiellonian University in Poland.

Kaye said he began his research with the hope of being the second person to find preserved dinosaur tissues. In addition to the acid bath procedure used in the previous work, he added examination by electron microscope before the bones were dissolved. He was surprised by the findings.

The researchers found that what previously had been identified as remnants of blood cells, because of the presence of iron, were actually structures called framboids, microscopic mineral spheres bearing iron. They found similar spheres in a variety of other fossils from various time periods, including an extinct sea creature

called an ammonite. In the ammonite they found the spheres in a place where the iron they contain could not have had any relationship to the presence of blood.

"We determined that these structures were too common to be exceptionally preserved tissue. We realized it couldn't be a one-time exceptional preservation," Kaye said.

The scientists also dissolved bone in acid, as had been done previously, and found the same soft tissue structures. They conducted a comparison using infrared mass spectroscopy and determined the structures were more closely related to modern biofilm than modern collagen, extracellular proteins associated with bone. Carbon dating placed the origin at around 1960.

Using an electron microscope, the researchers saw coatings on the vascular canal walls that contained gas bubbles, which they associated with the presence of methane-producing bacteria. In addition, they examined what looked like tiny cracks within the vascular canals and found that they were actually small troughs, or channels. Study at high magnification revealed the channels had rounded bottoms and bridged each other, indicating they were organically created, likely by bacteria moving in a very thick solution.

"From this evidence, we could determine that what had previously been reported as dinosaurian soft tissues were in fact biofilms, or slime," Kaye said.

For more information, contact Kaye at (307) 334-4018 or tomkaye@u.washington.edu
The paper is available at http://www.plosone.org/doi/pone.0002808

T. rex 'tissue' may just be bacterial scum

* 00:01 30 July 2008
* NewScientist.com news service
*** Jeff Hecht**

When palaeontologists reported that they had recovered soft tissue from a 65-million-year-old Tyrannosaurus rex fossil, the excitement was palpable.

Without going all Jurassic Park, the discovery seemed to open the door to studying biomolecules from dinosaurs and other long-extinct creatures.

Now, however, Tom Kaye of the University of Washington says the soft material is more likely to be remnants of biofilms deposited by bacteria.

Kaye set out to find his own dinosaur tissue in bones from rocks like those that had apparently yielded the T. rex tissue.

Dental plaque

"We cracked open a lot of bones and spent hundreds of hours on an electron microscope examining them," said Kaye. He concluded the soft material was not from dinosaurs, but from bacterial films which grew on cavities inside the bone long after the animal had died.

More familiar biofilms are thin, sticky layers like dental plaque, but Kaye says the biofilms he found produced branching hollow filaments when they coated the inside of blood vessel cavities in the bone.

Mary Schweitzer of North Carolina State University, who made the original soft tissue claim and who also reported evidence for dinosaur collagen, is not convinced.

Schweitzer points to immunological studies that show her T. rex samples were close to chicken collagen, as expected because birds evolved from predatory dinosaurs.

Original protein

Kaye, she says, "did not offer any explanation for how 'biofilm' proteins from dinosaur could cluster with chicken, while 'biofilm' from mammoth and mastodon cluster with elephant."

That indicates at least some of the long-dead animals' original protein survives.

It is clear that some biomarker molecules can survive for tens or hundreds of millions of years in fossils, says David Martill of the University of Portsmouth, UK.

"This is why we should not abandon hope of finding fossil biomolecules," he says.

Bees join hunt for serial killers

By Jennifer Carpenter Science reporter, BBC News

The team's bees were identified with small numbers

The way bumblebees search for food could help detectives hunt down serial killers, scientists believe.

Just as bees forage some distance away from their hives, so murderers avoid killing near their homes, says the University of London team.

This "geographic profiling" works so well in bees, the scientists say future experiments on the animals could now be fed back to improve crime-solving.

The team's work is reported in the Royal Society journal Interface.

"We're really hopeful that we can improve the model for criminology," Dr Nigel Raine, from Queen Mary, University of London (QMUL), told BBC News.

The scientist is working with colleagues Steve Le Comber and Kim Rossmo, a former detective in the US, to tag bees with tiny coloured numbers and follow them from their nests to flower patches.

The researchers' analysis describes how bees create a "buffer zone" around their hive where they will not forage, to reduce the risk of predators and parasites locating the nest. It turns out that this pattern of behaviour is similar to the geographic profile of criminals stalking their victims.

"Most murders happen close to the killer's home, but not in the area directly surrounding a criminal's house, where crimes are less likely to be committed because of the fear of getting caught by someone they know," Dr Raine explained.

Food importance

Understanding the geographic profiles of animals is interesting to biologists as it helps them predict the locations of important feeding grounds, and knowing these areas will inform more effective conservation measures.

This approach works well for very different creatures, from bees and bats to great white sharks.

Please turn on JavaScript. Media requires JavaScript to play.

The team has also been attaching radio tags to find out more about bee behaviour.

But what is more unusual is that models used to describe bee foraging can be applied back to human behaviour, the researchers say.

Instead of using information about the distribution of flowers visited by bees to explain the insects' behaviour, criminologists' models will use details about crime scenes, robbery locations, abandoned cars, even dead bodies, to hone the search for a suspect.

"Bees have much simpler brains and so understanding how bees are recruited to flowers is much easier than understanding the complex thoughts of a serial murderer," Dr Raine said.

More broadly, the London-based team hopes its work will lead to a better understanding of how one of the most familiar animals in nature goes about its daily business.

"Bees are hugely important to ecosystems and also important to humans," Dr Raine told BBC News.

"Bees' pollination 'services' account for about one in three mouthfuls of food that we eat as humans. They pollinate a huge diversity of our fruit and vegetable crops.

"If we don't know how bees forage then we don't really understand pollination, and that is quite detrimental to how we feed ourselves; which is becoming an increasing problem with bigger populations."

Dr Raine's team is also using tiny Radio Frequency Identification (RFID) tags - the same technology used to track stock in warehouses or supermarkets - to monitor the movements of bees.

The miniature tags are glued to the backs of the insects to record their movements in and out of the hive.

Digestive specialists freeze out esophagus cancer with new therapy

DALLAS — July 29, 2008 — UT Southwestern Medical Center gastroenterologists are using a new method to freeze damaged cells in the esophagus, preventing them from turning cancerous.

The Food and Drug Administration-approved cryoablation therapy helps Barrett’s esophagus patients with dysplasia, a condition in which normal cells are transformed into potentially cancerous ones.

“Due to damage from chronic stomach acid, they are people who have a higher risk of developing esophagus cancer,” said Dr. Jayaprakash Sreenarasimhaiah, assistant professor of internal medicine in the division of digestive and liver disease at UT Southwestern. “The goal of this therapy is to literally freeze the damage in its tracks and stop it before it turns to cancer.” Gastroenterologists, using a special catheter, spray liquid nitrogen on the damaged tissue to freeze the superficial lining of the esophagus, the long tube that carries food from the throat to the stomach. The treated tissue eventually falls off, allowing normal cells to grow and replace the damaged cells in about six to eight weeks.

“Repeated treatments can actually help get rid of Barrett’s esophagus with dysplasia and prevent the progression to cancer,” said Dr. Sreenarasimhaiah, a gastroenterologist who specializes in endoscopic technology.

The minimally invasive cryoablation therapy has recently been approved by the FDA for treating Barrett’s, but it requires special training and equipment available in only a handful of centers in Texas and a few dozen nationally.

Barrett’s esophagus can result from ongoing heartburn, which allows a constant splashing of acid from the stomach into the esophagus. Untreated, it can become Barrett’s with dysplasia, in which cells start to transform.

Typical treatment includes endoscopic mucosal resection (EMR), in which the damaged lining is scraped away, a procedure that takes hours and can have side effects such as bleeding or narrowing of the esophagus. The most aggressive approach includes surgery to remove damaged portions of the tube.
Some patients, however, are too sick or elderly to be candidates for surgery. Others simply want another option.

"This is a disease we see in a lot of older patients with other illnesses, so the decision to send them to surgery requires careful consideration," Dr. Sreenarasimhaiah said. "Cryoablation therapy is particularly attractive for older patients who may have complications or other medical issues — such as accompanying heart or lung diseases — that make traditional surgeries for Barrett's with dysplasia too risky."

Cryoablation therapy takes about 30 to 40 minutes and requires sedation. As with an endoscopy, a tube down the patient's throat is used to insert a tiny camera and instruments. No incisions are required.

Early results from studies show the therapy – similar to that used by dermatologists to freeze off warts — works well inside the esophagus, though further study is needed, Dr. Sreenarasimhaiah said.

"Patients may feel a little pain in the first couple of days, like a heartburn-type pain, but that starts to improve after a few days and after that they usually don't feel anything," he said. "They can eat immediately after they wake. They are not on a special diet, but they do continue their anti-reflux medications."

Visit http://www.utsouthwestern.org/digestive to learn more about UT Southwestern's clinical services in digestive disorders.
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Frankincense provides relief to arthritis sufferers

An enriched extract of the 'Indian Frankincense' herb Boswellia serrata has been proven to reduce the symptoms of osteoarthritis. Research published today in BioMed Central's open access journal Arthritis Research & Therapy has shown that patients taking the herbal remedy showed significant improvement in as little as seven days.

Osteoarthritis is the most common form of arthritis; it commonly affects weight-bearing joints such as the knees and hips, along with the hands, wrists, feet and spine. The symptoms include pain, stiffness and limited movement. This randomised, double-blinded, placebo-controlled trial of 70 patients will be of great interest to sufferers, especially those who don't get adequate relief from existing treatments.

The study was led by Siba Raychaudhuri, a faculty member of the University of California, Davis, in the United States. According to Raychaudhuri, "The high incidence of adverse affects associated with currently available medications has created great interest in the search for an effective and safe alternative treatment". The extract the authors used was enriched with 30% AKBA (3-O-acetyl-11-keto-beta-boswellic acid), which is thought to be the most active ingredient in the plant. Raychaudhuri said, "AKBA has anti-inflammatory properties, and we have shown that B. serrata enriched with AKBA can be an effective treatment for osteoarthritis of the knee". This is a proprietary product developed by Laila Nutraceuticals.

B. serrata has been used for thousands of years in the Indian system of traditional medicine known as 'Ayurveda'. This study is the first to prove that an enriched extract of the plant can be used as a successful treatment.

The same authors have previously tested the safety of their remedy in animal experiments. They say that, "In this study, the compound was shown to have no major adverse effects in our osteoarthritis patients. It is safe for human consumption and even for long-term use".

Notes to Editors

1. A double blind, randomized, placebo controlled study of the efficacy and safety of 5-Loxin(R) for treatment of osteoarthritis of the knee
Krishanu Sengupta, Krishnaraju V Alluri, Andey Rama Sathis, Simanchala Mishra, Trimurtulu Golakoti, Kadainti VS Sarma, Dipak Dey and Siba P Raychaudhuri
Arthritis Research & Therapy (in press)
During embargo, article available here: http://arthritis-research.com/imedia/1806060114163435_article.pdf
After the embargo, article available at journal website: http://arthritis-research.com/

Alzheimer's drug 'halts' decline

By Emma Wilkinson Health reporter, BBC News

UK scientists have developed a drug which may halt the progression of Alzheimer's disease.

Trials of the drug, known as Rember, in 321 patients showed an 81% difference in rate of mental decline compared with those not taking the treatment.

The Aberdeen University researchers said the drug targeted the build-up of a specific protein in the brain.

Alzheimer's experts were optimistic about the results, but said larger trials were now needed.

Presenting the results at the International Conference on Alzheimer's Disease, Professor Claude Wischik said the drug may be on the market by 2012.
Patients with mild to moderate Alzheimer's disease were given either 30, 60 or 100mg of the drug or a placebo.

The 60mg dose produced the most pronounced effect - over 50 weeks there was a seven-point difference on a scale used to measure severity of dementia.

At 19 months there was no significant decline in mental function in patients taking the drug, the researchers said. Imaging data also suggests the drug may be having its biggest effect in the parts of the brain responsible for memory.

The link between clumps or "tangles" of protein inside nerve cells in the brain and Alzheimer's disease was first made over 100 years ago.

Later shown to be made up of a protein called Tau, the tangles build up inside cells involved in memory, destroying them in the process.

SUCCESS STORY

Among the trial patients was Jimmy Hardie, 72. He began taking Rember in March 2006.
His wife said his improvement was gradual, but he is now much more confident.
She said he used to panic when faced with something difficult to do, but now copes much better.
He keeps busy maintaining old tractors, running a trout fishery, and doing a lot of gardening.
Mr Hardie said: "It has made a difference to my life. I have my off days - but I had a lot before."

Rember, or methylthioninium chloride, is the first treatment specifically designed to target the Tau tangles.

Other treatments for Alzheimer's tend to focus on combating a waste protein in the brain, beta-amyloid, which is known to form hard plaques. The latest work suggests targeting Tau may produce better results.

Methylthioninium chloride is more commonly used as a blue dye in laboratory experiments.

Professor Wischik discovered it by accident 20 years ago, when a drop in a test tube led to the disappearance of the Tau protein he had been working on.

"We have demonstrated for the first time that it may be possible to arrest the progression of this disease by targeting the tangles which are highly correlated with the disease," he said.

"We did an analysis of the effect size at 24 weeks and at 50 weeks compared to the average effect size of the current treatments and it was about two and a half times better," he added.

Larger trials of the drug are planned to start in 2009, and researchers are also investigating whether the drug has a role in prevention of the disease in the first place.

Professor Clive Ballard, head of research at the Alzheimer's Society, said: "This is a major new development in the fight against dementia. "It is the first realistic evidence that a new drug can improve cognition in people with Alzheimer's by targeting the protein tangles that cause brain cell death. "This first modestly sized trial in humans is potentially exciting. "It suggests the drug could be over twice as effective as any treatment that is currently available."

Rebecca Wood, chief executive of the Alzheimer's Research Trust, said: "In this exploratory trial, rember reduced the decline in blood flow to parts of the brain that are important for memory.

"This bodes well but we need more human trials to assess the treatment's possible side effects."

She added the fact the trial was funded by a pharmaceutical company highlighted the lack of funding for Alzheimer's research in the UK.

More on the same topic:

Alzheimer's disease patients show improvement in trial of new drug

A new drug has been shown to improve the brain function of people with early stage Alzheimer's disease and reduce a key protein associated with the disease in the spinal fluid, in a small study published today in the journal Lancet Neurology and presented at the 2008 Alzheimer's Association International Conference on Alzheimer's Disease.

The drug, known as PBT2, counteracts the production and build-up of a protein called amyloid-beta that occurs in Alzheimer's disease. This protein, which can build up into a 'plaque', is believed to be toxic to brain cells and to prevent them from functioning properly.

Seventy-eight participants with early stage Alzheimer's disease took either 50mg or 250mg doses of the drug PBT2, or a placebo, over the course of 12 weeks in a randomised, double-blind clinical trial, led by a researcher from Imperial College London working with colleagues in Australia and Sweden. Both doses of PBT2 capsules were observed to be safe and well tolerated during the course of the study.

Participants undertook a number of tests to assess their cognitive function, prior to beginning treatment and at the end of the 12-week period. In two of these tests of executive function, which involves the ability to organise information, sequence events and plan, those on a 250mg dose of PBT2 showed a significant improvement over the placebo group.

The researchers also measured how the levels of amyloid-beta in spinal fluid changed during the course of the trial. They found that levels of amyloid-beta 42 in the cerebrospinal fluid of those on the 250mg dose of PBT2 were reduced by approximately 13 percent compared to placebo at the end of the 12-week period.

Amyloid-beta needs the metals zinc and copper in order to accumulate in the brain and these two metals become abnormally distributed in the brains of people with Alzheimer's disease. PBT2 works by interrupting the interaction between the metal ions and amyloid-beta, and returns levels of zinc and copper in the brain to normal levels.

In the cognitive tests, those on a 250mg dose of PBT2 were able to complete the task in a test known as Trail Making Part B an average of 42 seconds faster than they had at the beginning of the trial. The placebo group was an average of 6 seconds slower.

In the Category Fluency Test, which looks at a person's ability to come up with as many relevant words as possible in relation to a specified category, those in the 250mg group were able to produce an average of 2.4 more words than at the beginning of the trial. This compared with a decrease of 0.3 words in the placebo group.

Although memory loss is the problem most often associated with Alzheimer's disease, the executive cognitive functions assessed by these two tests typically begin to deteriorate in the early stages of the disease, though are sometimes less obvious than memory symptoms.

There were no significant differences in participants' scores on tests assessing their memory function in the new study, but the researchers believe this may be because the memory function deteriorates at a slower rate than the executive functions at this stage of illness, making changes harder to detect in a short study.

Dr Craig Ritchie, from the Division of Neurosciences and Mental Health at Imperial College London, who led the study, said: "Alzheimer's disease is a devastating condition and it affects hundreds of thousands of people in the UK. The results of our trial are very encouraging, although it was a relatively small study, which took place over a short period of time. Our findings certainly engender much optimism that this drug may have a significant effect on the underlying pathology of Alzheimer's, with a tangible clinical benefit for patients.

"We now need further research to see how PBT2 performs in larger, longer-term trials. Our hope is that we might be able to see treatments that can substantially improve the lives of people with early Alzheimer's disease within the next five or so years," added Dr Ritchie, who has been assisting the Australian company Prana Biotechnology with the clinical development of its new drugs for ten years.

The next step for the research is to move forward with PBT2 in further trials with a view to gaining a license for the drug.

These study results follow on from a recently published study of mice which showed that PBT2, in the space of a few days, cleared amyloid-beta, improved cognition and reduced the damage to brain cells. The parent compound to PBT2, clioquinol, was shown in a small study of 36 patients in 2003 to slow the progression of Alzheimer's disease. PBT2 was developed to be even more effective than clioquinol at attacking the core pathology of the disease.

Note to people with scarred and stiffened lungs: Monitor your sleep before severe fatigue sets in

Mother's legacy shows impact of severe fatigue, $2M in research funding to help study disease

Family, friends and neighbors remember Lisa Sandler Spaeth as an active mother of two in Potomac, Md., with a lot on the go, juggling her son's baseball games and her daughter's horseback-riding lessons with numerous committee obligations, organizing women's activities at her local synagogue. Add to this Spaeth's thriving home business turned wholesale supplier - making custom hair accessories for children - which she founded with her mother.

But Spaeth was also diagnosed with pulmonary fibrosis, a hard-to-treat disease that progressively damages the lungs and starves the body of oxygen. For two years after her diagnosis, until her death in May 2007, at age 44, Spaeth was beset by fatigue. Her energy levels sank as her lungs deteriorated. Breathing became difficult, and she could no longer attend many of the sporting events, trade fairs and women's groups that filled her life.

It is with people like Spaeth in mind that researchers at Johns Hopkins and elsewhere have found what is likely to be the first evidence linking the extreme fatigue in the lung-scarring disease, which has no known cause, to the poor quality of sleep that results - as much as a 25 percent loss in body-rejuvenating R.E.M. sleep. And they have also gauged the detrimental effects this has on people's daily lives, nearly halving test scores used to assess physical and mental quality of life.

In a report appearing this month in the journal Chest, senior study investigator and pulmonologist Sonye Danoff, M.D., Ph.D., who treated Spaeth, found more than twice the amount of nighttime sleep disturbances and double the number of daytime episodes of drowsiness among 41 men and women with so-called idiopathic pulmonary fibrosis than in people with healthy lungs.

"Physicians should strongly consider monitoring people with this scarring lung disease for sleep disorders as part of their standard care, because poor sleep has a profound effect on their quality of life," says Danoff, an assistant professor at the Johns Hopkins University School of Medicine.

The latest study results back up previous research by Danoff and other sleep experts at Johns Hopkins, which showed that 18 of 22 people with fibrosed lungs had problems breathing while asleep. The majority of them dropped out of R.E.M. sleep during the night, losing 25 percent of total R.E.M. sleep time.

It is during the R.E.M. period that rapid eye movements occur (hence the name), that people dream and that the body recovers from the previous day and builds up energy for the next.

Pulmonary fibrosis makes people highly vulnerable to sleep problems, Danoff says, because they often breathe twice as fast to supply the body with oxygen. And just as breathing and other body functions naturally slow down at the onset of R.E.M. sleep, these people who depend on a higher rate of breathing are constantly being pushed to wake up from a lack of oxygen.

"Essentially," she adds, "the body's internal alarms go off as people enter the most rejuvenating part of sleep. And when people don't get a good night's sleep, they cannot function normally the next day. It's a slippery slope that gets progressively worse over time."

Also in this latest Johns Hopkins study are survey results assessing quality of life and quality of sleep, which showed that people with stiffened lungs and sleep problems have 40 percent lower scores in physical activities compared to the general U.S. population. Rated activities included basic tasks, such as going to the mailbox and walking to the car. Mental and social activities, such as carrying on a conversation with a store clerk or telephoning friends and family, were reduced 48 percent.

Sleep quality was assessed on a scale comprising 36 different sleep measurements, such as the length of time it took to fall asleep and overall time spent sleeping.

Moreover, the team's analysis showed that sleep problems could not be predicted by other demographic factors, such as age, gender, race or weight. Nor were they linked, researchers say, with other lung function and more noticeable disease symptoms, including shortness of breath and cough.

"Because there is so much about pulmonary fibrosis that we cannot yet fix, we need to focus on what we can fix while we wait for research to catch up with treatments that can prevent or reverse the disease," says Danoff.

Current treatments for pulmonary fibrosis are limited to steroids and other immune-system-lowering drugs that help slow down lung tissue deterioration as the thin walls of the air sacs stiffen and lose capacity to freely expand and contract.

More than 200,000 Americans suffer from pulmonary fibrosis, whose cause remains unknown. And the lung disease kills nearly 40,000 each year.

"If we had been able to treat Lisa Spaeth's fatigue from poor quality sleep, then she might have had more time to lead her life as fully as she had been prior to getting sick," says Danoff.

Despite Spaeth's death, her zest for life carries on. Her mother, Froma Sandler, maintains the business. And through the encouragement of family and friends, more than a thousand people have donated to medical research in Spaeth's honor. The largest-ever contributions arrived in May, just prior to the first anniversary of Spaeth's death, when the Maryland-based Robert M. Fisher Memorial Foundation pledged $2 million to Johns Hopkins to help fund Danoff's future studies into pulmonary disease.

"This research funding will lay the groundwork for a more consolidated and comprehensive look at the many factors that may improve and extend the lives of patients with pulmonary fibrosis: from rehabilitation of the lungs to the development and testing of new medications to offset losses in quality of life from fatigue," says Danoff.

Danoff plans to use some of the funding to support studies that monitor patients with pulmonary fibrosis for problems in sleep patterns, especially in deep-sleep R.E.M. patterns, to target for treatment.

Another phase of research, she says, involves testing new devices to support breathing during sleep and to see if these devices improve quality sleep time and abate fatigue.

Funding for this latest study was provided by a fellowship grant from the CHEST Foundation, the philanthropic arm of the American College of Chest Physicians, which also publishes the journal Chest, and by The Johns Hopkins Hospital's General Clinical Research Center.

In addition to Danoff, other Hopkins researchers involved in these studies, conducted solely in Balimore, were Vidya Krishnan, M.D.; Meredith McCormack, M.D., M.H.S.; Stephen Mathai, M.D., M.H.S.; Maureen Horton, M.D.; and Nancy Collop, M.D. Additional assistance was provided by Shikhar Agarwal, M.D., from the Johns Hopkins University's Bloomberg School of Public Health; Brittany Richardson, from the University of Maryland; and Albert Polito, M.D., from Mercy Medical Center.

Women end up less happy than men

Less able to achieve their life goals, women end up unhappier than men later in life – even though they start out happier, reveals new research by Anke Plagnol of the University of Cambridge, and University of Southern California economist Richard Easterlin.

Plagnol and Easterlin's study, forthcoming in the Journal of Happiness Studies, is the first to use nationally representative data spanning several decades to examine the role of unfulfilled desires in a person's sense of well-being.

As the researchers explain, expectations of success may vary among those raised in different generations (i.e., an economic depression). Data sets from a range of time periods may also have different demographic compositions.

In their analysis, the researchers control for birth cohort and demographic characteristics such as race and education. They find that women are, on average, happier than men in early adulthood – but the glow wears off with time. Specifically, after the age of 48, men's overall happiness exceeds women's happiness.

These gender patterns of overall happiness correlate to patterns in two significant aspects of life satisfaction: family and finances.

As Plagnol explains: In later life it is "men [who] come closer to fulfilling their aspirations, are more satisfied with their family lives and financial situations, and are the happier of the two."

Women and men have fairly similar life goals when it comes to love, the study reveals. Nine out of 10 people of both genders reach adult life wanting a happy marriage.

"Differences between men and women in aspirations for marriage and children are fairly small," says Plagnol, who received her Ph.D. from USC in 2007. "Gender differences in satisfaction depend largely on attainment."

The saddest period of the average man's life – his 20s – is also the period when he is most likely to be single.

Young men are also more dissatisfied than young women with their financial situations, not because they are worse off, but because they want more and therefore experience a greater "shortfall," the researchers explain.

But age alters many things, including men's money woes and lackluster love lives.

After 34, men are more likely to be married than women, and the gap only widens with age, mirroring men's growing satisfaction with family life.

Men also become more satisfied with their financial situations over time, as reflected in their increased spending power. The researchers found that men tend to covet big-ticket items that might not be within reach until later in life, such as a car or vacation home.

(A notable exception: women want more "nice clothes" than men, the researchers found.)

These findings are consistent with an earlier study by Easterlin showing that recent generations are less satisfied than previous generations, despite having more.

"Of course, one doesn't have to be married to be happy, but if that's something you really want – and it is for most people – then the failure to attain it can have an impact on your overall happiness," Plagnol says, adding that those in a relationship also tend to be in a stronger financial position than those who must depend solely on their own resources.

Some age milestones:

41: Age at which men's financial satisfaction exceeds women's financial satisfaction
48: Age at which men's overall happiness exceeds women's overall happiness
64: Age at which men's satisfaction with family life exceeds women's satisfaction

Plagnol, Anke C. and Richard A. Easterlin, "Aspirations, Attainments, and Satisfaction: Life Cycle Differences Between American Women and Men." Journal of Happiness Studies; DOI: 10.1007/s10902-008-9106-5.

Improved estrogen reception may sharpen fuzzy memory

GAINESVILLE, Fla. — Estrogen treatments may sharpen mental performance in women with certain medical conditions, but University of Florida researchers suggest that recharging a naturally occurring estrogen receptor in the brain may also clear cognitive cobwebs.

The discovery suggests that drugs can be developed to offset "senior moments" related to low estrogen levels, as well as to protect against neurological diseases, all while avoiding the problems associated with adding estrogen to the body.

Writing online in Molecular Therapy in July, scientists with UF's McKnight Brain Institute describe how they improved thought processes in female mice bred with the inability to produce estrogen receptor-alpha, a protein apparently necessary for healthy learning and memory.

"We were able to restore function in these animals, not by dosing them with estrogen, but by enabling them to use the estrogen that was naturally present in their bodies," said Tom Foster, Ph.D., the Evelyn F. McKnight

chair for brain research in memory loss at the UF College of Medicine. "We discovered that you can affect the estrogen receptor directly in the hippocampus, right where it's needed to address memory and spatial learning."

Changes in the estrogen receptor have been associated with age-related memory deficits and an increased incidence of Alzheimer's disease among women. In addition, previous studies have shown estrogen replacement may improve cognition in postmenopausal women and younger women with low estrogen levels. Estrogen also appears to protect against Alzheimer's disease and dementia.

The downside is that estrogen is a powerful hormone that has far-reaching effects throughout the body. It has been associated with a slight increase in women's risk for breast cancer, heart disease in patients with existing cardiovascular problems, and stroke.

"Estrogen may act as a growth agent for cancer, but in the brain, it appears to maintain health and counteract stress," Foster said. "We wanted to come back and enhance the signaling pathway that makes estrogen functional. We used a gene therapy technique that enables us to target the brain, but ultimately there could be a pharmaceutical that enhances the signaling pathway solely in the brain."

The mice had unusually low levels of estrogen because their ovaries were removed at an early age. However, scientists were still able to rescue learning ability by delivering the correct gene to produce estrogen receptor-alpha directly to the hippocampus.

Mice that lacked the estrogen receptor showed poor ability to locate a platform hidden in a small swimming tank over a training period of several days. After receiving the gene, the mice learned to locate the platform in two days of training.

"This research shows that when the estrogen receptor-alpha is restored to adult mice that have been missing it their entire lives, it is still possible to enhance memory and learning," said John H. Morrison, Ph.D., dean of basic sciences and the Graduate School of Biological Sciences at Mount Sinai School of Medicine, who did not participate in the research. "This is good news for moving forward to develop clinical interventions and therapeutics because it appears critical damage was not done to brain circuitry during early development. There has also been debate about which of at least two estrogen receptors is key to synaptic health. Clearly estrogen receptor-alpha plays a critically important role in hippocampal organization and function."

Recordings made from the brain tissue of treated mice showed signals were strongly communicated across the gaps, or synapses, between hippocampal cells, similar to what would happen with estrogen replacement.

"Investigating the impact of genetically replacing the estrogen receptor at the cellular, synaptic and behavioral levels is a scientific tour de force which provides a strong foundation for the role of estrogen receptor alpha in mediating estrogen action in the hippocampus to restore select types of memory function," said Roberta Diaz Brinton, Ph.D., a professor of pharmacology and pharmaceutical sciences and biomedical engineering at the University of Southern California, who was not involved in the study. "From a technology perspective, their technique to transfect the estrogen receptor is an exciting advance for researching steroid receptors in the brain."

Studying the effects of increasing the estrogen receptor in other brain regions may shed additional light on memory processes.

"The research brings up the idea that local activation of non-nuclear estrogen receptor-alpha is important for regulating memory processes in the hippocampus," said Teresa A. Milner, Ph.D., a professor of neuroscience at Weill Cornell Medical College, who also was also not involved in the research.

UF neuroscience associate Asha Rani and UF scientists Ashok Kumar, Ph.D.; Li Cui, Ph.D.; and Susan L. Semple-Rowland, Ph.D., participated in the study, which was supported by the National Institutes of Health and the Evelyn F. McKnight Brain Research Foundation.

Summer Heat too Hot for you? What is Comfortable?

Johns Hopkins Researchers Discover How Animals Sense the "Comfort Zone"

Extreme heat or cold is not only uncomfortable, it can be deadly-causing proteins to unravel and malfunction.

For many years now, scientists have understood the molecular mechanisms that enable animals to sense dangerous temperatures; such as extremely high temperatures that directly trigger heat sensor proteins known as TRP channels. However, much more poorly understood is how animals sense very small temperature differences in the comfortable range, and choose their favorite temperature.

Reporting this week at Nature Neuroscience, Johns Hopkins researchers now have discovered that the fruit fly uses TRPA1 to sense single degree changes in the comfortable range. However, rather than sensing temperature changes directly, TRPA1 functions in the last step of a multistep process that uses many of the same proteins that function in vision. Just as the early events involved in vision allow animals to adapt to different light intensities, the multistep process involved in temperature detection potentially allows animals to adapt to different temperatures in the comfortable range as well.

"It's an exciting discovery, yet in a lot of ways it just makes a lot of sense," says Craig Montell, Ph.D., a professor of biological chemistry and member of Johns Hopkins' new Center for Sensory Biology. "You clearly don't want to hang around or adapt to a temperature that could kill you, but on the other hand, if you can't find your favorite temperature, it is OK to adapt to another comfortable temperature."

Montell and his team use fruit flies as their experimental model because it is easy to perform genetic manipulations on these animals. Temperatures colder than 16 degrees Celsius (61 degrees Fahrenheit) or warmer than 26 degrees C (79 degrees F) are known to trigger an avoidance response. Fruit fly maggots (larvae), explains Montell, prefer 18 degrees C (64 degrees F), but are comfortable at temperatures ranging from 18 to 24 degrees C (64 to 75 degrees F).

To first figure out if the larvae could even sense small temperature differences in the 18 to 24 degree "comfort zone," Montell's team set up a preference test that consisted of a plastic plate where one half of the plate was kept at 18 degrees and the other half at a different temperature, from 19 to 24 degrees. After 15 minutes, they counted the number of larvae on each side of the plate.

"It turns out these larvae can discriminate one degree differences-they prefer 18 over 19 degrees" says Montell. "The question then was: How do they do this?"

Since TRP channels are known to open in response to changes in temperature, Montell's team then tested flies containing mutations in 12 fruit fly TRPgenes to see if any were required for the ability to sense temperature changes within the comfort zone.

Eleven of the 12 TRPmutants still preferred 18 degrees to other temperatures in this range. Only the TRPA1 mutant larvae showed no temperature preference, suggesting to the researchers that only TRPA1 is required for comfort zone temperature sensing.

The known "thermoTRPs" all open directly in response to changes in temperature. TRP proteins also are involved in other types of sensory biology, including vision, explains Montell. But rather than being directly triggered by light, a different light sensor molecule activates the TRP vision protein indirectly. Since TRPA1 is not turned on by changes in temperature in the comfortable range, Montell's team reasoned that perhaps, in this range, TRPA1 might be triggered indirectly through a series of steps similar to those that function in vision.

The team then tested flies with mutations disrupting proteins known to work with TRP proteins required for fly vision and found that they, too, were unable to discern temperature differences in the 18 to 24 C range.

Thus, Montell and co-workers have found a new way that TRP channels function in thermosensation, and this "is quite reminiscent of how we detect light."

"We think it's important for adaptation; if a fly finds itself at 34 degrees (93 degrees F), it should never try to adapt to that temperature, because it will die," says Montell. "But flies living at 22 degrees could adapt to this environment because, while this temperature isn't their optimal choice, it still isn't deleterious." The multistep vision-like strategy for sensing changes in temperature could also be well suited for amplifying very small differences in temperature, such as 18 and 19 degrees C. This strategy could allow animals to respond to one degree changes that might otherwise not be possible through a process involving just one protein.

The team's work raises the possibility that similar multistep processes may allow mammals to sense small changes in internal body temperature.

The research was funded by the National Eye Institute and the National Institute of General Medical Sciences.
Authors on the paper are Young Kwon, Hye-Seok Shim, Xiaoyue Wang and Montell, all of Hopkins.
On the Web: http://biolchem.bs.jhmi.edu/members/facultydetail.asp?PersonID=674 http://www.nature.com/neuro/index.html
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Personal Health

The Treadmill's Place in Evaluating Hearts

By JANE E. BRODY

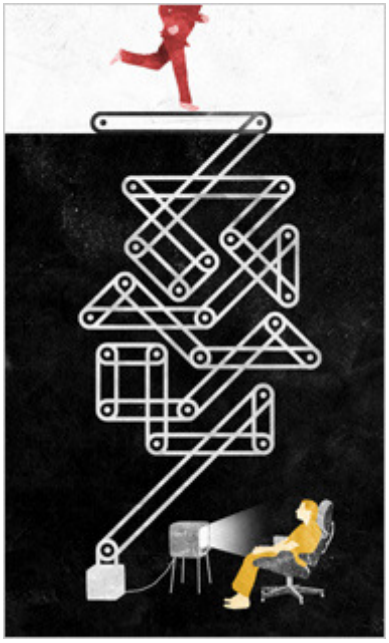
Each year hundreds of thousands of Americans, including some 700,000 Medicare recipients, get on a treadmill not for exercise but to try to determine if their hearts are healthy.

Tim Russert, the NBC journalist, had such an exam, called an exercise or treadmill stress test, six weeks before he died of a heart attack last month at age 58. His results had been deemed normal, prompting people to question how worthwhile this test could be.

Two weeks before Mr. Russert died, Dr. Todd D. Miller, a cardiologist and co-director of the Mayo Clinic's Nuclear Cardiology Laboratory in Rochester, Minn., published an assessment of the test's ability to predict the presence of potentially life-threatening cardiac problems. Dr. Miller elaborated on his report, in The Cleveland Clinic Journal of Medicine, in a telephone interview.

The test is meant to be used “almost exclusively” for people who have symptoms of heart disease, Dr. Miller emphasized.

“But in the real world,” he said, “it is often used as a screening test for people without symptoms who are worried about their risk. The accuracy of the test depends on whom it is used. It is most accurate among populations with a high prevalence of coronary disease. But in most people without symptoms, the prevalence of disease is so low that the accuracy of the test is low, too.”



Jez Burrows

Limitations and Advantages

In fact, this test is unable to detect the kind of problem that caused Mr. Russert’s death — a plaque within the wall of a coronary artery that ruptured, resulting in a clot that set off a rapidly fatal heart rhythm abnormality. If not for the rhythm disturbance, Mr. Russert would have had a far greater chance of surviving his heart attack, said Dr. Miller, who was not one of his physicians.

Mr. Russert’s treadmill test may have put him in the low-risk category, Dr. Miller said, “but that doesn’t mean no risk.” “Maybe 3 patients in 1,000 with a low-risk test will die from heart disease within a year,” he said. “Among those deemed at high risk, more than 3 patients in 100 would die within a year.”

Furthermore, when the stress test is used for people who are at low risk for heart disease, an abnormal finding is most often a false positive that prompts further testing that is far more costly, Dr. Miller said.

The stress test’s main advantages are its rapidity and low cost — one-fifth to one-quarter the cost of more definitive and often more time-consuming tests like a nuclear stress test, CT coronary angiogram or standard angiogram. Medicare pays about $150 for a standard stress test, though hospitals typically charge three to four times that when the test is done on younger patients.

Regardless of cost, the test has no value unless its findings are interpreted in the context of a person’s other risk factors for heart disease: age, sex and heart disease symptoms, as well as smoking, being overweight, hypertension, high cholesterol, diabetes and family history.

Three main arteries feed the heart, and the ability of a stress test to pick up narrowing of an artery depends on which one is involved, Dr. Miller said. It is better at picking up coronary disease if more than one artery is clogged. The treadmill test seeks to answer two questions: “Does the patient have coronary artery disease, and is he or she likely to die or suffer a coronary event soon?” Dr. Miller wrote in the Cleveland Clinic journal. But at best it can provide only an estimate of someone’s risk of having a heart attack or dying of heart disease within a given period of time.

Interpreting the Results

During a treadmill test, patients are hooked up to an electrocardiogram machine (often abbreviated EKG, for the German spelling) that records the workings of the heart as the duration, speed and difficulty of the exercise increase.

Measurements taken during and immediately after the workout are indicators of cardiovascular fitness and how well a person’s autonomic nervous system is functioning: how long the person can continue as the treadmill’s speed and incline gradually increase; whether blood pressure drops instead of rising; whether the heart rate increases to an age-appropriate level and how fast it recovers when the test ends; and whether the pumping chambers of the heart develop abnormal beats.

Doctors used to rely mainly on an EKG finding called ST-segment depression to indicate heart trouble. But scores of studies have zeroed in on other, more reliable findings. Exercise duration has the strongest prognostic value, Dr. Miller said. “The longer the patient can keep going on the treadmill, the less likely he or she is to die soon of coronary artery disease — or of any cause,” he wrote.

Even people who have three diseased coronary arteries can be expected to survive four years or more if they can stay on the treadmill for 12 or more minutes, a study in the 1980s of 4,083 patients with symptoms of heart disease showed.

But duration on the treadmill may be limited by lack of physical fitness, back problems or other unrelated disorders, leading to other, more expensive evaluations.

“When a middle-age couch potato is done in after only three minutes on the treadmill, you scratch your head,” Dr. Miller said. “Is this heart disease or just deconditioning?”

Measurements and Diagnoses

Duration on a treadmill is a measure of exercise capacity — the workload the body can achieve expressed as metabolic equivalents, or METs, a multiple of the amount of oxygen the body uses at rest. The average middle-age man can reach 10 to 12 METs, about 2 METs more than the average woman, Dr. Miller said.

Blood pressure that is lower during the treadmill exercise than when the person is standing at rest often indicates severe coronary disease — a heart unable to meet the demand — and has been linked to a threefold increase in the risk of a cardiac event within two years, a study of 2,036 patients showed.

A normal heart beats faster during exercise and slows as soon as exercise stops. Failure of the heart rate to increase as expected, a condition called chronotropic incompetence, is associated with an increased risk of death from heart disease, a study by the Cleveland Clinic Foundation showed. The risk of death within six years is also doubled if the person's heart rate fails to fall quickly when the treadmill stops.

Finally, various heart rhythm abnormalities may occur during the treadmill test. Though most are benign, a rhythm disturbance after the test called ventricular ectopy is linked to a somewhat raised death rate over the next five years.

The bottom line? A stress test result is only one factor in estimating a person's risk of dying soon of heart disease. All other risk factors must be taken into account and, if possible, treated to reduce or eliminate them. To this advice Dr. Miller added, "We'd all be a lot better off if we became more active."

News Analysis

Climate Experts Tussle Over Details. Public Gets Whiplash.

By ANDREW C. REVKIN

DATA DELUGE From left, Greenland ice, lemur leaf frog, hurricanes tracks and a plot of buoys used in sea temperature studies. Discordant findings aside, the theory of rising human influence on climate endures. **Michael Kappeler/Agence France-Presse — Getty Images; Erik S. Lesser for NYT; NOAA; NASA**

When science is testing new ideas, the result is often a two-papers-forward-one-paper-back intellectual tussle among competing research teams.

When the work touches on issues that worry the public, affect the economy or polarize politics, the news media and advocates of all stripes dive in. Under nonstop scrutiny, conflicting findings can make news coverage veer from one extreme to another, resulting in a kind of journalistic whiplash for the public.

This has been true for decades in health coverage. But lately the phenomenon has been glaringly apparent on the global warming beat.

Discordant findings have come in quick succession. How fast is Greenland shedding ice? Did human-caused warming wipe out frogs in the American tropics? Has warming strengthened hurricanes? Have the oceans stopped warming? These questions endure even as the basic theory of a rising human influence on climate has steadily solidified: accumulating greenhouse gases will warm the world, erode ice sheets, raise seas and have big impacts on biology and human affairs.

Scientists see persistent disputes as the normal stuttering journey toward improved understanding of how the world works. But many fear that the herky-jerky trajectory is distracting the public from the undisputed basics and blocking change. "One of the things that troubles me most is that the rapid-fire publication of unsettled results in highly visible venues creates the impression that the scientific community has no idea what's going on," said **W. Tad Pfeffer**, an expert on Greenland's ice sheets at the University of Colorado.

"Each new paper negates or repudiates something emphatically asserted in a previous paper," Dr. Pfeffer said. "The public is obviously picking up on this not as an evolution of objective scientific understanding but as a proliferation of contradictory opinions."

Several experts on the media and risk said that one result could be public disengagement with the climate issue just as experts are saying ever more forcefully that sustained attention and action are needed to limit the worst risks. Recent polls in the United States and Britain show that the public remains substantially divided and

confused over what is happening and what to do. Some environmentalists have blamed energy-dependent industries and the news media for stalemates on climate policy, arguing that they perpetuate a false sense of uncertainty about the basic problem.

But scientists themselves sometimes fail to carefully discriminate between what is well understood and what remains uncertain, said **Kimberly Thompson**, an associate professor of risk analysis and decision science at Harvard.

And, Dr. Thompson said, the flow of scientific findings from laboratory (or glacier) to journal to news report is fraught with "reinforcing loops" that can amplify small distortions.

For example, she said, after scientists learn that accurate, but nuanced, statements are often left out of news accounts, they may pre-emptively oversimplify their description of some complex finding. Better, but more difficult, Dr. Thompson said, would be to work with the reporter to characterize the weight of evidence behind the new advance and seek to place it in context.

To support clarity, **Stephen H. Schneider**, a climatologist at Stanford, helped create a glossary defining what is meant by phrases like "very likely" (greater than 90 percent confidence) in the reports from the Intergovernmental Panel on Climate Change. In a news media universe where specialized reporting is declining and a Web mash-up of instant opinion and information is emerging, Dr. Schneider said, it is ever more important for scientists to take responsibility for communicating in ways that stick, while sticking with the facts.

Dr. Thompson said climate science presented particularly tough challenges, given the long time lag before the worst effects kick in and the persistent uncertainty about the likelihood of worst-case outcomes. She said the news media sometimes overplayed the uncertainty by balancing opposing views in a story without characterizing the overall level of confidence in either side. And sometimes they do the opposite, sacrificing accuracy for impact, she said.

"Words that we as scientists use to express uncertainty routinely get dropped out to make stories have more punch and be stronger," she said, adding that those words are important to include because "they convey meaning to readers not only in the story at hand, but more generally about science being less precise than is typically conveyed."

Public-relations offices at leading scientific journals and hubs for research also could do more to avoid overplaying incremental research results, she and several other experts said.

Donald Kennedy, a Stanford professor emeritus who was the editor in chief of the journal Science from 2000 until earlier this year, said the flow of papers on climate, glaciology and relevant ocean sciences greatly increased in his tenure. "I do think we grew more sensitive to the need for critical review of papers likely to initiate or continue the kind of controversy that results in a whiplash effect," Dr. Kennedy said.

Roger A. Pielke Jr., a political scientist at the University of Colorado, warned that the focus by the public and media on the stream of evolving climate science could distract from the need for policies now that made sense regardless of uncertainties. "The example of reducing losses to hurricanes is a good one," Dr. Pielke said, "where the actions that make the most sense are really independent of the debate over greenhouse gases and hurricane behavior."

"The same might be said for many health studies on fat, coffee, carbs," he added. "The lesson from experts is to eat a balanced diet and get plenty of exercise," which stays the same despite the various disputes.

He said his advice for scientists who wanted to "dampen the whiplash effect" was to "discuss the 'So what?' implications of the work explicitly, rather than leaving that step to advocates or politicians, or reporters."

Increasingly, scientists are taking their message straight to the public. Realclimate.org, Climatepolicy.org and Climateethics.org are among Web sites where issues are explored in an ongoing way, rather than in response to news releases and scientific papers. Other new Web ventures, like ClimateCentral.org at Princeton and the Yale Forum on Climate Change and the Media, focus on improving media coverage.

Robert J. Brulle, a sociologist at Drexel University, said it was hard to be optimistic about such efforts. "In this public sphere," he said, "it is assumed that the better argument, backed up with solid scientific evidence, will prevail." He said many studies had shown that people tended to sift sources of information to reinforce existing views.

Morris Ward, the editor of the Yale effort (yaleclimatemediaforum.org), says that it will be up to the public to choose to be better informed on momentous issues that do not fit the normal template for news or clash with their ingrained worldviews. "At some point," he said, "the public at large has to step up to the plate in terms of scientific and policy literacy, in terms of commitment to education and strong and effective political leadership, and in terms of their own general self-improvement."

10 Things to Scratch From Your Worry List

By JOHN TIERNEY

For most of the year, it is the duty of the press to scour the known universe looking for ways to ruin your day. The more fear, guilt or angst a news story induces, the better. But with August upon us, perhaps you're in the mood for a break, so I've rounded up a list of 10 things not to worry about on your vacation.

Now, I can't guarantee you that any of these worries is groundless, because I can't guarantee you that anything is absolutely safe, including the act of reading a newspaper. With enough money, an enterprising researcher could surely identify a chemical in newsprint or keyboards that is dangerously carcinogenic for any rat that reads a trillion science columns every day.

Viktor Koen

What I can guarantee is that I wouldn't spend a nanosecond of my vacation worrying about any of these 10 things. (You can make your own nominations in the TierneyLab blog.)

1. Killer hot dogs. What is it about frankfurters? There was the nitrite scare. Then the grilling-creates-carcinogens alarm. And then, when those menaces ebbed, the weenie warriors fell back on that old reliable villain: saturated fat.

But now even saturated fat isn't looking so bad, thanks to a rigorous experiment in Israel reported this month. The people on a low-carb, unrestricted-calorie diet consumed more saturated fat than another group forced to cut back on both fat and calories, but those fatophiles lost more weight and ended up with a better cholesterol profile. And this was just the latest in a series of studies contradicting the medical establishment's predictions about saturated fat.

If you must worry, focus on the carbs in the bun. But when it comes to the fatty frank — or the fatty anything else on vacation — I'd relax.

2. Your car's planet-destroying A/C. No matter how guilty you feel about your carbon footprint, you don't have to swelter on the highway to the beach. After doing tests at 65 miles per hour, the mileage experts at edmunds.com report that the aerodynamic drag from opening the windows cancels out any fuel savings from turning off the air-conditioner.

3. Forbidden fruits from afar. Do you dare to eat a kiwi? Sure, because more "food miles" do not equal more greenhouse emissions. Food from other countries is often produced and shipped much more efficiently than domestic food, particularly if the local producers are hauling their wares around in small trucks. One study showed that apples shipped from New Zealand to Britain had a smaller carbon footprint than apples grown and sold in Britain.

4. Carcinogenic cellphones. Some prominent brain surgeons made news on Larry King's show this year with their fears of cellphones, thereby establishing once and for all that epidemiology is not brain surgery — it's more complicated.

As my colleague Tara Parker-Pope has noted, there is no known biological mechanism for the phones' non-ionizing radiation to cause cancer, and epidemiological studies have failed to find consistent links between cancer and cellphones.

It's always possible today's worried doctors will be vindicated, but I'd bet they'll be remembered more like the promoters of the old cancer-from-power-lines menace — or like James Thurber's grandmother, who covered up her wall outlets to stop electricity from leaking.

Driving while talking on a phone is a definite risk, but you're better off worrying about other cars rather than cancer.

5. Evil plastic bags. Take it from the Environmental Protection Agency : paper bags are not better for the environment than plastic bags. If anything, the evidence from life-cycle analyses favors plastic bags. They require much less energy — and greenhouse emissions — to manufacture, ship and recycle. They generate less air and water pollution. And they take up much less space in landfills.

6. Toxic plastic bottles. For years panels of experts repeatedly approved the use of bisphenol-a, or BPA, which is used in polycarbonate bottles and many other plastic products. Yes, it could be harmful if given in huge doses to rodents, but so can the natural chemicals in countless foods we eat every day. Dose makes the poison.

But this year, after a campaign by a few researchers and activists, one federal panel expressed some concern about BPA in baby bottles. Panic ensued. Even though there was zero evidence of harm to humans, Wal-Mart pulled BPA-containing products from its shelves, and politicians began talking about BPA bans. Some experts fear product recalls that could make this the most expensive health scare in history.

Nalgene has already announced that it will take BPA out of its wonderfully sturdy water bottles. Given the publicity, the company probably had no choice. But my old blue-capped Nalgene bottle, the one with BPA that survived glaciers, jungles and deserts, is still sitting right next to me, filled with drinking water. If they ever try recalling it, they'll have to pry it from my cold dead fingers.

7. Deadly sharks. Throughout the world last year, there was a grand total of one fatal shark attack (in the South Pacific), according to the International Shark Attack File at the University of Florida.

8. The Arctic's missing ice. The meltdown in the Arctic last summer was bad enough, but this spring there was worse news. A majority of experts expected even more melting this year, and some scientists created a media sensation by predicting that even the North Pole would be ice-free by the end of summer.

So far, though, there's more ice than at this time last summer, and most experts are no longer expecting a new record. You can still fret about long-term trends in the Arctic, but you can set aside one worry: This summer it looks as if Santa can still have his drinks on the rocks.

9. The universe's missing mass. Even if the fate of the universe — steady expansion or cataclysmic collapse — depends on the amount of dark matter that is out there somewhere, you can rest assured that no one blames you for losing it. And most experts doubt this collapse will occur during your vacation.

10. Unmarked wormholes. Could your vacation be interrupted by a sudden plunge into a wormhole? From my limited analysis of space-time theory and the movie "Jumper," I would have to say that the possibility cannot be eliminated. I would also concede that if the wormhole led to an alternate universe, there's a good chance your luggage would be lost in transit.

But I still wouldn't worry about it, In an alternate universe, you might not have to spend the rest of the year fretting about either dark matter or sickly rodents. You might even be able to buy one of those Nalgene bottles.

Increased burden of rare genetic variations found in schizophrenia

2 new sites of deletions implicated in largest study of its kind

People with schizophrenia bear an "increased burden" of rare deletions and duplications of genetic material, genome-wide, say researchers supported in part by the National Institute of Mental Health (NIMH), a component of the National Institutes of Health (NIH).

"Although many of us have these changes in our genetic material, they are about 15 percent more frequent in people with schizophrenia," explained Pamela Sklar, M.D., Ph.D., of Harvard University and the Stanley Center for Psychiatric Research. "We also discovered two large areas of chromosomal deletions that confer a great deal of risk for schizophrenia and confirm involvement of a third previously reported area."

Sklar and colleagues in the International Schizophrenia Consortium team, representing 11 research institutes worldwide, report on the largest study of its kind to date, online July 30, 2008, in the journal Nature.

"By implicating two previously unknown sites, this study triples the number of genomic areas definitely linked to schizophrenia," said NIMH Director R Thomas Insel, M.D. "It also confirms in a large sample that unraveling the secrets of rare structural genetic variation may hold promise for improved diagnosis, treatment and prevention of such neuro-developmental disorders."

Although recent smaller studies had identified such structural genetic glitches in schizophrenia, this genome-wide association study is the first large enough to detect weak signals that might otherwise be drowned out amid a din of statistical noise. Genetic factors are thought to account for 73 to 90 percent of schizophrenia, but most of these have so far eluded detection.

In search of rare illness-linked genetic variations, Sklar and colleagues scanned the genomes of 3,391 schizophrenia cases and 3,181 controls in a European sample.

The cases showed a subtle, but statistically significant increased number of such variations, which were found in 13.1 percent of cases and 10.4 percent of controls. Variations affected 1.41-fold more genes in people with schizophrenia, who also had a 1.45-fold higher prevalence of the rarest glitches – those that occurred only once.

The large sample also allowed the researchers to pinpoint previously undiscovered chromosomal locations associated with schizophrenia. An area on Chromosome 15 harbored deletions in 9 cases and no controls, while an area on Chromosome 1 had deletions in 10 cases and only one control.

"This tells us that variations in both of these areas are very potent risk factors for schizophrenia," said Sklar.

The researchers also confirmed in 13 cases a previously-reported association between schizophrenia and a deletion on chromosome 22 known to cause velo-cardio-facial syndrome. Other suspect sites identified were on Chromosomes 12 and 16 and in genes relevant to neural development and growth.

Exactly how the subtly increased number of structural variations in schizophrenia might translate into illness remains to be discovered, say the researchers.

The same sites of deletions on Chromosomes 1 and 15 reported by Sklar and colleagues, as well as an additional area on Chromosome 15, are also implicated in schizophrenia by another large study published online the same day in Nature by another international group of researchers supported in part by NIMH.

The International Schizophrenia Consortium is composed of researchers at: Cardiff University, Karolinska Institute/University of North Carolina at Chapel Hill, Trinity College Dublin, University College London, University of Aberdeen, University of Edinburgh, Queensland Institute of Medical Research, University of Southern California, Massachusetts General Hospital, Stanley Center for Psychiatric Research and Broad Institute of MIT and Harvard.

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The National Institute of Mental Health (NIMH) mission is to reduce the burden of mental and behavioral disorders through research on mind, brain, and behavior. More information is available at the NIMH website, http://www.nimh.nih.gov.

MGH study suggests how amyloid plaques may damage brain cells in Alzheimer's disease

Elevated calcium levels near plaques can disrupt neuronal function, lead to cellular degeneration

One of the major unanswered questions surrounding Alzheimer's disease – whether and how the amyloid plaques found in the brains of patients with the neurodegenerative disorder actually damage neurons – may be closer to an answer. Using an advanced imaging technique that reveals how brain cells are functioning, researchers from the MassGeneral Institute for Neurodegenerative Disease (MGH-MIND) have found that levels of intracellular calcium are significantly elevated in neurons close to plaques in the brains of an Alzheimer's mouse model. The study in the July 31 issue of Neuron also shows how this calcium overload can interfere with the transmission of neuronal signals and activate a pathway leading to further cell damage.

"While a connection between calcium regulation and Alzheimer's pathology has been predicted for many years, this is the first direct observation of a connection between amyloid plaques, calcium accumulation and a neurodegenerative mechanism in the most relevant animal model," says Brian Bacskai, PhD, of MGH-MIND, the study's senior author.

Calcium ions play an essential role in transmitting signals from one neuron to another. Many earlier studies have suggested that alterations in calcium regulation may be involved in the neurodegeneration that characterizes Alzheimer's disease, but the mechanism behind that association has been unclear. The current study was designed to investigate whether it was possible to measure changes in brain function, reflected by alterations in calcium levels, that may be occurring in response to plaque formation. To do so the investigators combined an advanced imaging technique they developed to measure structural changes in the brain – including plaque formation and changes in the physical appearance of neurons – with the use of a fluorescent probe that reports cellular calcium levels, developed by researchers from the Riken Institute in Japan.

After first verifying that their strategy could accurately depict neuronal calcium levels, including specific levels in the projections that carry neuronal signals, the researchers showed that dendrites, which receive nerve signals, were almost six times more likely to have excessive levels of calcium in transgenic mice with amyloid plaques than in normal mice. Those excess calcium levels were even higher – nearly doubling – in neurons adjacent to plaques.

They then found how this calcium overload probably interferes with neuronal communication. Normally specific signals being transmitted are reflected by distinct calcium levels in structures called dendritic spines, but in mice with the plaque-associated elevations, calcium levels were the same throughout a dendrite instead of changing at the locations of the spines. Those dendrites in which calcium levels were highest also had structural changes similar to those seen in the brains of patients who have died with Alzheimer's disease.

Cellular calcium overload can damage cells through a pathway involving the action of an enzyme called calcineurin, and a previous study found that treatment with a calcineurin inhibitor appeared to improve cognition in an Alzheimer's mouse model. After the MGH-MIND team treated plaque-bearing mice with the same calcineurin inhibitor, they found that neuronal calcium levels were partially moderated and dendrites did not continue to degenerate, indicating that the calcineurin pathway may be a potential therapeutic target.

"We need to keep in mind that animal models are not a complete reflection of what happens in human disease, so we can't extrapolate too far down the road," Bacskai says. "But our data do suggest that calcineurin inhibition should be investigated in future studies, which also should look at how amyloid-beta causes calcium

overload and whether removing plaques really does improve neuronal health." He also noted that dietary calcium has no effect on the cellular calcium levels examined in this study, so people concerned about the risk of Alzheimer's should not hesitate to take calcium supplements to address other health issues.

Bacskai is an associate professor of Neurology at Harvard Medical School. The first author of the Neuron report is Kishore Kuchibhotla, a doctoral student in the Harvard University Biophysics program; additional co-authors, all from MGH-MIND, are Samuel Goldman, Carli Lattarulo, Hai-Yan Wu, PhD, and Bradley Hyman, MD, PhD. The work was supported by grants from the National Institutes of Health.

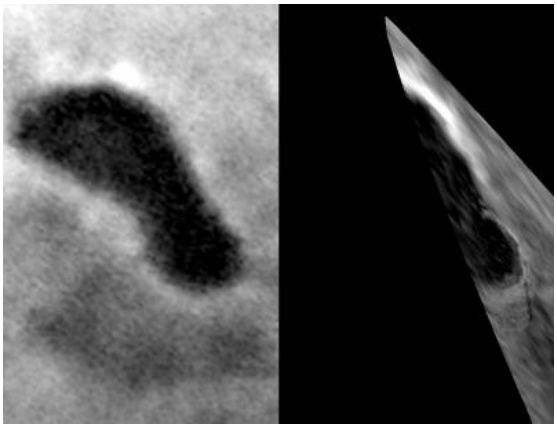
Cassini instrument confirms liquid surface lake on Titan

Scientists have confirmed that at least one body in our solar system, other than Earth, has a surface liquid lake.

Using an instrument on NASA's Cassini orbiter, they discovered that a lake-like feature in the south polar region of Saturn's moon, Titan, is truly wet. The lake is about 235 kilometers, or 150 miles, long.

The visual and infrared mapping spectrometer, or VIMS, an instrument run from The University Arizona, identifies the chemical composition of objects by the way matter reflects light.

When VIMS observed the lake, named Ontario Lacus, it detected ethane, a simple hydrocarbon that Titan experts have long been searching for. The ethane is in liquid solution with methane, nitrogen and other low-molecular weight hydrocarbons.



RIGHT IMAGE: The visual and infrared mapping spectrometer (VIMS) aboard NASA's Cassini orbiter captured this detailed, partial view of Titan's Ontario Lacus at 5 microns wavelength from 1,100 kilometers away, or about 680 miles away, on Dec. 4, 2007. Only part of the lake is visible on Titan's sunlit side. What appears to be a 'beach' is seen in the lower right of the image, below the bright lake shoreline. LEFT IMAGE: Cassini's Imaging Science System took this image of Lacus Ontario in June 2005. **Right image - NASA/JPL/University of Arizona Left image - NASA/JPL/Space Science Institute**

"This is the first observation that really pins down that Titan has a surface lake filled with liquid," VIMS principal investigator and professor Robert H. Brown of UA's Lunar and Planetary Laboratory said. Brown and his team report their results in the July 31 issue of the journal Nature.

"Detection of liquid ethane in Ontario Lacus confirms a long-held idea that lakes and seas filled with methane and ethane exist on Titan," said Larry Soderblom of the U.S. Geological Survey, Flagstaff, Ariz.

The fact that the VIMS could detect the spectral signatures of ethane on the moon's dimly lit surface while viewing at a highly slanted angle through Titan's thick atmosphere "raises expectations for exciting future lake discoveries by the infrared spectrometer," Soderblom, an interdisciplinary Cassini scientist, said.

The ubiquitous hydrocarbon haze in Titan's atmosphere hinders the view to Titan's surface. But there are transparent atmospheric "windows" at certain infrared light wavelengths through which Cassini's VIMS can see to the ground. VIMS observed Ontario Lacus on Cassini's 38th close flyby of Titan in December 2007.

The lake is roughly 20,000 square kilometers, or 7,800 square miles, just slightly larger than North America's Lake Ontario, Brown said. Infrared spectroscopy doesn't tell the researchers how deep the lake is, other than it must be at least a centimeter or two, or about three-quarters of an inch, deep.

"We know the lake is liquid because it reflects essentially no light at 5-micron wavelengths," Brown said. "It was hard for us to accept the fact that the feature was so black when we first saw it. More than 99.9 percent of the light that reaches the lake never gets out again. For it to be that dark, the surface has to be extremely quiescent, mirror smooth. No naturally produced solid could be that smooth."

VIMS observations at 2-micron wavelengths shows the lake holds ethane. The scientists saw the specific signature of ethane as a dip at the precise wavelength that ethane absorbs infrared light. Tiny ethane particles almost as fine as cigarette smoke are apparently filtering out of the atmosphere and into the lake, Brown said.

Ethane is a simple hydrocarbon produced when ultraviolet light from the sun breaks up its parent molecule, methane, in Titan's methane-rich, mostly nitrogen atmosphere.

Before the Cassini mission, several scientists thought that Titan would be awash in global oceans of ethane and other light hydrocarbons, the byproducts of photolysis, or the action of ultraviolet light on methane over 4.5 billion years of solar system history. But 40 close flybys of Titan by the Cassini spacecraft show no such oceans exist.

The observations also suggest the lake is evaporating. The lake is ringed by a dark beach, where the black lake merges with the bright shoreline.

"We can see there's a shelf, a beach, that is being exposed as the lake evaporates," Brown said.

That the beach is darker than the shoreline could mean that the "sand" on the beach is wet with organics, or it could be covered with a thin layer of liquid organics, he said.

The VIMS measurements rule out the presence of water ice, ammonia, ammonia hydrate and carbon dioxide in Ontario Lacus.

The VIMS result gives researchers new insight on Titan's chemistry and weather dynamics. Titan, which is one-and-a-half times the size of Earth's moon and bigger than either Mercury or Pluto, is one of the most fascinating bodies in the solar system when it comes to exploring environments that may give rise to life.

Cassini cameras and radar and the UA-built camera aboard the European Space Agency's Huygens probe that landed on Titan in January 2005 have shown that methane saturates and drains from Titan's atmosphere, creating river-like and lake-like features on the surface. Just as water cycles through the hydrologic regime on Earth, methane cycles through a methanological cycle on Titan.

'Hidden' Van Gogh painting revealed

30 July 2008 **by M&C**

A new technique allows pictures which were later painted over to be revealed once more. An international research team including members from Delft University of Technology (The Netherlands) and the University of Antwerp (Belgium), has successfully applied this technique for the first time to the painting entitled Patch of Grass by Vincent van Gogh. Behind this painting is a portrait of a woman.

It is well-known that Vincent van Gogh often painted over his older works. Experts estimate that about one third of his early paintings conceal other compositions under them. A new technique, based on synchrotron radiation induced X-ray fluorescence spectroscopy, reveals this type of hidden painting. The techniques usually used to reveal concealed layers of paintings, such as conventional X-ray radiography, have their limitations. Together with experts from the Deutsches Elektronen-Synchrotron in Hamburg and the Kröller-Müller Museum, TU Delft materials expert and art historian Dr Joris Dik, and University of Antwerp chemistry professor Koen Janssens therefore chose to adopt a different approach. The painting is subjected to an X-ray bundle from a synchrotron radiation source, and the fluorescence of the layers of paint is measured. This technique has the major advantage that the measured fluorescence is specific to each chemical element. Each type of atom (e.g. lead or mercury) and also individual paint pigments can therefore be charted individually. The benefit of using synchrotron radiation is that the upper layers of paint distort the measurements to a lesser degree. Moreover, the speed of measurement is high, which allows relatively large areas to be visualised.

Patch of Grass

This method was applied to a painting by Vincent van Gogh. The work in question, Patch of Grass, was painted by Van Gogh in Paris in 1887 and is owned by the Kröller-Müller Museum. Previous research had already discovered the vague outline of a head behind the painting. It was scanned at the synchrotron radiation source DORIS at Deutsches Elektronen-Synchrotron DESY in Hamburg using an intense but very small X-ray bundle. Over the course of two days, the area covering the image of a woman's head was scanned, measuring 17.5 x 17.5 cm.

The measurements enabled researchers to reconstruct the concealed painting in unparalleled detail. In particular the combination of the distribution of the elements mercury and antimony (from specific paint pigments) provided a 'colour photo' of the portrait which had been painted over.

The reconstruction enables art historians to understand the evolution of Van Gogh's work better. The applied technique is expected to pave the way for research into many other concealed paintings.

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The original scientific article can be found at: http://pubs.acs.org/cgi-bin/abstract.cgi/ancham/asap/abs/ac800965g.html

Click here for a film explaining the research (QuickTime, 10 Mb) or the high res version, and a film of the work in progress.

The Power of Peter Piper: How alliteration enhances poetry, prose, and memory

From nursery rhymes to Shakespearian sonnets, alliterations have always been an important aspect of poetry whether as an interesting aesthetic touch or just as something fun to read. But a recent study suggests that this literary technique is useful not only for poetry but also for memory.

In several experiments, researchers R. Brooke Lea of Macalester College, David N. Rapp of Northwestern University, Andrew Elfenbein and Russell Swinburne Romine of University of Minnesota and Aaron D. Mitchel of the Pennsylvania State University had participants read works of poetry and prose with alliterative sentences to show the importance of repetitive consonants on memory.

Previous studies have shown that alliteration can act as a better tool for memory than both imagery and meaning, however the reason for this has never been established. In their experiments the researchers hoped to demonstrate that alliterations retrieve similar sounding words and phrases from a person's memory, making it a useful tool for poetry comprehension and memorization.

In one experiment, a group of participants read aloud poems with similar alliterative sounds throughout it while other participants had to read aloud poems with either different alliterative sounds or no alliterations at all. A second experiment had the same conditions, except that participants read a series of poems silently. The final experiment had participants read a work of narrative prose, also with the same conditions in regards to alliterative sounds in the literature. In each experiment, participants had to recall both content and thematic aspects from the works that they read.

The results of all three experiments underscore the interaction between alliteration and memory. In each of the experiments, participants in the same-alliteration condition were able to recall the most from the literature they read.

"In our experiments, concepts presented early in a poem (or prose passage) were more available when alliterative sounds overlapped between lines than when there was no overlap," the researchers reported.

Additionally, the results of the other experiments, published in the July issue of Psychological Science, a journal of the Association for Psychological Science, show that alliteration's affect on memory is not lessened by either the type of work it is used in or whether or not the literature is read silently or aloud. Most importantly, the results demonstrate alliteration only works as a tool for memory when the alliterative sounds are similar; while the participants in the same-alliteration condition did well in each experiment, those in the other two conditions had similar, less impressive results. *Author Contact: R. Brooke Lea lea@macalester.edu*

Study identifies changes to DNA in major depression and suicide

Autopsies usually point to a cause of death but now a study of brain tissue collected during these procedures, may explain an underlying cause of major depression and suicide. The international research group, led by Dr. Michael O. Poulter of Robarts Research Institute at The University of Western Ontario and Dr. Hymie Anisman of the Neuroscience Research Institute at Carleton University, is the first to show that proteins that modify DNA directly are more highly expressed in the brains of people who commit suicide. These proteins are involved in chemically modifying DNA in a process called epigenomic regulation. The paper is published in Biological Psychiatry.

The researchers compared the brains of people who committed suicide with those of a control group who died suddenly, from heart attacks and other causes. They found that the genome in depressed people who had committed suicide was chemically modified by a process that is normally involved in regulating the essential characteristics of all cells in the body. As Poulter explains, "We have about 40,000 genes in every cell and the main reason a brain cell is a brain cell is because only a small fraction of the genes are turned on. The remaining genes that are not expressed are shut down by an epigenetic process called DNA methylation."

The rate of methylation in the suicide brains was found to be much greater than that of the control group. Importantly, one of the genes they studied was shown to be heavily chemically modified and its expression was reduced. This particular gene plays a major role in regulating brain activity. "Interestingly, the nature of this chemical modification is long term and hard to reverse, and this fits with depression," says Poulter.

"The whole idea that the genome is so malleable in the brain is surprising. Finding that epigenetic mechanisms continue to influence gene expression is pretty unusual," says Poulter, who is also a professor in the Department of Physiology and Pharmacology at Western's Schulich School of Medicine & Dentistry. "These observations open an entirely new avenue of research and potential therapeutic interventions." The research was funded through the Canadian Institutes of Health Research.

Cartilage that repairs itself? OHSU research reveals important clues

Mice with natural ability to regenerate cartilage may help scientists find ways to significantly improve treatment of human injuries – such as Tiger Woods' damaged knee cartilage

PORTLAND, Ore. – A strain of mice with the natural ability to repair damaged cartilage may one day lead to significant improvements in treatment of human knee, shoulder and hip injuries.

Researchers at Oregon Health & Science University have discovered males from a strain of mice called MRL/MpJ have the innate ability to repair their own knee cartilage. "We think there is something special about these mice," said Jamie Fitzgerald, Ph.D., assistant professor of orthopedics and rehabilitation in the OHSU School of Medicine. "They have the ability to regenerate cartilage."

"Knee pain is one of the most common musculoskeletal complaints that bring people to their doctor," Fitzgerald said. Cartilage is a key culprit. "Human cartilage injuries heal poorly and can lead to cartilage degeneration and osteoarthritis. This is an enormous clinical problem. It is estimated that one quarter of the adult population will have some kind of arthritis by 2020."

Knee injuries are a significant issue for professional athletes. The National Football League Charities provided the initial grant to launch the study. "Cartilage injuries can be career-ending for football players," Fitzgerald said.

Greg Oden missed his rookie season with the Blazers because of a cartilage injury. Although it's not his primary injury, champion golfer Tiger Woods was sidelined for two months this spring after surgery to deal with damaged cartilage in his left knee.

Fitzgerald and his fellow OHSU researchers Andrea Herzka, M.D., and Cathleen Rich studied knee injuries in 150 mice. Three months after the cartilage in their knees was damaged, male MRL mice had replaced a significant amount of the injured tissue with healthy cartilage. The results of their study were recently published in Osteoarthritis and Cartilage.

Chris Little, director of the Raymond Purves Bone and Joint Research Laboratories in Sydney, Australia, and one of the scientists involved in the project, says the finding is significant for human health. "The research we have published is an early, but important step in unraveling the important pathways that will facilitate development of new treatments."

The next step is understanding why these mice are able to restore the cartilage in their knees. "If we can identify what genes or proteins are necessary for cartilage to heal, we can work toward finding similar genes and proteins in humans," Herzka says. An actual treatment, however, "is many years away."

Fitzgerald became interested in studying the MRL strain of mice in 2005 while working at the Murdoch Childrens Research Institute in Melbourne, Australia. His work followed the observation that MRL mice had the ability to heal ear wounds without scarring, including replacing cartilage, hair follicles, skin and blood vessels. Little helped design the experiments and taught Fitzgerald and the OHSU team surgical techniques used in the effort.

Was ancient Greek 'computer' an astronomical tool?

* 30 July 2008

*** Jo Marchant**

See video of the Antikythera mechanism here.

INSCRIPTIONS on a mysterious 2000-year-old clockwork device suggest that the artefact was inspired by earlier devices made by the great Greek mathematician Archimedes.

The so-called "Antikythera mechanism" has puzzled historians since it was salvaged from an ancient shipwreck near the Greek island of Antikythera in 1901. It dates back to about 100 BC, and consists of more than 30 bronze gear wheels and pointers, enclosed in a wooden case.

The device is by far the most advanced scientific instrument to survive from antiquity - nothing else close to its complexity shows up in archaeological records for more than 1200 years, when mechanical clocks appeared in medieval Europe.

The Antikythera mechanism

The Antikythera mechanism is thought to be a mechanical computer, which used sophisticated algorithms to calculate the motions of celestial bodies. A dial on the front showed the position of the sun, moon and probably the planets in the zodiac, while the back displayed a 19-year lunisolar calendar, as well as the timing of eclipses (Nature, DOI: 10.1038/nature05357; Interdisciplinary Science Reviews, vol 32, p 27).

The mechanism may have been used by philosophers to show the workings of the heavens, as suggested by the Roman author Cicero, who wrote in the 1st century BC of bronze devices that erroneously modelled the movements of the sun, moon and planets around Earth.

The origin of the Antikythera mechanism was a mystery, but newly deciphered inscriptions show that its calendar used local month names. They match those used by Greek colonies founded by the city of Corinth, and a prime candidate is Syracuse, in Sicily (Nature, DOI: 10.1038/nature07130).

Alexander Jones of the Institute for the Study of the Ancient World in New York, who helped decipher the inscriptions, says the presence of a local calendar supports the idea that rather than being used by astronomers, the mechanism was intended for demonstrations, albeit to a small, educated elite.

Jones and his colleagues say the identification of Syracuse is intriguing because one of the models Cicero mentioned in his writings was made by Archimedes in the 3rd century BC. Archimedes worked in Syracuse, so the Antikythera mechanism, made at least a century later, might be part of a tradition of geared mechanisms begun by the legendary mathematician.

But this also prompts a new mystery, because the wreck on which the mechanism was found was a Roman ship, sailing not from Sicily but from the eastern Mediterranean in 70-60 BC, mostly likely taking looted Greek treasures back to Rome.

"The route of the ship is puzzling," says Paul Cartledge, a professor of Greek history at the University of Cambridge, UK. "It was going from east to west, and Antikythera is well to the east of Syracuse."

Cartledge says it's not impossible that the instrument was designed in the east – Rhodes or Alexandria say – for use in Syracuse.

However the mechanism seems to have been several decades old when it was taken on its final journey. So perhaps it was made in Syracuse for a wealthy owner who subsequently moved to the eastern Mediterranean, or was carried there as a gift or votive offering, before later becoming part of booty taken for Rome.

Jo Marchant is author of Decoding the Heavens, a book about the Antikythera mechanism to be published in November 2008.

First performance-enhancing drugs for exercise endurance?

While steroids can help build the bulky muscles that lend athletes and body builders power and speed, there hadn't been a drug capable of building the endurance needed to run a marathon or to ride a bike through the Alps. Now, there just might be, suggests a new study in mice reported in the journal Cell, a Cell Press publication.

The report shows that a drug developed for the treatment of metabolic disease, when taken in combination with exercise, gives mice the ability to run farther than exercise training alone can.

“When we gave the mice a small amount of daily exercise in the presence or not of the drug, all showed an increased ability to run. But those on the drug gained an additional hour," said Ronald Evans of the Salk Institute.

Moreover, they found, treatment with another compound endowed mice with greater endurance, even without the exercise. "It's tricking the muscle into 'believing' it's been exercised daily," Evans said. "It's basically the couch potato experiment, and it proves you can have a pharmacologic equivalent to exercise."

Both chemicals work by tapping into the molecular pathways that normally reprogram muscle in response to exercise. The findings could be a boon to those with health problems that make exercise difficult, he said. However, they also have a "high potential for abuse" by athletes, despite the fact that the effects seen in the mice may or may not work as well in highly trained individuals who may be "pushing the limits" already.

Skeletal muscle comes in two main types: bulky fast twitch muscles for power and speed and slender slow twitch muscles for endurance. Fast twitch muscles burn sugar that must be stored in the muscle itself while slow twitch muscle burns fat.

Earlier studies by Evans' team showed they could genetically engineer, or "pre-program" mice to produce more of the fat-burning slow twitch muscle fibers, turning them into "marathon mice" with nearly 100 percent greater running endurance as untrained adults. The key was ramping up activity of a gene in muscle called PPARd, known to control other genes important to skeletal muscle metabolism.

But could you re-program rather than pre-program the muscles of adult animals by simply giving a drug that acts on PPARd?

To find out, they gave mice an experimental drug, known only as GW1516, that increases the activity of PPARd. The drug is being tested for the treatment of metabolic disease, but Evans wanted to know what effects it might have on muscle.

"It was a spectacular failure," Evans said. "The drug by itself had no impact on running ability" even though their were changes in muscle gene activity.

Something was missing from the equation, so the researchers took a different tack. They gave the PPARd drug to mice that were undergoing exercise training. The same dose and duration of GW1516 treatment that previously failed to alter performance, when paired with four weeks of exercise training, increased the animals' running time by 68 percent and their running distance by 70 percent over trained mice given a placebo, they report.

The muscles of those mice also showed a unique "endurance gene signature," including patterns of gene activity not seen with either the drug or exercise alone. That pattern did bear a striking resemblance to the one seen years earlier in the genetically engineered marathon mice, they noted.

Since PPARd on its own wasn't enough, the researchers decided to try one more thing: a chemical known as AICAR that was known to act on a gene called AMPK. Evans group suspected AMPK might be the link between exercise and PPARd.

To their surprise, even in sedentary mice, four weeks of AICAR treatment alone induced metabolic genes and enhanced running endurance by 44 percent. "We were blown away that AICAR alone mimicked exercise—not to the same level but a healthy boost," Evans said.

"In this study, we revealed that synthetic PPARd activation and exercise or more importantly AMPK activation alone, provides a robust transcriptional cue that re-programs the skeletal muscle genome and dramatically enhances endurance," the researchers concluded. "We believe that the strategy of re-organizing the preset genetic imprint of muscle (as well as other tissues) using exercise mimetic drugs has therapeutic potential in treating certain muscle diseases such as wasting and frailty as well as obesity where exercise is known to be beneficial."

Given the potential for abuse by athletes set on winning at any cost, Evans said his group has already spoken to the World Anti-Doping Agency and is developing a test aimed at detecting use of the PPARd-boosting drug. That test won't be available in time for this summer's Olympic games, he said. It also wouldn't detect the use of AICAR, a chemical that is available but isn't an FDA-approved drug.

While the potential for important health benefits is substantial, "both [compounds] are very logical targets for athletic abuse, and we need to be aware of that," Evans said.

The researchers include Vihang A. Narkar, Salk Institute, La Jolla, CA; Michael Downes, Salk Institute, La Jolla, CA; Ruth T. Yu, Salk Institute, La Jolla, CA; Emi Embler, Salk Institute, La Jolla, CA; Yong-Xu Wang, University of Massachusetts Medical School, Worcester, MA; Ester Banayo, Howard Hughes Medical Institute, La Jolla, CA; Maria M. Mihaylova, Salk Institute, La Jolla, CA; Michael C. Nelson, Salk Institute, La Jolla, CA; Yuhua Zou, Salk Institute, La Jolla, CA; Henry Juguilon, Salk Institute, La Jolla, CA; Heonjoong Kang, Marine Biotechnology Laboratory, School of Earth and Environmental Sciences, Seoul National University, Seoul, South Korea; Reuben J. Shaw, Salk Institute, La Jolla, CA; and Ronald M. Evans, Salk Institute, La Jolla, CA, Howard Hughes Medical Institute, La Jolla, CA

'Major discovery' from MIT primed to unleash solar revolution

Scientists mimic essence of plants' energy storage system

CAMBRIDGE, Mass. -- In a revolutionary leap that could transform solar power from a marginal, boutique alternative into a mainstream energy source, MIT researchers have overcome a major barrier to large-scale solar power: storing energy for use when the sun doesn't shine.

Until now, solar power has been a daytime-only energy source, because storing extra solar energy for later use is prohibitively expensive and grossly inefficient. With today's announcement, MIT researchers have hit upon a simple, inexpensive, highly efficient process for storing solar energy.

Requiring nothing but abundant, non-toxic natural materials, this discovery could unlock the most potent, carbon-free energy source of all: the sun. "This is the nirvana of what we've been talking about for years," said MIT's Daniel Nocera, the Henry Dreyfus Professor of Energy at MIT and senior author of a paper describing the work in the July 31 issue of Science. "Solar power has always been a limited, far-off solution. Now we can seriously think about solar power as unlimited and soon."

Inspired by the photosynthesis performed by plants, Nocera and Matthew Kanan, a postdoctoral fellow in Nocera's lab, have developed an unprecedented process that will allow the sun's energy to be used to split water into hydrogen and oxygen gases. Later, the oxygen and hydrogen may be recombined inside a fuel cell, creating carbon-free electricity to power your house or your electric car, day or night.

The key component in Nocera and Kanan's new process is a new catalyst that produces oxygen gas from water; another catalyst produces valuable hydrogen gas. The new catalyst consists of cobalt metal, phosphate and an electrode, placed in water. When electricity — whether from a photovoltaic cell, a wind turbine or any other source — runs through the electrode, the cobalt and phosphate form a thin film on the electrode, and oxygen gas is produced.

Combined with another catalyst, such as platinum, that can produce hydrogen gas from water, the system can duplicate the water splitting reaction that occurs during photosynthesis.

The new catalyst works at room temperature, in neutral pH water, and it's easy to set up, Nocera said. "That's why I know this is going to work. It's so easy to implement," he said.

'Giant Leap' For Clean Energy

Sunlight has the greatest potential of any power source to solve the world's energy problems, said Nocera. In one hour, enough sunlight strikes the Earth to provide the entire planet's energy needs for one year.

James Barber, a leader in the study of photosynthesis who was not involved in this research, called the discovery by Nocera and Kanan a "giant leap" toward generating clean, carbon-free energy on a massive scale.

"This is a major discovery with enormous implications for the future prosperity of humankind," said Barber, the Ernst Chain Professor of Biochemistry at Imperial College London. "The importance of their discovery cannot be overstated since it opens up the door for developing new technologies for energy production thus reducing our dependence for fossil fuels and addressing the global climate change problem."

'Just the beginning'

Currently available electrolyzers, which split water with electricity and are often used industrially, are not suited for artificial photosynthesis because they are very expensive and require a highly basic (non-benign) environment that has little to do with the conditions under which photosynthesis operates.

More engineering work needs to be done to integrate the new scientific discovery into existing photovoltaic systems, but Nocera said he is confident that such systems will become a reality.

"This is just the beginning," said Nocera, principal investigator for the Solar Revolution Project funded by the Chesonis Family Foundation and co-Director of the Eni-MIT Solar Frontiers Center. "The scientific community is really going to run with this."

Nocera hopes that within 10 years, homeowners will be able to power their homes in daylight through photovoltaic cells, while using excess solar energy to produce hydrogen and oxygen to power their own household fuel cell. Electricity-by-wire from a central source could be a thing of the past.

The project is part of the MIT Energy Initiative, a program designed to help transform the global energy system to meet the needs of the future and to help build a bridge to that future by improving today's energy systems. MITEI Director Ernest Moniz, Cecil and Ida Green Professor of Physics and Engineering Systems, noted that "this discovery in the Nocera lab demonstrates that moving up the transformation of our energy supply system to one based on renewables will depend heavily on frontier basic science."

The success of the Nocera lab shows the impact of a mixture of funding sources – governments, philanthropy, and industry. This project was funded by the National Science Foundation and by the Chesonis Family Foundation, which gave MIT $10 million this spring to launch the Solar Revolution Project, with a goal to make the large scale deployment of solar energy within 10 years.

Living with a partner reduces risk of Alzheimer's

Living with a spouse or a partner decreases the risk of developing Alzheimer's and other dementia diseases. This according to a study by Krister Håkansson, researcher in psychology at Växjö University and Karolinska Institutet, Sweden. The results were presented for the first time yesterday at the world's largest dementia conference.

"This is, for me, an overwhelming start," says Mr Håkansson. "It's the first study I've done in this field, and the results are astounding. They indicate a very strong correlation between this type of social factor and the risk of developing dementia."

The new findings are based on data from a Finnish study, which was unique in that 2,000 people were examined at the age of around 50 and again twenty-one years later. Normally, dementia researchers only study late-life individuals. Previous research has shown that an active lifestyle, both intellectually and socially, can decrease the risk of developing dementia; since a shared life often entails considerable social and intellectual stimulation, the point of inquiry of this present study was whether living with a spouse or a partner can help to ward off dementia.

The results show that people living with a spouse or a partner in midlife ran a 50 per cent lower risk of developing dementia than people living alone, even when controlled for other risk factors, such as age.

How long a person had been single and for what reasons also affected the chances of developing dementia. Those who had lived alone their entire adult life ran twice the risk, while those who were divorced in midlife and remained subsequently single ran three times the risk.

Widows and widowers ran the greatest risk. Those at greatest risk of developing dementia diseases were people who had lost their partner before middle age and then continued to live as a widow or widower. The study showed that the chances of developing Alzheimer's for these individuals were six times greater than for married couples.

"This suggests two influencing factors – social and intellectual stimulation and trauma," says Mr Håkansson. "In practice, it shows how important it is to put resources into helping people who have undergone a crisis. If our interpretation will hold, such an intervention strategy could also be profitable for society considering the costs for dementia care."

The new results were presented at the 2008 Alzheimer's Association International Conference on Alzheimer's Disease (ICAD 2008), the world's largest in the field, which is currently being help in Chicago. For more news, visit the conference press room at http://www.alz.org/icad/press_room.asp

Krister Håkansson can already see several interesting lines of inquiry leading from this study. "Does it matter, for instance, if the relationship is a happy one or not? And does it matter if someone has always intended to live a single life or not?"

New discovery may lead to immunization against cardiovascular disease

Low levels of naturally occurring antibodies may represent an increased risk of developing cardiovascular disease, particularly stroke in men. This discovery, published in the academic journal Atherosclerosis, has now led to attempts to develop an immunization against cardiovascular disease.

Atherosclerosis (hardening of the arteries) is an inflammatory disease in which the walls of the blood vessels are thickened and become less elastic. It can cause blood clots and other cardiovascular diseases. It is not known precisely what causes atherosclerosis, but the immune system probably plays an important role. Research scientists suspect that various oxidised forms of what is known as bad cholesterol, LDL (low-density lipoprotein), contribute to the development of the disease. A research team from Karolinska Institutet, in cooperation with Lund University, has now shown that a particular type of naturally occurring antibodies, anti-PC, which are targeted against the lipid portion of the LDL molecule, play an important role in the development of cardiovascular disease.

The findings show that individuals who have low levels of anti-PC are at increased risk of cardiovascular disease. The risk is particularly high in men who develop stroke, with an almost fourfold increase.

This newly discovered risk factor, low levels of anti-PC, is independent of previously known risk factors such as high blood pressure, high blood lipids, diabetes and smoking.

"Our findings suggest that anti-PC can be used as a complement to the traditional risk factors to improve diagnosis and treatment. In addition we are currently developing anti-PC as a vaccine for atherosclerosis and cardiovascular disease," says Professor Johan Frostegård, who directed the study.

The study is based on data from 349 people who at some time over a 12-year period have suffered a heart attack or stroke and 693 individuals without symptoms of cardiovascular disease. The research has been carried out under the EU consortium CVDIMMUNE, http://www.cvdimmune.com/, which is led by Johan Frostegård at Karolinska Institutet.

Publication: "Low levels of IgM antibodies against phosphorylcholine - a potential risk marker for ischemic stroke in men." Beatrice Sjöberg, Jun Su, Ingrid Dahlbom, Hans Grönlund, Max Wikström, Bo Hedblad, Göran Berglund, Ulf de Faire and Johan Frostegård. Atherosclerosis 2008, in press, accepted manuscript, available online.

Liver damage in hepatitis C patients could be treated with warfarin, says study

The drug warfarin may help prevent liver failure in thousands of people with Hepatitis C, according to new research.

In a study published tomorrow (1 August) in the Journal of Thrombosis and Haemostasis, researchers show that warfarin reduces the scarring on the liver caused by Hepatitis C. This scarring, or fibrosis, replaces normal liver cells and can lead to cirrhosis of the liver and ultimately liver failure.

Following the new findings in mouse models, the Imperial College London researchers are now embarking on a clinical trial of warfarin as a treatment for people with Hepatitis C, funded by the Medical Research Council (MRC).

There are an estimated 300,000 people in the UK with chronic Hepatitis C. The disease progresses much more quickly in some patients than in others and around one in five of those infected will develop cirrhosis.

Treatment to clear the infection is currently effective in only around 50 percent of patients and can have considerable unpleasant side effects such as fatigue, nausea and depression. If this treatment fails, there are no currently effective therapies to slow the progression of fibrosis.

The new research looks at how warfarin affects the progression of fibrosis in mice with chronic liver injury. Warfarin is already used to prevent and treat blood clots in people with artificial heart valves, deep vein thrombosis, and a host of other conditions.

A previous study by the same researchers demonstrated that in Hepatitis C, scarring of the liver accelerates in those patients who are prone to form blood clots. This led the researchers to believe that warfarin's anti-clotting properties might enable the drug to fight the disease.

The new study showed that treatment with warfarin significantly reduces the progression of fibrosis in normal mice with chronic liver injury. It also shows that warfarin reduces the progression of fibrosis in mice with chronic liver injury and a genetic mutation known as Factor V Leiden (FVL), which causes fibrosis to progress at a much faster rate than usual because it amplifies the body's clotting mechanisms.

Professor Mark Thursz, one of the authors of the study from the Division of Medicine at Imperial College London, said: "At the moment there are a great many people with Hepatitis C who have no treatment options left and it would transform their lives if we could prevent them from developing liver failure. We are looking forward to seeing the results of our upcoming trial in humans now that we've had such promising results in the trial in mice."

Dr Quentin Anstee, an MRC Clinical Research Fellow and the corresponding author of the study from Imperial College London, added: "If we have positive results from the new trial, we will have a potential treatment that is already available and very cheap, and which should be safe enough for people to take. If we are successful in Hepatitis C patients, we are hopeful that such treatment might benefit people with liver damage from other causes, and this is something we would be keen to study further."

The researchers are recruiting 90 patients for the new trial who have undergone a liver transplant as a result of liver failure caused by hepatitis C. A third of such patients progress very rapidly to fibrosis following transplantation.

The researchers hope that treating these patients with warfarin will prevent this liver damage and improve their prognosis. Transplant patients have a liver biopsy every year following transplantation to assess their progress, and the researchers will analyse data from this biopsy to establish the effectiveness of the warfarin treatment. The two-year trial will take place across five centres including Imperial College Healthcare NHS Trust, which has integrated with Imperial College London to form the UK's first Academic Health Science Centre.

The trial is taking place in transplant patients because the researchers estimate that it would take 10-15 years to conduct a trial in patients in whom the disease was progressing at a normal rate.

New Study Shows Compounds From Soy Affect Brain and Reproductive Development

Matt Shipman, News Services, (919) 515-3470

Two hormone-like compounds linked to the consumption of soy-based foods can cause irreversible changes in the structure of the brain, resulting in early-onset puberty and symptoms of advanced menopause in research animals, according to a new study by researchers at North Carolina State University. The study is a breakthrough in determining how these compounds can cause reproductive health problems, as well as in providing a key building block for how to treat these problems.

The study is the first to show that the actual physical organization of a region of the brain that is important for female reproduction can be significantly altered by exposure to phytoestrogens – or plant-produced chemicals that mimic hormones – during development. Specifically, the study finds that the compounds alter the sex-specific organization of the hypothalamus – a brain region that is essential to the regulation of puberty and ovulation. The study also shows that the phytoestrogens could cause long-term effects on the female reproductive system.

While the study examined the impact of these compounds on laboratory rats, neurotoxicologist Dr. Heather Patisaul – who co-authored the study – says the affected "circuitry" of the brain is similar in both rats and humans. Patisaul is an assistant professor in NC State's Department of Zoology. Her co-author is Heather Bateman, a doctoral student in the department.

Patisaul says this finding is extremely important because, while the changes in brain structure cannot be reversed, "if you understand what is broken, you may be able to treat it." Patisaul says she is in the process of evaluating the effects of these compounds on the ovaries themselves.

Patisaul says that this study is also "a step towards ascertaining the effects of phytoestrogens on developing fetuses and newborns." Patisaul adds that these phytoestrogenic compounds cross the placental barrier in humans and that, while many people are concerned about the effects of man-made compounds on human health, it is important to note that some naturally occurring substances can have similar effects.

In the study, which will be published in an upcoming issue of Neurotoxicology, the researchers exposed newborn rats to physiologically relevant doses of the phytoestrogens genistein and equol, and then looked at reproductive health markers in the rats throughout their adulthood. The neonatal stage of development in rats is comparable to the latter stages of pregnancy for humans, Patisaul says. Genistein is a phytoestrogen that is found in various plants, including soybeans and soy-based foods. Equol is a hormone-like compound that is formed when bacteria found in the digestive system metabolize another phytoestrogen. However, only approximately a third of humans have the necessary bacteria to produce equol.

The study shows that both genistein and equol result in the early disruption of the rats' estrus cycle – which would be corollary to early onset of menopause in a human. The study also showed that genistein caused the early onset of puberty. The disruption of the estrus cycle could stem from problems with the brain or the ovaries, so the researchers decided to determine if the compounds had any effect on brain development or function.

Patisaul explains that the brains of both female rats and female humans have a region that regulates ovulation. "That part of the brain," Patisaul says, "is organized by hormones during development – which is the neonatal stage for rats and during gestation for humans." Patisaul says the new study shows that the female brain is "critically sensitive" to genistein and equol during this crucial stage of development – and that this may indicate that the brain is also especially sensitive during this period to all phytoestrogens and possibly other man-made chemicals, such as bisphenol-A.

Note to editors: The study's abstract follows.

"Disrupted female reproductive physiology following neonatal exposure to phytoestrogens or estrogen specific ligands is associated with decreased GnRH activation and kisspeptin fiber density in the hypothalamus"

Authors: Dr. Heather B. Patisaul, Heather L. Bateman, North Carolina State University

Published: July 2008, online by Neurotoxicology

Abstract: It is well established that estrogen administration during neonatal development can advance pubertal onset and prevent the maintenance of regular estrous cycles in female rats. This treatment paradigm also eliminates the preovulatory rise of gonadotropin releasing hormone (GnRH). It remains unclear, however, through which of the two primary forms of the estrogen receptor (ERα or ERβ) this effect is mediated. It is also unclear whether endocrine disrupting compounds (EDCs) can produce similar effects. Here we compared the effect of neonatal exposure to estradiol benzoate (EB), the ERα specific agonist 1,3,5-tris(4-Hydroxyphenyl)-4-propyl-1H-pyrazole (PPT), the ERβ specific agonist diarylpropionitrile (DPN) and the naturally occurring EDCs genistein (GEN) and equol (EQ) on pubertal onset, estrous cyclicity, GnRH activation, and kisspeptin content in the anteroventral periventricular (AVPV) and arcuate (ARC) nuclei. Vaginal opening was significantly advanced by EB and GEN. By ten weeks postpuberty, irregular estrous cycles were observed in all groups except the control group. GnRH activation, as measured by the percentage of immunopositive GnRH neurons that were also immunopositive for Fos, was significantly lower in all treatment groups except the DPN group compared to the control group. GnRH activation was absent in the PPT group. These data suggest that neonatal exposure to EDCs can suppress GnRH activity in adulthood, and that ERα plays a pivotal role in this process. Kisspeptins (KISS) have recently been characterized to be potent stimulators of GnRH secretion. Therefore we quantified the density of KISS immunolabeled fibers in the AVPV and ARC. In the AVPV, KISS fiber density was significantly lower in the EB and GEN groups compared to the control group but only in the EB and PPT groups in the ARC. The data suggest that decreased stimulation of GnRH neurons by KISS could be a mechanism by which EDCs can impair female reproductive function.

Biological Fathers Not Necessarily the Best, Social Dads Parent Well too

Madison, WI – July 30, 2008 – A large number of U.S. children live or will live with a “social father,” a man who is married to or cohabiting with the child’s mother, but is not the biological father. A new study in the Journal of Marriage and Family examined differences in the parenting practices of four groups of fathers according to whether they were biologically related to a child and whether they were married to the child’s mother. Researchers found that married social fathers exhibited equivalent or higher quality parenting behaviors than married and cohabiting biological fathers.

Furthermore, whereas married and cohabiting biological fathers displayed relatively similar quality parenting, the parenting practices of married social fathers were of higher quality than those of cohabiting social fathers. Married social fathers were more engaged with children, took on more shared responsibility in parenting, and were more trusted by mothers to take care of children.

Led by Lawrence M. Berger, PhD, MSW, of the University of Wisconsin-Madison, participants were drawn from the Fragile Families and Child Wellbeing Study, a longitudinal study of children born in 20 large U.S. cities in the late 1990s and early 2000s. Sample children were mostly born to unmarried parents and had been followed from birth to approximately age five.

Analyses and regression results from interviews with mothers revealed that they perceived married social fathers to be engaged in relatively high quality parenting practices with the five-year-old children. Most notably, social fathers exhibited significantly higher levels of cooperation in parenting than biological fathers.

“On the whole, our findings suggest that marriage is a better predictor of parenting quality with regard to social fathers than biological fathers,” the authors conclude. “Our study is relevant to understanding the quality of parental care that children receive from resident fathers across a range of family configurations that are now commonly experienced by children.”

Simian foamy virus found in several people living and working with monkeys in Asia

A research team led by University of Washington scientists has found that several people in South and Southeast Asian countries working and living around monkeys have been infected with simian foamy virus (SFV), a primate virus that, to date, has not been shown to cause human disease. The findings provide more evidence that Asia, where interaction between people and monkeys is common and widespread, could be an important setting for future primate-to-human viral transmission. The study appears in the August issue of the journal Emerging Infectious Disease.

Though SFV has not been found to cause any human disease, it is a slow-acting retrovirus, so it could take many years before scientists determine the effects of infection. SFV could also change at the genetic level, resulting in a new strain of the virus that would affect humans. Scientists believe that a similar process occurred with HIV, which probably originated as a virus in non-human primates in Africa before jumping the species barrier to human hosts.

In this study, researchers from the University of Washington visited several countries in Asia, interviewing and testing about 300 people who live or work closely with any one of several species of small-bodied monkeys called macaques. Eight of those participants tested positive for SFV. The people who had contracted the virus came from a variety of places and contexts: one person lived in an urban area in Bangladesh that had a large monkey population, for instance, while two other people lived near a monkey temple in Thailand. Monkey temples are places of religious worship that have become refuges for populations of primates.

Though much of the research on viral transmission between humans and other primates has focused on Africa, UW researcher Dr. Lisa Jones-Engel has led multiple studies examining the issue in Asia. Some Asian countries are prime areas for viral transmission between monkeys and humans, she explained, because of the huge populations of both and the widespread interaction between the species. People are in close contact with monkeys in many settings in Asia: in cities, religious temples, open-air markets, street performances, nature preserves, hunting areas, zoos, and even homes, where monkeys are kept as pets.

"So much of the focus on this issue has been in Africa, but there, the interface between humans and other primates is decreasing," said Jones-Engel, a senior research scientist in the Division of International Programs at the UW's Washington National Primate Research Center. "The intensity of bush meat hunting and infectious diseases have taken a huge toll on primate populations there. Individuals in Africa who are interacting with other primates are often very isolated from other humans – they live in small, rural villages, which limits the potential spread of pathogens."

In Asia, however, monkeys are often respected or revered because of cultural and religious traditions. The rapid expansion of cities and the decline of wild habitats have driven many monkey populations into urban areas, Jones-Engel said, where they interact more closely with large, interconnected populations of people.

In one state in northern India, for example, researchers estimate that more than a quarter-million rhesus macaques, or about 86 percent of the wild population, live in urban areas because of habitat loss. Unlike the great apes, such as chimpanzees or gorillas, rhesus macaques and other species of monkeys are very adaptable to new habitats.

"Some macaque species thrive in human-altered environments, given the tolerance of the local people," said Dr. Gregory Engel, clinical assistant professor of family medicine at the UW and a co-author on this study.

The group's findings support the notion that viral transmission could occur in any one of many settings in Asia, from religious temples to urban areas, and that the issue could affect many different people, from temple workers to pet owners. One of the people infected was a farmer in Thailand who had trained monkeys to help him harvest coconuts.

"This is a heterogeneous sample – subjects reported contact with primates in a variety of contexts," explained Gregory Engel, who is also a physician at Swedish Medical Center in Seattle. "It seems that some of these contexts are going to be very important, but they haven't been studied much. Zoo workers and bush meat hunters have been typically considered at the highest risk for viral transmission, but none of the zoo workers or hunters in our sample tested positive for SFV."

The researchers suggest that better disease monitoring and further study of monkey-human interaction could help cut down on the risks associated with viral transmission. People living, working, or visiting areas of Asia with monkey populations can also reduce their risk by limiting their close contact with the animals. Tourists can reduce their risk by wearing long pants around monkeys, and by not trying to feed, pet, or hold the animals.

This research project included scientists at the Fred Hutchinson Cancer Research Center in Seattle; the University of Toronto; Notre Dame University in Indiana; Udayana University, Bali, Indonesia; Tribhuvan University, Kathmandu, Nepal; Chiang Mai University, Thailand; Jahangirnagar University, Dhaka, Bangladesh; and the Southwest Foundation for Biomedical Research, San Antonio, Texas.

Physicians ask EPA, 'Antibiotics to cure sick apples, or sick children?'

Arlington, VA—A federal decision to permit the State of Michigan to spray the state's apple orchards with gentamicin risks undermining the value of this important antibiotic to treat blood infections in newborns and other serious human infections, according to the Infectious Diseases Society of America (IDSA).

The Environmental Protection Agency (EPA) on Wednesday granted the state of Michigan "emergency" permission to use gentamicin to fight a tree disease called fire blight.

"At a time when bacteria are becoming increasingly resistant to many of our best antibiotics, it is an extremely bad idea to risk undermining gentamicin's effectiveness for treating human disease by using it to treat a disease in apples," said IDSA President Donald Poretz, MD.

Gentamicin is a crucial antibiotic used to treat dangerous gastrointestinal and urinary tract infections, and is particularly valuable for treating blood infections in newborn children. As rates of antibiotic-resistant infections rise across the country, effective drugs like gentamicin become increasingly valuable. The Food and Drug Administration classifies gentamicin as, "highly important." The Environmental Protection Agency (EPA) currently bans its use on imported fruits and vegetables and EPA officials have previously stated that using gentamicin in agriculture could reduce its value in treating human infections.

But in an ill-advised reversal, EPA granted Michigan special permission to use the antibiotic. The reason, ironically, is that fire blight has become resistant to the antibiotic apple growers had been using, streptomycin.

Microbes evolve resistance quickly, whether they cause human disease or apple disease. What worries infectious diseases physicians is that microbes pass those resistance traits on to other microbes. So when some species of microbe inevitably evolves resistance to gentamicin, IDSA is very concerned that that trait will show up in bacteria that cause human infections.

IDSA is urging EPA to rescind its decision. "The threat of antibiotic resistance is growing, and the number of effective antibiotics is dwindling," Dr. Poretz said. "Our priority must be to save these effective antibiotics for whom they are needed most: for humans, not for agriculture."

Congress is currently considering new legislation, the Strategies To Address Antimicrobial Resistance (STAAR) Act, intended to improve the U.S. response to antimicrobial resistance. IDSA and more than twelve other major medical, health care, and public health organizations have endorsed the STAAR Act. For more information, see www.idsociety.org/staaract.htm.

Free articles get read but don't generate more citations

When academic articles are "open access" or free online, they get read more often, but they don't -- going against conventional wisdom -- get cited more often in academic literature, finds a new Cornell study.

The reason, suggest Cornell graduate student Philip Davis and colleagues, including three Cornell professors, is that most researchers probably already have all the access they need to relevant articles.

"It appears that higher quality articles -- in other words, more citable articles -- are simply made freely available," said Davis. "Previous studies using different methods simply got cause and effect reversed." The study is published online in the British Medical Journal and will be published in the print edition Aug. 9.

The findings are particularly relevant to academic researchers, because the frequency with which a researcher's work is cited can be a factor in tenure and promotion decisions.

The researchers conducted the first controlled study of open-access publishing, randomly making some journal articles freely available while keeping others available by subscription only, to determine whether increased access to journal articles results in more article downloads and citations.

They found that in the year after the articles were published, open-access articles were downloaded more but were no more likely to be cited than subscription-based articles.

"The established dogma is that freely available scientific articles are cited more because they are read more," said Davis, a former science librarian who designed the study. "We found that open-access publishing may reach more readers than subscription-access publishing, but there is no evidence that freely accessible articles are cited any more than subscription-access articles."

The researchers randomly assigned 247 articles in 11 scientific journals, to free access. They measured how many times these articles were downloaded, the number of unique visitors to each article and how many times each article was cited. "There were definitely more article downloads for freely accessible articles," said Davis. "Yet nearly half of these downloads were by Internet indexing robots like Google, crawling the Web for free content." "There are many reasons to provide free access to the literature," said Davis. "A citation advantage, however, is not one of them."

Other co-authors are Bruce V. Lewenstein, professor of communication; Daniel H. Simon, assistant professor of economics; James G. Booth, professor of statistics; and Matthew J.L. Connolly, programmer and analyst, all at Cornell. The research was funded by the Andrew W. Mellon Foundation. *http://www.news.cornell.edu/stories/July08/openaccess.cites.sl.html*

Turned-off cannabinoid receptor turns on colorectal tumor growth

Researchers find CB1 suppresses tumors, a new potential path for treatment, prevention

HOUSTON - New preclinical research shows that cannabinoid cell surface receptor CB1 plays a tumor-suppressing role in human colorectal cancer, scientists report in the Aug. 1 edition of the journal Cancer Research.

CB1 is well-established for relieving pain and nausea, elevating mood and stimulating appetite by serving as a docking station for the cannabinoid group of signaling molecules. It now may serve as a new path for cancer prevention or treatment.

"We've found that CB1 expression is lost in most colorectal cancers, and when that happens a cancer-promoting protein is free to inhibit cell death," said senior author Raymond DuBois, M.D., Ph.D., provost and executive vice president of The University of Texas M. D. Anderson Cancer Center.

DuBois and collaborators from Vanderbilt-Ingram Cancer Center also show that CB1 expression can be restored with an existing drug, decitabine. They found that mice prone to developing intestinal tumors that also have functioning CB1 receptors develop fewer and smaller tumors when treated with a drug that mimics a cannabinoid receptor ligand. Ligands are molecules that function by binding to specific receptors. Agonists are synthetic molecules that mimic the action of a natural molecule.

"Potential application of cannabinoids as anti-tumor drugs is an exciting prospect, because cannabinoid agonists are being evaluated now to treat the side-effects of chemotherapy and radiation therapy," DuBois said. "Turning CB1 back on and then treating with a cannabinoid agonist could provide a new approach to colorectal cancer treatment or prevention."

Cannabinoids are a group of ligands that serve a variety of cell-signaling roles. Some are produced by the body internally (endocannabinoids). External cannabinoids include manmade versions and those present in plants, most famously the active ingredient in marijuana (THC).

Receptor shutdown by methylation

Endocannabinoid signaling is important to the normal functioning of the digestive system and has been shown to protect the colon against inflammation. Since chronic inflammation is a known risk factor for colorectal cancer, the researchers decided to look into the role of cannabinoid receptors in a mouse model of colon cancer.

"People have looked at cannabinoids in cancer earlier, mainly in cell culture experiments," DuBois said. "The molecular mechanisms for loss of the receptor and its effect on cancer have not been previously shown."

First, the team found that CB1 was largely absent in 18 of 19 human tumor specimens and in 9 of 10 colorectal cancer cell lines. Further experimentation showed that the gene that encodes the CB1 protein was not damaged, but shut down chemically by the attachment of methyl groups - a carbon atom surrounded by three hydrogen atoms - to the gene encoding CB1.

Treating cell lines with decitabine, a demethylating agent approved for some types of leukemia, removed the methyl groups, restoring gene expression in 7 of 8 cell lines and full expression of CB1 protein in three lines.

Next, the group found that deletion of the CB1 gene in a strain of mice that spontaneously develops precancerous polyps resulted in a 2.5-to-3.8-fold increase in the number of polyps and a 10-fold increase in the number of large growths, those most likely to develop into cancer.

Treating mice that had the CB1 receptor with an endocannabinoid agonist resulted in a decline in polyps ranging from 16.7 percent to 50 percent. The reduction was greater for larger polyps.

CB1 thwarts survivin, a protein that protects cancer

Cannabinoids previously had been shown to kill cancer cells in lab experiments by inducing apoptosis - programmed cell death. The team confirmed the role of CB1 in apoptosis, showing that tumor cells with high CB1 expression were sensitive to apoptosis when treated by a cannabinoid agonist. Cell lines with silenced CB1 resisted cell death.

A series of experiments showed that CB1 increases cancer cell death by stifling a protein called survivin. Survivin is overexpressed in nearly every human tumor but is barely detectable in normal tissue, DuBois noted. Overexpression of survivin is associated with poor outcome and reduced apoptosis in colorectal cancer patients. The researchers pinpointed a cell signaling pathway by which activated CB1 cuts down survivin.

"Just increasing the levels of cannabinoids to treat colorectal cancer won't work if the CB1 receptor is not present," DuBois said. This suggests that treating first with a demethylating agent, such as decitabine, to reactivate CB1 in the tumor and following up with a cannabinoid might be an effective attack on colorectal cancer.

Scarcity of CB1 also is associated with Huntington's disease, Alzheimer's disease and multiple sclerosis. Further investigation, the researchers note, is needed to define its role in those diseases and other types of

cancer. The team also analyzed the other main cannabinoid receptor, CB2, and found no role for it in colorectal cancer.

They also treated the mice with a CB1 antagonist, a compound that binds to the receptor but does not activate it. Mice with CB1 blocked in this manner also showed an increase in the number and size of polyps. A CB1 antagonist called rimonabant is currently marketed overseas for weight loss. The researchers note that a patient's risk for colorectal cancer should be assessed when use of such drugs is being considered.

The study was funded by grants from the National Cancer Institute and the National Colorectal Cancer Research Alliance. Co-authors with DuBois are first author Dingzhi Wang, Ph.D., Haibin Wang, Ph.D., Wei Ning, Michael Backlund, Ph.D., and Dushansu K. Dey, Ph.D., all of the Vanderbilt-Ingram Cancer Center.

First Stars Were Brutes, but Died Young, Astronomers Say

By DENNIS OVERBYE

The first stars in the universe were short-lived brutish monsters, and they changed the nature of the cosmos forever, blazing away a dark fog that had smothered space for 300 million years and beginning to enrich the cosmos with the stuff of life. That is the news from a new computer simulation of the early years of the universe, performed by a group of astronomers led by Naoki Yoshida of Nagoya University in Japan.

The calculations show how small lumps in the distribution of matter and energy could draw in more matter by gravity, heat up, shrink and become the first “cosmic objects” — tiny seeds or proto-stars one one-hundredth the mass of the Sun. In a mere 10,000 years or so, by sucking in surrounding clouds of gas, they probably grew into giant stars at least 100 times as massive as the Sun.

Poetically, those first stars would have blazed brightly and died young, burning out in only a million years, which means that such computer simulations are the only telescopes through which these original stars can be observed. “The simulations offer a very clear picture of how the first stars formed,” Dr. Yoshida said, in a telephone news conference Wednesday. He and his colleagues reported their findings in a paper published in Science on Friday.

Volker Bromm, an astronomer at the University of Texas, Austin, who was not part of the team, said that Dr. Yoshida’s work had taken simulations of the early universe to a new level, although much work remained to be done. “The ultimate goal of predicting the mass and properties of the first stars is now within reach,” he wrote in a commentary that accompanied the Science paper.

Lars Hernquist of the Harvard-Smithsonian Center for Astrophysics, a member of Dr. Yoshida’s team, described the calculations as an attempt to fill a gap in cosmological knowledge.

Astronomers have a good idea of what the universe was like at an age of 400,000 years from studying a relict haze of microwaves left over from the Big Bang, and they know what it is like today. “This study is designed to understand how objects came into the universe,” he said, “and how they affected what came afterwards.”

The emergence of the first stars, about 300 million years after the Big Bang, was an epochal event for two reasons. First, they lighted up a universe that had been dark since shortly after the Big Bang fires had cooled. Through thermonuclear fusion, they also got the ball rolling on the alchemical transformation of the cosmos, from being composed essentially of pure hydrogen and helium to being littered today with heavier elements like carbon, oxygen, nitrogen and iron.

More massive stars burn hotter and faster and produce heavy elements more copiously than less massive ones. So Dr. Yoshida’s result would mean that this process of enrichment got off to a fast start, which astronomers could test by looking at the abundances of such elements in the lowest-mass and thus oldest stars around.

These massive stars would also have been prodigious producers of ultraviolet radiation needed to ionize hydrogen, which filled the universe like an opaque fog after the Big Bang cooled, and make it transparent to visible light, thus ending what cosmologists call the “dark ages.”

Astronomers have long reasoned that the first stars would have been massive, because without the heavy elements, which astronomers call metals, clouds of helium and hydrogen, the primordial gases, can’t easily cool off. So as the lumps compress under the pressure of incoming material, they heat up and push back. Only for very large amounts of gas can gravity overcome the pressure and the star start to form.

Astronomers have been using computers for decades to simulate the motions of cosmic particles coming together under gravity, but they typically have had to stop when the agglomerations became dense and hot enough for other forces — radiation, heat and gas dynamics — to complicate things. Dr. Yohsida said that his simulations were the first to be able to follow the complex interactions of gas and radiation that dominate evolution of the protostar.

Dr. Yoshida said his computer program, “like a piece of art,” had been seven or eight years in development. The simulations, performed on a network of 70 computer processors, begin with the universe as a nearly

smooth mixture of hydrogen, helium and the mysterious dark matter— perhaps clouds of as-yet-unidentified elementary particles — whose gravity shapes the distribution of matter in the universe.

As time goes on, small ripples in the dark matter cause ordinary matter to puddle, heat up, lose energy by radiation and then shrink, eventually forming stable seeds about one one-hundredth the density of water and about one one-hundredth the mass of the Sun. For now that is as far as the rigorous calculations go.

The seeds, however, are surrounded by huge amounts of gas, from which they are likely to grow. By how much depends on further calculations.

Significantly, the computations did not show the gas fragmenting into smaller clumps on the way to becoming the protostar. If the material had fragmented, Dr. Hernquist explained, the first stars would have been closer to the Sun in their masses and life histories and how they died. “It is vitally important to decide in the end exactly how massive these stars are,” he said. That would help astronomers deduce what might have happened to them. Were they scattered to the heavens in supernova explosions or did they perhaps collapse into black holes? “We don’t know how they die,” said Dr. Hernquist.

Scientists 'reprogram' cells from sick, elderly patients

* 19:00 31 July 2008
* NewScientist.com news service
*** Peter Aldhous**

You can think of it as recreating a deadly disease in the Petri dish. Scientists have grown motor neurons by "reprogramming" skin cells taken from a patient with the neurodegenerative disease amyotrophic lateral sclerosis (ALS).

Now they aim to study the cells to gain a better understanding of what goes wrong in the condition, and to screen for drugs that might help prevent the damage.

ALS affects cells in the spinal cord that send nerves into the muscles, controlling movement. Patients with the disease become progressively paralysed, and may eventually be unable to breathe. Famous sufferers include the US baseball player Lou Gehrig, who died of the condition in 1941, and the British theoretical physicist Stephen Hawking.

Reprogrammed cells

It is not possible to culture the affected cells directly from a patient's spinal cord. So researchers led by Kevin Eggan of the Harvard Stem Cell Institute, and Christopher Henderson of Columbia University, New York, took skin cells from an 82-year-old woman with ALS, and her sister, aged 89, who also has the disease.

The researchers first used the genetic reprogramming technique pioneered by Shinya Yamanaka of Kyoto University in Japan to make cells known as induced pluripotent stem cells (iPS cells) from both women's skin cells. Eggan and Henderson deliberately chose very old patients, as the same technique could be used to study cells from people with diseases that typically strike only late in life, such as Alzheimer's.

Tailor-made cells

Encouragingly, making iPS cells from old and sick people did not seem much more difficult than creating them from healthy, younger volunteers. "There's not an enormous difference in the efficiency," Eggan says.

Like stem cells taken from human embryos shortly after fertilisation, iPS cells have the potential to grow into any other type of cell. So the researchers then took the iPS cells derived from the 82-year-old patient and cultured them under conditions previously used to grow motor neurons from embryonic stem cells. The resulting cells carried "marker" molecules typical of motor neurons.

Researchers have long wanted to grow cells that are genetically matched to patients with devastating diseases. "This is the first time that this has been achieved, and is an interesting step forward," says Ian Wilmut of the University of Edinburgh, UK, who is also working to create iPS cells from patients with ALS.

Cancer risk

Until Yamanaka devised his reprogramming technique, the best hope of creating patient-matched cells was employing the cloning techniques used by Wilmut to create Dolly the sheep. But no-one has yet succeeded – partly because of the difficulty in obtaining the large numbers of human eggs needed for the cloning step.

Because iPS cells can so far only be created using viruses that insert copies of genes that can trigger cancer, the motor neurons will not be used to treat patients with ALS.

In any case, says Henderson, it is unclear whether transplanted cells could survive and form neural connections in patients whose spinal cords are damaged by the disease. "It's a very hostile environment," he says.

Instead, Eggan and Henderson plan to use their motor neurons to study the cellular processes that cause the symptoms of ALS, by comparing patient-derived cells with similar neurons grown from healthy people.

Functioning neurons

The two sisters who donated skin cells have a rare, inherited form of ALS caused by a mutation in a gene called SOD1, and experiments with cells from mice carrying SOD1 mutations suggest that support cells called astrocytes release a toxic factor that kills the motor neurons. This means Eggan may have to also grow astrocytes, but he is confident that they can be created from iPS cells. The researchers also need to show that the cells they have created can function as motor neurons. "Expressing a marker or two is not sufficient," notes Arnold Kriegstein, director of the Institute for Regeneration Medicine at the University of California, San Francisco.

Eggan says the cells' function will be tested by transplanting them into the spinal cords of chick and mouse embryos. His team also aims to create motor neurons and astrocytes from patients with other forms of ALS.

Journal reference: Science (DOI: 10.1126/science.1158799)

Phoenix Mars lander 'tastes' first sample of water ice

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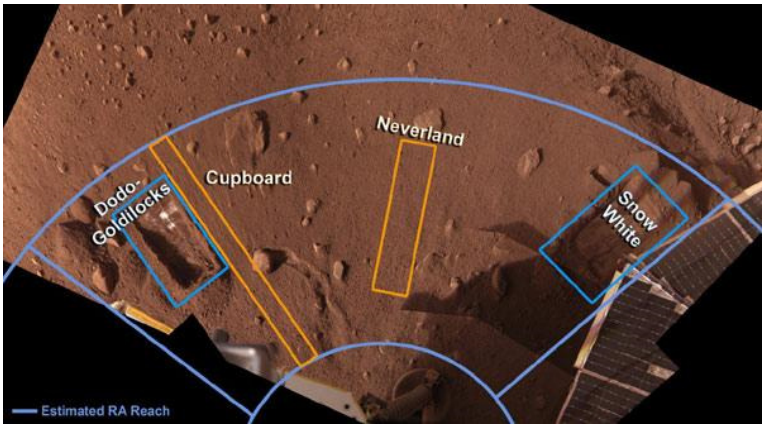
* NewScientist.com news service

*** Devin Powell**

After weeks of struggling to scrape icy material from just below the surface of Mars, NASA's Phoenix lander has collected and analysed its first sample of water ice.

"We've finally touched it and tasted it. It tastes very fine," said team member William Boynton of the University of Arizona in Tucson.

On Wednesday, Phoenix's robotic arm scooped out a sample of dirt from a 5-centimetre deep trench called "Snow White", which it began digging in June. The soil was transferred to one of the lander's eight TEGA (Thermal Evolved-Gas Analyzer) ovens and slowly warmed to 2 °Celsius (36 °Fahrenheit).



Phoenix plans to dig two new trenches called Cupboard and Neverland **(NASA/JPL-Caltech/U of A/Texas A and M)**

When the temperature reached 0 °C (32 °F), the instrument had to add extra heat to continue warming the sample – the signature of frozen ice melting. TEGA's mass spectrometer also directly detected minute traces of water.

Speaking at a televised press conference, Boynton put on a pointy green hat and gave the sample its official fairy tale name: "Wicked Witch."

"We named it after the witch from Hansel and Gretel, who saw her final demise by being pushed into an oven," said Boynton.

Tough work

The existence of water ice on Mars is not unexpected. Previous observations by NASA's Odyssey spacecraft detected signs of ice just below the surface. And images sent back from Phoenix in June showed bright chunks of material in the Snow White trench. These chunks disappeared over the course of days, which the team interpreted as the vaporisation, or sublimation, of ice in Mars's cold, low-pressure atmosphere.

Digging up the ice has been tricky, though, because the bright layer under the soil is too hard for Phoenix's scoop to penetrate, despite the blades attached to its front.

Sticky soil

On 15 July, the team used a sort of drill called a rasp attached to the scoop to cut cores out of Snow White and collect the shavings in a compartment on the back side of the scoop. But when the scoop was turned upside down, the sample stuck to the walls inside. Martian salt may have melted the ice and made the soil sticky, says Boynton.

While NASA worked to solve this problem, Boynton's team used the front of the scoop to collect the overlying soil, which is thought to be ice-free. They sprinkled this dirt slowly and carefully into their instruments – trying to avoid problems with clumpy soil experienced during an earlier attempt to dump soil from a nearby trench called "Dodo-Goldilocks".

Discovering ice was a surprise for the team. The amount is miniscule – at most a few percent of the sample. "We usually think of soil as the impurity in the ice," says Boynton. "In this case you could almost say the ice is the impurity in the soil."

Digging for life

The finding was accompanied by an announcement that NASA had decided to extend the 90-day mission by five weeks, until the end of September. This decision will add $2 million to the $420 price tag of the Phoenix lander, says Michael Meyer, NASA's chief scientist for the Mars exploration programme.

If its equipment holds out, Phoenix will dig two new trenches in its immediate surroundings. "Cupboard" will be located in a trough between two mounds, where wind-blown material collects. "Neverland" will be dug next to a rock, which may help to warm the surrounding soil.

The TEGA team will continue to analyse its Wicked Witch sample, heating it to a variety of temperatures to release gases and test for the presence of organic compounds.

"We're looking beyond finding water to finding habitats for life," says Meyer. To answer this question, NASA scientists will need to find evidence that their ice sometimes turns into liquid water.

Guilt on their hands: tiny 'tags' could help to solve and deter gun crime

Criminals who use firearms may find it much harder to evade justice in future, thanks to an ingenious new bullet tagging technology developed in the UK.

The tiny tags – just 30 microns* in diameter and invisible to the naked eye – are designed to be coated onto gun cartridges. They then attach themselves to the hands or gloves of anyone handling the cartridge and are very difficult to wash off completely.

Crucially, some of these 'nanotags' also remain on the cartridge even after it has been fired. This should make it possible to establish a robust forensic link between a cartridge fired during a crime and whoever handled it.

To date it has been extremely hard to establish such a link because of the difficulty in retrieving fingerprints or significant amounts of DNA from cartridge surfaces, which are shiny and smooth. The nanotags, which are quite unlike anything previously used in the fight against gun crime, could therefore lead to a significant increase in successful convictions.

This breakthrough has been achieved by a team of chemists, engineers, management scientists, sociologists and nanotechnologists from Brighton, Brunel, Cranfield, Surrey and York Universities, with funding from the Engineering and Physical Sciences Research Council (EPSRC).

"The tags primarily consist of naturally-occurring pollen, a substance that evolution has provided with extraordinary adhesive properties," says Professor Paul Sermon from the University of Surrey, who has led the research. "It has been given a unique chemical signature by coating it with titanium oxide, zirconia, silica or a mixture of other oxides. The precise composition of this coating can be varied subtly from one batch of cartridges to another, enabling a firm connection to be made between a particular fired cartridge and its user."

In addition to this breakthrough, the team has also developed a method of trapping forensically-useful amounts of DNA on gun cartridges. It involves increasing the abrasive character of the cartridge case with micro-patterned pyramid textures, or adding an abrasive grit, held in place by a thin layer of resin, to the cartridge base. This rough surface is able to retain dead skin cells from a thumb as it loads a cartridge into a firearm. A key benefit is also the affordability – a cost-effective way of reliably capturing sufficient DNA from a gun cartridge has never been available before. The technology has been designed to avoid damage to the DNA captured which is caused (i) by temperatures generated as the gun is fired, when heat is rapidly transferred from the burning propellant into the cartridge case and (ii) when copper is extracted from the cartridge case by lactic acid in sweat.

The nanotag and DNA capture technologies could potentially be available for use within as little as 12 months. There may also be scope to apply them in other fields, such as knife crime, in future.

"We're currently focusing on understanding the precise requirements of the police and cartridge manufacturers," comments Professor Sermon. "But our work clearly could make a valuable contribution not only to solving gun crime but also to deterring criminals from resorting to the use of firearms in the first place."

Notes for Editors

The 18-month 'DNA Receptors with Nanotags on Cartridges' initiative has consisted of two parallel projects receiving total EPSRC funding of nearly £379,000. Project partners are the Forensic Science Service, BAE Systems and coatings manufacturer Andura.

The original concept for the initiative was identified through the EPSRC Ideas Factory 'sandpit' process. A sandpit is a five-day interactive workshop involving a multidisciplinary mix of participants, some being active researchers and some being potential users of research outcomes, to drive lateral thinking and radical approaches to addressing particular research challenges.

New Male Circumcision Device for HIV Prevention Studied by NewYork-Presbyterian/Weill Cornell

Research on Innovative ShangRing Device Planned for Africa

NEW YORK (July 31, 2008) — With the recent endorsement by the World Health Organization (WHO) and scientists worldwide of adult male circumcision as an important strategy for HIV prevention, there is increased urgency to develop safe and cost-effective circumcision services. This is especially the case in Africa where HIV/AIDS continues to spread at an epidemic rate.

Studying this method are Dr. Marc Goldstein and physician-scientists at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, who are evaluating an innovative circumcision device developed in China and will initiate a study of the device in Africa in the coming months.

The device, named the ShangRing after its inventor, Mr. Jian-Zhong Shang, consists of two concentric plastic rings that sandwich the foreskin, allowing it to be cut away without suturing and with minimal bleeding. Performed in a clinic under local anesthesia, the procedure takes less than five minutes, compared with approximately 20 to 30 minutes for a traditional "free hands" circumcision that requires suturing. The patient returns in one week for device removal.

"Circumcision with this technique promises to be faster, safer and more acceptable to patients than conventional surgical circumcision methods," says Dr. Goldstein, the study's principal investigator. He is urologist and specialist in reproductive medicine at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, the Matthew P. Hardy Distinguished Professor of Reproductive Medicine and Urology at Weill Cornell Medical College, and senior scientist at The Population Council, Center for Biomedical Research, located on the campus of The Rockefeller University.

The hope is that with these advantages, circumcision will become more commonplace (currently only between 15 and 50 percent of sub-Saharan males are circumcised). Its advantages include reduced risk of a variety of sexually transmitted diseases (STDs), notably HIV.

"Circumcision is the only new HIV prevention method to demonstrate consistent efficacy in randomized controlled trials," notes co-principal investigator Dr. Philip S. Li, associate research professor of urology and reproductive medicine and director of microsurgical research and training at the Center for Male Reproductive Medicine and Microsurgery at Weill Cornell Medical College.

Three randomized controlled trials in Kenya, Uganda and South Africa reported a protective effect (up to 60 percent) of circumcision against HIV infection. The World Health Organization, the Joint United Nations Programme on HIV/AIDS (UNAIDS), and other global reproductive health organizations such as EngenderHealth have recognized circumcision as an important method to reduce HIV infection.

The ShangRing has been used to circumcise several thousand Chinese men since 2005. Preliminary reports of 1,200 patients indicate good results with minimal complications. The ShangRing, with 15 patents pending in 85 countries, is currently available only in China. FDA evaluation is under way.

"The beauty of this device is its simple, innovative design," says Dr. Howard Kim, a fellow in male reproductive medicine and microsurgery at NewYork-Presbyterian Hospital/Weill Cornell Medical Center and member of the Weill Cornell team that traveled to China to learn this new technique. "Although many male circumcision devices are available, they have not gained widespread acceptance due to high complication rates or difficulties with surgical technique."

"Even non-physician health care providers will be able to learn this procedure to safely perform circumcisions in resource-poor regions," adds Dr. Richard Lee, a chief resident in urology at NewYork-Presbyterian Hospital/Weill Cornell Medical Center and another member of the China team.

The NewYork-Presbyterian/Weill Cornell team, in collaboration with the nonprofits EngenderHealth and The Population Council, are planning a small pilot study in Nyanza, Kenya, to test efficacy, safety and acceptability of the technique. Local health providers who perform circumcisions in a clinical setting will be recruited and trained in the procedure by the NewYork-Presbyterian/Weill Cornell team. The pilot study is expected to be followed by a multicenter clinical trial that will compare the ShangRing technique to traditional circumcision methods.

Male circumcision has been performed as far back as ancient Egypt, and the practice has continued through the ensuing centuries for religious, cultural and sociopolitical reasons. Performing circumcision for potential health benefits gained momentum in the 19th century with the advent of anesthesia and the initial epidemiological studies demonstrating lower rates of venereal diseases in circumcised men. Recent studies have shown that circumcised men are at significantly lower risk of urinary tract infections and sexually transmitted infections such as syphilis and chancroid. Additional studies point to lower risk of invasive penile carcinoma, gonorrhea and chlamydia (in female partners).

Stinging Tentacles Offer Hint of Oceans' Decline

By ELISABETH ROSENTHAL

BARCELONA, Spain — Blue patrol boats crisscross the swimming areas of beaches here with their huge nets skimming the water's surface. The yellow flags that urge caution and the red flags that prohibit swimming because of risky currents are sometimes topped now with blue ones warning of a new danger: swarms of jellyfish.

A jellyfish in the Mediterranean off the coast of the Spanish island of Mallorca. **Dani Cardona/Reuters**

In a period of hours during a day a couple of weeks ago, 300 people on Barcelona's bustling beaches were treated for stings, and 11 were taken to hospitals.

From Spain to New York, to Australia, Japan and Hawaii, jellyfish are becoming more numerous and more widespread, and they are showing up in places where they have rarely been seen before, scientists say. The faceless marauders are stinging children blithely bathing on summer vacations, forcing beaches to close and clogging fishing nets.

But while jellyfish invasions are a nuisance to tourists and a hardship to fishermen, for scientists they are a source of more profound alarm, a signal of the declining health of the world's oceans.

"These jellyfish near shore are a message the sea is sending us saying, 'Look how badly you are treating me,' " said Dr. Josep-María Gili, a leading jellyfish expert, who has studied them at the Institute of Marine Sciences of the Spanish National Research Council in Barcelona for more than 20 years.

The explosion of jellyfish populations, scientists say, reflects a combination of severe overfishing of natural predators, like tuna, sharks and swordfish; rising sea temperatures caused in part by global warming; and pollution that has depleted oxygen levels in coastal shallows.

These problems are pronounced in the Mediterranean, a sea bounded by more than a dozen countries that rely on it for business and pleasure. Left unchecked in the Mediterranean and elsewhere, these problems could make the swarms of jellyfish menacing coastlines a grim vision of seas to come.

"The problem on the beach is a social problem," said Dr. Gili, who talks with admiration of the "beauty" of the globular jellyfish. "We need to take care of it for our tourism industry. But the big problem is not on the beach. It's what's happening in the seas."

Jellyfish, relatives of the sea anemone and coral that for the most part are relatively harmless, in fact are the cockroaches of the open waters, the ultimate maritime survivors who thrive in damaged environments, and that is what they are doing.

Within the past year, there have been beach closings because of jellyfish swarms on the Côte d'Azur in France, the Great Barrier Reef of Australia, and at Waikiki and Virginia Beach in the United States.

In Australia, more than 30,000 people were treated for stings last year, double the number in 2005. The rare but deadly Irukandji jellyfish is expanding its range in Australia's warming waters, marine scientists say.

While no good global database exists on jellyfish populations, the increasing reports from around the world have convinced scientists that the trend is real, serious and climate-related, although they caution that jellyfish populations in any one place undergo year-to-year variation.

"Human-caused stresses, including global warming and overfishing, are encouraging jellyfish surpluses in many tourist destinations and productive fisheries," according to the National Science Foundation, which is issuing a report on the phenomenon this fall and lists as problem areas Australia, the Gulf of Mexico, Hawaii, the Black Sea, Namibia, Britain, the Mediterranean, the Sea of Japan and the Yangtze estuary.

In Barcelona, one of Spain's most vibrant tourist destinations, city officials and the Catalan Water Agency have started fighting back, trying desperately to ensure that it is safe for swimmers to go back in the water.

Each morning, with the help of Dr. Gili's team, boats monitor offshore jellyfish swarms, winds and currents to see if beaches are threatened and if closings are needed. They also check if jellyfish collection in the waters near the beaches is needed. Nearly 100 boats stand ready to help in an emergency, said Xavier Duran of the water agency. The constant squeal of Dr. Gili's cellphone reflected his de facto role as Spain's jellyfish control and command center. Calls came from all over.

Officials in Santander and the Basque country were concerned about frequent sightings this year on the Atlantic coast of the Portuguese man-of-war, a sometimes lethal warm-water species not previously seen regularly in those regions.

Farther south, a fishing boat from the Murcia region called to report an off-shore swarm of Pelagia noctiluca — an iridescent purplish jellyfish that issues a nasty sting — more than a mile long. A chef, presumably trying to find some advantage in the declining oceans, wanted to know if the local species were safe to eat if cooked. Much is unknown about the jellyfish, and Dr. Gili was unsure.

In previous decades there were jellyfish problems for only a couple of days every few years; now the threat of jellyfish is a daily headache for local officials and is featured on the evening news. “In the past few years the dynamic has changed completely – the temperature is a little warmer,” Dr. Gili said.

Though the stuff of horror B- movies, jellyfish are hardly aggressors. They float haplessly with the currents. They discharge their venom automatically when they bump into something warm — a human body, for example — from poison-containing stingers on mantles, arms or long, threadlike tendrils, which can grow to be yards long. Some, like the Portuguese man-of-war or the giant box jellyfish, can be deadly on contact. Pelagia noctiluca, common in the Mediterranean, delivers a painful sting producing a wound that lasts weeks, months or years, depending on the person and the amount of contact.

In the Mediterranean, overfishing of both large and small fish has left jellyfish with little competition for plankton, their food, and fewer predators. Unlike in Asia, where some jellyfish are eaten by people, here they have no economic or epicurean value.

The warmer seas and drier climate caused by global warming work to the jellyfish’s advantage, since nearly all jellyfish breed better and faster in warmer waters, according to Dr. Jennifer Purcell, a jellyfish expert at the Shannon Point Marine Center of Western Washington University.

Global warming has also reduced rainfall in temperate zones, researchers say, allowing the jellyfish to better approach the beaches. Rain runoff from land would normally slightly decrease the salinity of coastal waters, “creating a natural barrier that keeps the jellies from the coast,” Dr. Gili said.

Then there is pollution, which reduces oxygen levels and visibility in coastal waters. While other fish die in or avoid waters with low oxygen levels, many jellyfish can thrive in them. And while most fish have to see to catch their food, jellyfish, which filter food passively from the water, can dine in total darkness, according to Dr. Purcell’s research.

Residents in Barcelona have forged a prickly coexistence with their new neighbors.

Last month, Mirela Gómez, 8, ran out of the water crying with her first jellyfish sting, clutching a leg that had suddenly become painful and itchy. Her grandparents rushed her to a nearby Red Cross stand. “I’m a little afraid to go back in the water,” she said, displaying a row of angry red welts on her shin.

Francisco Antonio Padrós, a 77-year-old fisherman, swore mightily as he unloaded his catch one morning last weekend, pulling off dozens of jellyfish clinging to his nets and tossing them onto a dock. Removing a few shrimp, he said his nets were often “filled with more jellyfish than fish.”

By the end of the exercise his calloused hands were bright red and swollen to twice their normal size. “Right now I can’t tell if I have hands or not — they hurt, they’re numb, they itch,” he said.

Dr. Santiago Nogué, head of the toxicology unit at the largest hospital here, said that although 90 percent of stings healed in a week or two, many people’s still hurt and itched for months. He said he was now seeing 20 patients a year whose symptoms did not respond to any treatment at all, sometimes requiring surgery to remove the affected area.

The sea, however, has long been central to life in Barcelona, and that is unlikely to change. Recently when the beaches were closed, children on a breakwater collected jellyfish in a bucket. The next day, Antonio López, a diver, emerged from the water. “There are more every year — we saw hundreds offshore today,” he said. “You just have to learn how to handle the stings.”

Epilepsy drug may help alcoholics recover from dependence, small study suggests

Further studies of nonaddictive drug gabapentin for insomnia during alcohol recovery are warranted, researchers say

ANN ARBOR, Mich. — It's a Catch-22 of the highest order. People with alcohol problems often use alcohol to get to sleep -- but it actually keeps them from getting good-quality sleep all night long.

At the same time, they're highly likely to suffer from full-blown chronic insomnia that keeps them from getting enough sleep night after night – and that condition has been shown to cut their chances of getting sober again.

Meanwhile, their doctors aren't likely to prescribe them insomnia medications, because most sleeping pills can be habit-forming or have adverse effects due to an alcohol-damaged liver.

Now, a small new pilot study from a team of University of Michigan alcoholism and sleep researchers offers some sign of a possible way out of this conundrum.

The study, published in the August issue of the journal Alcoholism: Clinical and Experimental Research, suggests that the drug gabapentin might be able to reduce insomnia in recovering alcoholics, and help them stay

away from alcohol more successfully. The drug, often used to treat epilepsy and chronic pain, is not habit-forming and is not processed by the liver.

Although the study involved only 21 insomniacs in recovery from alcohol dependence, and did not provide long-term gabapentin treatment or long-term follow-up on their sleep or their alcohol recovery, it was randomized, placebo-controlled, and double-blinded. In all, 30 percent of the patients who received gabapentin during alcohol recovery relapsed to drinking, compared with 80 percent of those who received a placebo.

Based on the results, the researchers have already launched additional studies of the potential role of gabapentin in alcohol recovery and sleep.

"We showed that the patients who got the real drug, rather than placebo, were less likely to relapse to drinking -- or if they relapsed it was later," says lead author Kirk Brower, M.D., FASAM, the executive director of U-M Addiction Treatment Services and a professor of psychiatry at the U-M Medical School. "In other words, gabapentin prevented and delayed relapse. Meanwhile, patients reported sleeping better in both the treatment and placebo groups, which may be due to the gabapentin in the first group and the resumption of drinking in the other."

Co-author Flavia Consens, M.D., an associate professor of neurology and member of the U-M Sleep Disorders Center, is cautiously optimistic that the new findings could open the door to better understanding of how to handle sleep problems in people who are trying to recover from their dependence on alcohol. As many as 70 percent of people with alcohol problems suffer insomnia, she says, while others cope with other sleep disturbances including breathing problems known as sleep apnea.

Nearly 14 million Americans meet the diagnostic criteria for alcohol abuse or alcoholism. Alcohol problems, alone or in combination with illicit drug problems, account for 40 percent of admissions to addiction treatment programs each year, according to the federal Substance Abuse and Mental Health Services Administration.

"There may be some underlying chemical changes in the brain that prompt alcoholics to report more insomnia as a co-existing condition than non-alcoholics," she says. "A possible explanation of these new findings is that the gabapentin might decrease the insomnia initially, and the patient may not need or crave alcohol as a treatment for the insomnia. We're also looking into other factors that may have an effect on the neurochemistry of the brain, and see how they could impact recovery and sleep."

The researchers caution that they did not observe differences in brain wave data collected during sleep studies conducted before and after patients received gabapentin. Neither did the drug appear to have a greater benefit for insomnia than placebo during the first 6 weeks of receiving study medication. Six weeks after stopping medication, however, those who had taken gabapentin reported worse insomina than those on placebo. Insomnia was measured using standardized questionnaires for a total of 12 weeks

All of the volunteers met national criteria for alcohol dependence, and were either in alcohol treatment or expressed a willingness to abstain from alcohol. They also all met criteria for insomnia that had lasted six months or more. They could not have other medical or mental health conditions, or be taking medications, that might affect their sleep, and underwent blood tests to rule out medical illnesses such as thyroid deficiency and liver disease.

Each of the study volunteers spent three nights in the U-M Sleep Disorders Center: two during the preparation for the study, and one three weeks after they began to receive gabapentin or placebo. All the volunteers received up to six brief sessions of behavioral therapy aimed not at sleep or alcohol issues, but rather at adherence to the study medication.

Fourteen of the volunteers successfully completed the entire study, including a follow-up appointment six weeks after they completed the six-week course of gabapentin or placebo, and three overnight sleep studies.

Brower notes that the medication dose and schedule used in the study may have contributed to the relatively weak effect on sleep that was seen from gabapentin. Patients took one dose each evening, rather than the three doses throughout the day that are routinely given for epilepsy or pain.

"These results raise more questions for us to explore, including the potential impact of gabapentin on people who are in recovery from alcohol dependence but do not report insomnia," he says.

The team has begun such a study, and is recruiting people who have a history of heavy drinking but have been sober for three to 12 weeks. These volunteers will spend a total of six nights in the recently opened eight-bed U-M Sleep & Chronophysiology Laboratory, and will receive study medication for one week. They'll also keep a sleep diary for 20 days, wear a wristwatch-like device to track their daily sleep/wake cycles, and come back for a follow-up visit. More information on this study is available at 734-232-0237 or by e-mailing dreamteam@umich.edu.

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