Antidepressants as treatment immediately following a stroke?

Rodent study highlights need for human clinical trials of drugs shown to increase growth of new neurons

A study at the Buck Institute for Age Research suggests a new strategy for the treatment of stroke. Research in rodents shows the growth of new neurons, also known as neurogenesis, lessens the severity of stroke and dramatically improves function following a stroke. The research suggests that drugs shown to promote neurogenesis in rodents could have benefits for human stroke victims and that those drugs–which include antidepressants and mood stabilizers such as lithium–may be suitable for study in human clinical trials. Results of the research appear the week of April 12 in the online edition of the Proceedings of the National Academy of Sciences.

"What this study shows more convincingly than in the past is that the production of new neurons after stroke is beneficial in rodents," said Buck faculty member and senior author David Greenberg, MD, PhD. "Assuming that neurogenesis is also beneficial in humans, drugs approved by the FDA for other purposes and already shown to promote new neuron growth in rodents might be worth studying as a potential treatment for stroke in humans. For example, antidepressants are often used to treat post-stroke depression, but their potential for improving outcome from stroke itself is less certain."

Previous research by the same group at the Buck Institute, which includes Drs. Kunlin Jin, Xiaomei Wang, Lin Xie and Xiao Mao, showed that the brain attempts to heal itself following stroke by growing new neurons, but it has not been shown clearly that those new neurons improve function.

About 795,000 Americans suffer a stroke each year. Stroke is the third leading cause of death in the U.S. and is the leading cause of serious long-term disability in this country. Treatments for stroke are limited. Clot busting drugs, which have to be given within hours of the stroke, have been of great benefit to a small number of patients, but stroke is not usually diagnosed in time for them to be used.

The Buck Institute study, which did not involve screening any of the existing drugs that support neurogenesis, compared stroke size and recovery in mice who were genetically altered and treated to either grow or not grow new neurons prior to stroke. Greenberg says strokes were about 30 percent larger in the animals that did not grow new neurons; the rodents that did grow new neurons showed dramatic improvement in motor function following the stroke. The exact mechanism by which the new neurons improve outcome is unknown.

Greenberg says future research at the Buck will likely involve testing drugs that stimulate neurogenesis at various dosages and treatment times to see if they improve outcome following stroke in rodents. Building on the Institute's collaborative approach to research involving other age-related disorders, Greenberg says its also likely that the impact of the growth of new neurons will be examined in animal models of Alzheimer's, Parkinson's and Huntington's disease.

Although the possibility of using existing drugs for the treatment of stroke is one that may excite patients and patient advocates, Greenberg urges caution. He says those suffering from stroke should not treat themselves, even with FDA-approved drugs, without medical advice. "Everything has potential side effects," said Greenberg. "Even taking something as seemingly innocuous as an antidepressant carries the possibility of making someone worse. These drugs need to be tested in a controlled clinical setting."

Contributors to this work: *Other Buck Institute scientists involved in the study include Kunlin Jin, Xiaomei Wang, Lin Xie and Xiao Mao. The work was supported by US Public Health Service Grants AG21980 and NS4491 and NS62414.*

Stress hormones accelerate tumor growth

Chronic stress has recently been implicated as a factor that may accelerate the growth of tumors. However, the mechanisms underlying this effect have not been determined. But now, Anil Sood and colleagues, at the University of Texas MD Anderson Cancer Center, Houston, have generated data using human ovarian cancer cell lines and tumor specimens that indicate that stress hormones, especially norepinephrine and epinephrine, can contribute to tumor progression in patients with ovarian cancer. They therefore suggest that targeting stress hormones and the signaling pathways that they activate might be of benefit to individuals with cancer.

Anoikis is the process by which cells are triggered to die when separated from their surrounding matrix and neighboring cells. Tumor cells that spread to other sites somehow escape anoikis. In the study, exposure of human ovarian cancer cells lines to either of the stress hormones norepinephrine or epinephrine protected them from anoikis. Similarly, in a mouse model of ovarian cancer, restraint stress and the associated increases in norepinephrine and epinephrine protected the tumor cells from anoikis and promoted their growth. This effect was associated with activation of the protein FAK. The clinical significance of these data was highlighted by the observation that in human ovarian cancer patients, behavioral states related to greater stress hormone activity were associated with higher levels of activated FAK, which was in turn linked to substantially accelerated mortality.

TITLE: *Adrenergic modulation of focal adhesion kinase protects human ovarian cancer cells from anoikis*
View this article at: http://www.jci.org/articles/view/40802?key=2596f6813536fc72a7f8

Study: Patients with amnesia still feel emotions, despite memory loss

A new University of Iowa study offers some good news for caregivers and loved ones of individuals with Alzheimer's disease. Patients might forget a joke or a meaningful conversation -- but even so, the warm feelings associated with the experience can stick around and boost their mood.

For the study, published this week in the Early Edition of the Proceedings of the National Academy of Sciences, researchers showed individuals with memory loss clips of happy and sad movies. Although the participants couldn't recall what they had watched, they retained the emotions elicited by the clips.

Justin Feinstein, lead study author and a student in the UI graduate programs of neuroscience and psychology, says the discovery has direct implications for Alzheimer's disease.

"A simple visit or phone call from family members might have a lingering positive influence on a patient's happiness even though the patient may quickly forget the visit or phone call," said Feinstein, a doctoral student in clinical neuropsychology. "On the other hand, routine neglect from staff at nursing homes may leave the patient feeling sad, frustrated and lonely even though the patient can't remember why."

Feinstein conducted the study with UI neuroscience faculty members Daniel Tranel, Ph.D., UI professor of neurology and psychology, and Melissa Duff, Ph.D., UI assistant professor of communication sciences and disorders.

The researchers studied five rare neurological patients with damage to their hippocampus, a part of the brain that's critical for transferring short-term memories into long-term storage. Damage to the hippocampus causes new memories to disappear. This same type of amnesia is an early sign of Alzheimer's disease.

The experiment started with an emotion-induction technique using powerful film clips. Each amnesic patient viewed 20 minutes of either sad or happy movies on separate days. The movies triggered the appropriate emotion, ranging from intense bouts of laughter during happy films to tears of sorrow during sad ones.

About 10 minutes after the clip ended, researchers gave patients a memory test to see if they could recall what they had watched. As expected, the patients were extremely impaired. A healthy person recalls about 30 details from each clip, but one patient couldn't recall a single detail.

After the memory test, patients answered questions to gauge their emotions.

"Indeed, they still felt the emotion. Sadness tended to last a bit longer than happiness, but both emotions lasted well beyond their memory of the films," Feinstein said. "With healthy people, you see feelings decay as time goes on. In two patients, the feelings didn't decay; in fact, their sadness lingered."

These findings challenge the popular notion that erasing a painful memory can abolish psychological suffering. They also reinforce the importance of attending to the emotional needs of people with Alzheimer's, which is expected to affect as many as 100 million people worldwide by 2050.

"Age is the greatest risk factor for Alzheimer's, and there's currently no cure," Feinstein said. "What we're about to face is an epidemic. We're going to have more and more baby boomers getting older, and more and more people with Alzheimer's disease. The burden of care for these individuals is enormous.

"What this research suggests is that we need to start setting a scientifically-informed standard of care for patients with memory disorders. Here is clear evidence showing that the reasons for treating Alzheimer's patients with respect and dignity go beyond simple human morals."

The study was funded by the Fraternal Order of Eagles, the National Institutes of Health, the National Science Foundation and the Kiwanis International Foundation.

Study identifies food combination associated with reduced Alzheimer's disease risk

Individuals whose diet includes more salad dressing, nuts, fish, poultry and certain fruits and vegetables and fewer high-fat dairy products, red meats, organ meats and butter appear less likely to develop Alzheimer's disease, according to a report posted online today that will appear in the June print issue of Archives of Neurology, one of the JAMA/Archives journals.

"Epidemiological evidence linking diet, one of the most important modifiable environmental factors, and risk of Alzheimer's disease is rapidly increasing," the authors write as background information in the article. "However, current literature regarding the impact of individual nutrients or food items on Alzheimer's disease risk is inconsistent, partly because humans eat meals with complex combinations of nutrients or food items that are likely to be synergistic."

Yian Gu, Ph.D., of Columbia University Medical Center, New York, and colleagues studied 2,148 older adults (age 65 and older) without dementia living in New York. Participants provided information about their diets and were assessed for the development of dementia every 1.5 years for an average of four years. Several dietary patterns were identified with varying levels of seven nutrients previously shown to be associated with

Alzheimer's disease risk: saturated fatty acids, monounsaturated fatty acids, omega-3 fatty acids, omega-6 fatty acids, vitamin E, vitamin B12 and folate.

During the follow-up, 253 individuals developed Alzheimer's disease. One dietary pattern was significantly associated with a reduced risk of the disease. This pattern involved high intakes of salad dressing, nuts, fish, tomatoes, poultry, fruits and cruciferous and dark and green leafy vegetables and low intakes of high-fat dairy, red meat, organ meat and butter.

The combination of nutrients in the low-risk dietary pattern reflect multiple pathways in the development of Alzheimer's disease, the authors note. "For example, vitamin B12 and folate are homocysteine-related vitamins that may have an impact on Alzheimer's disease via their ability of reducing circulating homocysteine levels, vitamin E might prevent Alzheimer's disease via its strong antioxidant effect and fatty acids may be related to dementia and cognitive function through atherosclerosis, thrombosis or inflammation via an effect on brain development and membrane functioning or via accumulation of beta-amyloid," they write.

"Our findings provide support for further exploration of food combination–based dietary behavior for the prevention of this important public health problem," they conclude.

(Arch Neurol. 2010;67[6]:(doi:10.1001/archneurol.2010.84). Available pre-embargo to the media at www.jamamedia.org.)

Prevalence of HIV in Africa is leading to new strains of Salmonella, say scientists

LIVERPOOL, UK – Scientists at the University of Liverpool have discovered that dangerous strains of Salmonella are beginning to emerge in people infected with HIV in Africa.

Their research has found that, in adults with HIV, new African Salmonellae can cause severe disease by invading cells in the blood and bone marrow, where they can hide away, allowing them to evolve into more dangerous, multi-drug resistant strains over time. This is made possible by the loss of immune cells that occurs in HIV which renders the body vulnerable to attack.

In Europe and the US, Salmonella normally causes diarrhoea and is rarely fatal, but in Africa, the new multi-drug resistant strains exploit vulnerable children and adults, causing severe infections that are difficult to treat and leading to death in one in four cases.

Previous work at the University of Liverpool in collaboration with the Wellcome Trust Sanger Institute, showed that new epidemic human strains of Salmonella are unique to Africa and have evolved to give a greater potential to cause serious disease. Researchers showed the strains, which were previously non-invasive, have now developed genetic similarities to the Salmonella bug that causes Typhoid Fever. This is significant because as well as being antibiotic resistant, their behaviour is likely to be intrinsically more invasive and aggressive than typical strains found in the US and Europe. This evolution has probably been driven by the context of the HIV epidemic.

The fact that the cells can persist inside cells in the blood and bone marrow confirms that these strains are behaving in a new and highly invasive fashion. It means that the infections are difficult to treat, and often persist and recur. This in turn means that conditions continue to be favourable for more bacterial adaptation, and for the evolution of more antibiotic resistance.

Dr Melita Gordon, Senior Lecturer and Consultant in Gastroenterology in the University of Liverpool, who carried out the work in partnership with Liverpool School of Tropical Medicine and the Malawi-Liverpool Wellcome Trust Major Overseas Unit, said: "This suggests that the high rate of HIV and other diseases that affect the immune system in Africa has provided an environmental niche in which new, more dangerous strains of Salmonella have been able to emerge.

"We are now studying ways in which these multi-drug resistant infections can be treated better without encouraging the emergence of newer forms of resistance to antibiotics. We should also be able to use the new genetic markers to track and understand the spread and habits of Salmonella in Africa much more effectively."

The research was funded by the Wellcome Trust and is published in Clinical Infectious Diseases.

U of I study: Lack of omega-6 fatty acid linked to severe dermatitis

URBANA – University of Illinois scientists have learned that a specific omega-6 fatty acid may be critical to maintaining skin health.

"In experiments with mice, we knocked out a gene responsible for an enzyme that helps the body to make arachidonic acid. Without arachidonic acid, the mice developed severe ulcerative dermatitis. The animals were very itchy, they scratched themselves continuously, and they developed a lot of bleeding sores," said Manabu Nakamura, a U of I associate professor of food science and human nutrition.

When arachidonic acid was added to the animals' diet, the itching went away, he said.

Nakamura's team has been focusing on understanding the function of omega-3 and -6 fatty acids, and doctoral student Chad Stroud developed a mouse model to help them understand the physiological roles of these fats. By knocking out genes, they can create deficiencies of certain fats and learn about their functions.

"Knocking out a gene that enables the body to make the delta-6-desaturase enzyme has led to some surprising discoveries. In this instance, we learned that arachidonic acid is essential for healthy skin function. This new understanding may have implications for treating the flaky, itchy skin that sometimes develops without an attributable cause in infants," he said.

Nakamura explained that our bodies make arachidonic acid from linoleic acid, an essential fatty acid that we must obtain through our diets. It is found mainly in vegetable oils.

Scientists have long attributed healthy skin function to linoleic acid, which is important because it provides the lipids that coat the outer layer of the skin, keeping the body from losing water and energy, which would retard growth, the scientist said. But skin function seems to be more complicated than that. These itchy mice had plenty of linoleic acid. They just couldn't convert it to arachidonic acid because the gene to make the necessary enzyme had been knocked out, he noted.

Arachidonic acid is also essential to the production of prostaglandins, compounds that can lead to inflammatory reactions and are important to immune function. Common painkillers like aspirin and ibuprofen work by inhibiting the conversion of arachidonic acid to prostaglandins.

"We usually think of inflammation as a bad thing, but in this case, prostaglandins prevented dermatitis, which is an inflammatory reaction. We measured prostaglandin levels in the animals' skin, and when we fed arachidonic acid to the knockout mice, they resumed making these important chemical compounds," he said.

Nakamura cautioned that there are still things they don't understand about the function of this omega-6 fatty acid. "This new knowledge is a starting point in understanding the mechanisms that are involved, and we need to do more research at the cellular level."

The study was published in a recent issue of the Journal of Lipid Research. Co-authors are Chad K. Stroud, Takayuki Y. Nara, Manuel Roqueta-Rivera, Emily C. Radlowski, Byung H. Cho, Mariangela Segre, Rex A. Hess, and Wanda M. Haschek, all of the U of I, and Peter Lawrence, Ying Zhang, and J. Thomas Brenna of Cornell University. Funding was provided in part by a USDA National Needs Fellowship Award and a grant from the National Institutes of Health.

U of I study: Lack of omega-3 fatty acid linked to male infertility

URBANA – According to a University of Illinois study, omega-3 fatty acids may be good for more than heart health. A little-known omega-3 may have implications for treating male infertility.

"In our experiment, we used 'knockout' mice that lacked the gene responsible for an enzyme important in making docosahexaenoic acid (DHA). In the absence of DHA, male mice are basically infertile, producing few if any misshaped sperm that can't get where they need to go," said Manabu Nakamura, a U of I associate professor of food science and human nutrition.

"We looked at sperm count, shape, and motility and tested the breeding success rate, and the mice lacking DHA simply were not able to breed," said Manuel Roqueta-Rivera, a U of I doctoral student who also worked on the study. In the DHA-deficient knockout mice, sperm counts were extremely low. The sperm that were produced were round instead of elongated and they were unable to move well, he said.

But, when DHA was introduced into the diet, fertility was completely restored. "It was very striking. When we fed the mice DHA, all these abnormalities were prevented," he said.

This is the first time that the importance of DHA to male fertility has been shown this directly, although some studies have suggested that male fertility patients with low sperm counts and less motile sperm tend to have low levels of this fatty acid.

The DHA study is part of the Nakamura team's efforts to understand the function of the omega-3 and -6 fatty acids. As part of that work, they have developed a mouse model to help them understand a particular fat's physiological role. By knocking out genes, they can create deficiencies of the fats they are interested in and learn about their functions.

"Knocking out the gene for the delta-6-desaturase enzyme has led to some surprising discoveries, including this one about the importance of DHA in sperm formation and mobility," he said. Nakamura said our body must make DHA from dietary alpha-linolenic acids, the parent compound of the omega-3 fatty acid family. Vegetable oils, including soybean and canola oil, are good sources of alpha-linolenic acid.

Nakamura's team plans to continue focusing on this omega-3's effects on fertility. But he cautioned that there are still things they don't understand.

"We get hints from looking at sperm in the DHA-deficient animals about what type of pathology we may be looking at and why these polyunsaturated fatty acids are important. But we're still at the starting point in understanding the mechanisms that are involved, and we need to do more research at the cellular level," he said.

The study was published in the February issue of the Journal of Lipid Research. Co-authors with Roqueta-Rivera and Nakamura are Chad K. Stroud, Wanda M. Haschek, Sandeep J. Akare, Mariangela Segre, and Rex A. Hess, all of the U of I, and Richard S. Brush, Martin-Paul Agbaga, and Robert E. Anderson, all of the University of Oklahoma Health Sciences Center.

Funding was provided in part by a CONACyT Mexico fellowship award, grants from the National Institutes of Health, the Foundation Fighting Blindness, and Research to Prevent Blindness.

Study Sees a Slant in Articles on Drug

By NICHOLAS BAKALAR

A new analysis of reviews and articles about the controversial diabetes drug Avandia has found that experts who were paid by its manufacturer have been significantly more likely than others to draw positive conclusions about the drug's safety and efficacy.

Since 2007, scientists have published hundreds of studies, reviews and opinion articles about Avandia in scientific journals and elsewhere, arriving at a range of conclusions, some sharply opposed to one another.

Avandia, or rosiglitazone, is prescribed, along with diet and exercise, to help control blood glucose levels in people with Type 2 diabetes. In 2007, The New England Journal of Medicine published a review of studies and concluded that its use was associated with a significant increase in the risk for heart attack.

After a Congressional investigation, the Food and Drug Administration imposed a "black box" safety warning on the medicine. In February, The New York Times described confidential F.D.A. reports recommending that Avandia be removed from the market.

To explore possible links between authors' financial interests and opinions, researchers reviewed 202 articles by 180 authors who wrote about Avandia and the risk of heart attack. Then they had independent reviewers with no conflicts of interest grade each article as favorable, neutral or unfavorable, based on the authors' positions on an association between Avandia and heart attacks and on their recommendations for continuing or ending its use. The study was published online on March 18 in the journal BMJ.

Often, authors with favorable opinions of the drug were paid both by Avandia's maker, GlaxoSmithKline, and by its competitors. Of those who offered favorable views, 87 percent had potential conflicts with Glaxo. Among authors who had unfavorable opinions, only 20 percent had received money from Glaxo.

Mary Anne Rhyne, a spokeswoman for Glaxo, said in an e-mail message: "Of the 202 articles, only 10 were original scientific research. Many of the articles reviewed were opinion pieces - editorials, commentaries or letters. It is important to note that the authors' conclusions do not impugn the validity of the scientific data."

interviews last week, Dr. Rudy Bilous and Dr. Mark W. Stolar, two of the scientists who reported favorable findings on Avandia, said drug company financing could create an appearance of bias.

"We can't have it both ways," said Dr. Bilous, an endocrinologist at James Cook University Hospital in Middlesbrough, England. "If people want drugs, the only people in the current environment doing the work and funding the research are the pharmaceutical industry, and their concern is for licensing, not necessarily the science."

Dr. Stolar, a professor of clinical medicine at Northwestern, had a similar view. "There is no broad enough funding on the national level for significant research," he said. "The problem is that the interpretation of the findings gets skewed because of that. There are very few people in whom I don't detect bias based on where their conflicts lie."

The BMJ review found that 90 of the 202 articles were by people with potential conflicts, but only 69 of them had a statement disclosing the fact. They uncovered the 21 remaining conflicts by searching the Internet and other publications by the same authors. The study's authors acknowledged that their work was observational and that they were unable to assign a monetary value to any of the relationships they found.

Dr. Amy T. Wang, the lead author and a resident in internal medicine at the Mayo Clinic, emphasized that the study drew no conclusions about the safety or efficacy of Avandia.

Ms. Rhyne said GlaxoSmithKline "will disclose research payments made to health care professionals and their institutions" beginning in 2011, with the disclosures covering research studies that began on or after Jan. 1, 2010.

This article has been revised to reflect the following correction: ***Correction: April 15, 2010***

An article on Tuesday about a study on financing of research into the diabetes drug Avandia referred incorrectly to a scientist who reported findings favorable to the drug. The scientist, Dr. Mark W. Stolar, an associate professor of medicine at Northwestern, has received payments from Takeda Pharmaceuticals, which makes diabetes drugs, but not from GlaxoSmithKline, which makes Avandia. (A co-author with Dr. Stolar did receive financing from Glaxo.)

UNC study offers first clinical evidence of anti-cancer drug triggering viral infection

Chapel Hill, NC - Important advances in the fight against cancer have come as researchers proved that viruses and cancers interact in ways that were previously unknown to scientists.

A new study led by UNC scientists shows that a common cancer drug can activate a viral infection that, paradoxically, can help anti-viral medications eradicate virus-associated cancer.

The cooperative study, conducted by a team of UNC School of Medicine scientists and the UNC Project in Malawi, demonstrated for the first time in humans that a common drug used to treat Burkitt lymphoma can activate infection by the Epstein-Barr virus (EBV), a virus which typically lies latent inside the tumor cells of affected patients. The finding paves the way for a future study using both a cancer drug and an antiviral agent to eradicate both the active virus infection and the tumor. The findings are reported in the April 1 issue of the journal Clinical Cancer Research.

Margaret Gulley, MD, professor of pathology and laboratory medicine, said, "What we have learned from this work is a potential means of capitalizing on presence of viral genomes within tumor cells to alter those tumor cells in a way that makes them more susceptible to treatment. Our findings have implications for other EBV- related malignancies that, overall, are among the most common cancers worldwide." Gulley is a member of UNC Lineberger Comprehensive Cancer Center.

EBV infects more than 90 percent of the world's population and is associated with diseases ranging from infectious mononucleosis to lymphomas, gastric cancer and cancer of the nose and throat.

Burkitt lymphoma, which is associated with EBV, is rare in most parts of the world, but is endemic in sub-Saharan Africa. Burkitt lymphoma is an aggressive, fast-growing type of non-Hodgkin lymphoma that often occurs in children. The disease may affect the jaw, bowel, lymph nodes, or other organs

The study demonstrated that initiating treatment with the anti-cancer drug cyclophosphamide in children with Burkitt lymphoma simultaneously triggered an active EBV infection. The increased replication of EBV in cancer tissue makes these cells more susceptible to the antiviral drugs that kill cells containing replicating virus. Antiviral agents such as ganciclovir and valacyclovir are already in routine clinical use for treating active viral infections.

Researchers enrolled 21 patients with a confirmed diagnosis of EBV-related Burkitt lymphoma. The patients ranged in age from 5-15 and were under treatment with cyclophosphamide for their cancer. Through laboratory analysis of biopsy samples, researchers found that cyclophosphamide seems to induce the phase of viral infection most susceptible to antiviral therapy.

"The next step," explains Gulley," is to design a clinical trial using both cytoxan and an antiviral agent simultaneously." Plans for such a trial are already underway under the leadership of Carol Shores, MD, PhD, associate professor of surgery in UNC's Department of Otolaryngology/Head and Neck Surgery and senior author of the study.

Other UNC scientists involved in the study are members of the departments of pathology, otolaryngology, and medicine/infectious disease division. Additional collaborators are affiliated with Kamuzu Central Hospital and the UNC Malawi Project, and Dr. Shannon Kenney who was Sarah Graham Kenan professor at UNC before joining the departments of medicine and oncology at the University of Wisconsin in Madison.

First Mention

Pertussis, 1913

By NICHOLAS BAKALAR

Whooping cough has been a well-known disease for hundreds of years, and the term “pertussis” has been in use since the 18th century. Its symptoms are vivid: severe coughing spells ending with a whooping gasp for breath and a face that turns red or purple, often followed by vomiting and then a return to feeling fine until the next episode. But until the early 20th century, no one knew what caused it.

During the 19th century, The New-York Daily Times, as it was then called, mentioned pertussis several times in passing. On March 19, 1853, it used the word in an account of the city inspector’s mortality report for the previous year, which listed 177 deaths caused by “teething,” 68 by “abscess” and 3 by “eruption.” No figure was given for pertussis.

The first substantive mention of pertussis came on Aug. 23, 1913, in an article that began, “It has just been definitely established that whooping cough is caused by a germ which has been named the bacillus pertussis by Bordet and Gengou, its discoverers.” On April 10, 1914, The Times ran an unsigned article under the headline “Physicians in War on Whooping Cough,” reporting on a medical meeting that recommended setting up special wards for the isolation and treatment of pertussis cases. “In New York City in 1913, from the imperfect statistics available,” the article said, “500 children fell victims to the disease.”

In the absence of an effective vaccine, treatment or cure, false hope flourished. On March 8, 1923, The Times reported that two Boston physicians had announced that “the X-ray may prove of more value in the treatment of whooping cough than any other form of treatment,” and told of “definite improvement” in “most of twenty-six cases of active pertussis treated with the X-ray.” The doctors admitted that “they could not give any rational explanation” for the effect, which we now know was imaginary.

Even though a number of vaccines and treatments of variable efficacy were developed starting soon after the discovery of the bacillus, The Times considered few worthy of serious attention until Oct. 18, 1941. That day, an unsigned article reported that the Michigan Department of Health had had "favorable results with pertussis vaccine, either alone or in combination with diphtheria toxoid." In December 1941, The Times reported that there had been 6,865 cases of pertussis in New York City that year, and 38 deaths.

After declining for some years after World War II, the number of pertussis infections rose steadily from 1990 to a peak of more than 25,000 cases nationwide in 2005, when the rate began to decline, possibly helped by the introduction of a new vaccine that year. There are now widely used pertussis vaccines and booster shots that are safe and effective for children and adults. Still, according to Dr. Thomas Clark, a medical epidemiologist with the Centers for Disease Control and Prevention, there were just over 13,000 pertussis infections nationwide in 2008, and 19 children, all less than a year old, died from whooping cough.

In Reporting Symptoms, Don't Patients Know Best?

By DENISE GRADY

About six years ago, my doctor gave me some samples of a drug to treat pain from an injury. I took it for a few days and then woke up one morning with a big red blister on my tongue. I'd never had anything like it before, and I wondered if the pills might be to blame. They weren't helping much anyway, so I quit taking them. The blister went away. I mentioned it the next time I saw the doctor, but he said it must have been a coincidence.

Not long after, the drug, Bextra, was taken off the market in the United States. It had been linked to heart attacks and also to a dangerous condition called Stevens-Johnson syndrome - which can cause mouth blisters, among other things. There's no way to know if Bextra caused my problem, but it seemed like a reasonable idea, and I never understood why my doctor was so quick to dismiss it.

The episode came to mind when I read an article in the March 11 New England Journal of Medicine by Dr. Ethan Basch, an oncologist who treats men with prostate cancer and does research at Memorial Sloan-Kettering Cancer Center in New York. He argues that doctors, researchers, drug makers and regulators should pay more attention to patients' firsthand reports of their symptoms while they take medicines, because their information could help to guide treatment and research, and uncover safety problems.

Direct reports from patients are rarely used during drug approval or in clinical trials, Dr. Basch says. If patients' comments are sought at all, they are usually filtered through doctors and nurses, who write their own impressions of what the patients are feeling.

In addition, he writes, doctors and nurses "systematically downgrade the severity of patients' symptoms" and sometimes miss side effects altogether. One result is "preventable adverse events" - for instance, suicidal thoughts in young people taking antidepressants, or severe constipation in people taking a drug for irritable bowel syndrome, both of which might have been detected earlier if symptoms had been systematically tracked.

Dr. Basch, 42, said he first became interested in this subject around 2003, when he attended a presentation of the results from a study of a new cancer drug. The researchers had not found fatigue to be much of a problem, but other doctors in the audience said their patients had suffered terribly from it while on the drug, so much that some had to quit taking it. Somehow, the study had completely missed that finding.

Intrigued, Dr. Basch began to study people receiving chemotherapy, and to compare symptom reports by patients with those from doctors and nurses. The differences were striking. For every problem - fatigue, nausea, appetite loss, vomiting, diarrhea, constipation - patients reported it earlier and more often than did doctors and nurses. Why does this happen so often? There's no simple answer.

"There is a sensibility among some old-school clinicians that they have a better sense of their patients' experience than patients do themselves," Dr. Basch said. "But doctors and nurses bring their own biases to the evaluation. They might say, 'Mrs. Smith always exaggerates her fatigue - she says 9, but I rate it a 6.' "

Three clinicians asked to rate the same patient's nausea will often give three different scores, he said.

The tendency to downgrade symptoms may be based on the doctor's knowledge that a patient is in the early stages of an illness and could be much worse. Or the doctor may be making mental comparisons with other patients who are sicker: "You think your nausea is bad, you should have seen the patient I saw this morning, let me tell you," as Dr. Basch put it. Sometimes, he said, the downgrading may reflect wishful thinking by doctors, who may think that a certain drug will help patients and don't want to take them off it.

Another reason, Dr. Basch said, is that "we live in a litigious society." Describing a problem in a chart creates a record that the doctor may have to act on. "There may be a defensive lack of documentation," he said.

But he went on, "Increasingly, scientifically, we believe that whatever Mrs. Smith says is what Mrs. Smith is experiencing, and it's important to know how patients themselves feel about how they're doing."

But the doctor's perspective is important, too, he said, and he suggested that symptoms be rated the way the Web site Metacritic rates movies: it posts two types of score, one from the public and one from professional critics. " want both," Dr. Basch said. Sometimes the information is lost altogether, when doctors and patients, distracted by test results and treatment plans, forget to discuss symptoms. "This is where a checklist could help," he said.

Mistakes and distortions in reporting symptoms can be compounded in studies, where one researcher collects the information, another retrieves it from the chart and enters it into the study record, and still others evaluate it. The results can be like playing telephone.

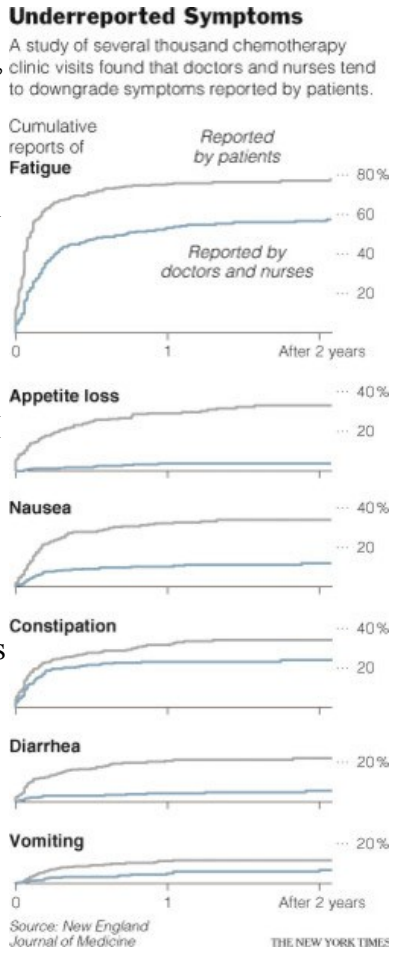
"There are multiple steps of transcription and information filtering," Dr. Basch said. "We know there are omissions and misinterpretations at every step of data transmission. We know information gets lost."

Patients may also tell doctors one thing and then write another in their own reports, Dr. Basch said; most say their written accounts are closer to reality.

The idea of not telling doctors the whole truth struck a guilty chord with me. Growing up, I got weekly hay fever shots that I don't think helped me at all. But I kept hoping they would, and the doctor was very kind, so whenever he asked if I was feeling better, I said yes, even though I actually spent most of August and September sneezing my brains out. This charade went on for years. Would I have been more honest in a diary? Maybe.

The Food and Drug Administration does have a system, Medwatch, that lets doctors and patients report problems that they think are adverse events from drugs already on the market. But it's a passive system that waits for reports instead of actively surveying patients. Many people don't know about it, and it has failed to catch some important adverse events, Dr. Basch said.

A better approach, he says, would be to have large numbers of patients filling out questionnaires before and after drugs are marketed. In an e-mail message, he said, "For example, in the postmarket setting we could ask 5,000 selected patients starting Bextra to report monthly (you would have reported the mouth sore without knowing if relevant or not, and this would then be pieced together with other reports)."



If patients had been asked to report their symptoms while the drug was still being tested, he added, problems might have been detected before it was even approved.

Gathering the patients' information would cost money, but not much compared with the overall cost of drug development and clinical trials, Dr. Basch said, adding that it would also save money by heading off potentially expensive problems. Dr. Basch said he was surprised to find drug companies enthusiastic about his research.

"You'd think it would not be appealing to them, because you're generating more adverse events," he said. "But the grade of the data is superior. You catch a lot of baseline symptoms before people start the drug, so you can understand what's probably related to the drug versus what's related to the patient's arthritis or whatever they had before the trial."

Although the regular reporting may sound like a nuisance for patients, researchers find that many people are eager to have their say. In one study, Dr. Basch said, subjects "typed volumes" into a small online text box, even though they couldn't see what they were typing after the first few sentences.

"We'd get two pages of stream of consciousness," Dr. Basch said. "The clinicians became overwhelmed."

The challenge is to create surveys that focus on what's relevant - and yet still provide a way to describe symptoms the researchers hadn't anticipated. Dr. Basch is working on it, for the National Cancer Institute.

"Patients have a lot to say," Dr. Basch said. We're just waiting for someone to listen.

A Lab Rat -- Created in the Lab

TAU is bioengineering tissues as an alternative to animal testing

It's illegal for health products with medical formulations to be accepted by the U.S. Food and Drug Administration without tests on animals - a situation that has serious ethical and moral implications. New research in the field of tissue engineering by Prof. Amit Gefen of Tel Aviv University's Faculty of Engineering holds a promise that far fewer lab animals will be needed for the necessary experimental trials.

Dr. Gefen's research into fat cells, published in a recent issue of Tissue Engineering , has led him to conclude that the necessary tissue can be produced from fat, skin, bone and muscle cells. His breakthrough study could have hundreds of applications in the pharmaceutical and medical world.

"Drugs make our lives better, and basic science is needed to push new drugs through clinical trials. But there is no doubt that an untold number of animals are sacrificed in the laboratory setting - both in basic research and in applied conditions when testing particular molecules," says Prof. Gefen, who heads TAU's Teaching Laboratory for Cell and Tissue Engineering. As a medical researcher himself, he was dependent on animal trials for testing new hypotheses he developed for living systems - until recently.

A more efficient road to scientific research

Bridging the worlds of biology and engineering, Prof. Gefen is now using adult rat stem cells - cells that can be stimulated to create skin, bone, fat and muscle tissue from an animal in a laboratory setting. In his own work on studying the mechanical properties of pressure ulcers, many tissue replications were needed. His new approach no longer requires the sacrifice of large numbers of animals. When an experiment is over, not one animal life has been lost.

The use of engineered tissues, says Prof. Gefen, may also be more scientifically efficient than using those from a living source. "The model we've created offers a very reliable method for researchers asking questions about basic science, and those investigating new drugs. We can injure tissue in a very controlled environment and grow muscle tissue without blood vessels, thereby neutralizing certain variables that often cloud what's happening in an experiment."

Saving lives and improving research at the same time

Though Prof. Gefen's method may not completely eliminate the need for animal testing, as few as 5% of the animals used today will need to be sacrificed in future tests, he predicts.

"It's a matter of proportion. Our tools spare an enormous number of lives," Prof. Gefen says. He is currently bringing together a number of discrete research directions from the separate fields of mechanics, tissue engineering and biology. He is also developing a new tool for researchers to investigate fat accumulation in cells (an important question for diabetes researchers) and weight loss drugs. Among his devices is one that can tell doctors how much mechanical stress is being placed on a person's foot, buttocks or other soft tissues. Another measures how much sensation is left in a diabetic limb. For all these approaches, Prof. Gefen has adopted tissue engineering methods to use fewer animals in his trials.

"We are now able to build a number of 'simplified' living tissues quite readily, and we're able to keep them 'alive,'" Prof. Gefen says. "They're genetically similar to the biological tissue of the animal, so we can factor out irrelevant physiological elements such as bleeding and pain response in an experiment. The fact that this tissue is genetically identical and the environmental factors are so well-controlled means that we can obtain far more experimental reproducibility than with experiments done on live animals."

In the future, Prof. Gefen hopes that similar models can be based on live human tissue, but that could be a number of years down the road.

Scientists find new genes for cancer, other diseases in plants, yeast and worms

AUSTIN, Texas - From deep within the genomes of organisms as diverse as plants, worms and yeast, scientists have uncovered new genes responsible for causing human diseases such as cancer and deafness.

The University of Texas at Austin scientists exploited the fact that all life on Earth shares common ancestry, and therefore shares sets of genes.

They found genes in yeast, for example, that humans use to make veins and arteries, even though yeasts have no blood vessels at all. Yeasts use those same genes to fix their cell walls in response to stress.

"Basically, we figured out a way to discover the genetic basis for disease by looking at organisms other than humans and finding disease equivalents," says Edward Marcotte, professor of chemistry and biochemistry.

To find the new genes, Marcotte and his graduate students developed a computer algorithm that first sifts through vast sets of existing genomic data for worms, mice, yeast, plants and humans. The algorithm pairs up sets of genes that overlap between these organisms and humans.

In doing so, it highlights genes that are known to work together to do one thing in the non-human organism, but the function of which are not yet known in humans. The scientists can then test those new genes in the lab to determine their function.

"The basic essence of the method is that there are ancient modules of genes that have been reused in different contexts over time," says Marcotte. "So the yeast uses a particular module with a particular set of inputs and outputs to do one task. Humans use this same module with different inputs and outputs to do another."

In the case of blood vessel formation, or angiogenesis, the scientists found 62 genes that yeast use to fix their cell walls that matched with a few genes known to be responsible for vein and artery formation in humans.

Developmental biologist John Wallingford and his graduate students then tested the human equivalents of the 62 yeast genes in developing frog embryos in the lab. This confirmed that eight of those 62 genes help build blood vessels in animals. Several of these genes were also confirmed in humans.

The newly found human angiogenesis genes are great candidates for drugs, says Marcotte.

"Tumors fool your body into feeding them by initiating blood vessel growth, and that's the reason we're interested in angiogenesis," says Marcotte. "So, genes for angiogenesis are common targets for chemotherapy. Some of the most effective chemotherapies block angiogenesis."

The scientists also found a set of genes in nematode worms involved in human breast cancer. Surprisingly, it is the same set of genes in the worms responsible for determining how many male offspring a parent worm births.

In plants, they found a gene that is involved with a genetic disorder called Waardenburg syndrome, which causes a significant fraction of cases of human deafness. (Strangely, plants use the gene as part of their system for sensing gravity, called gravitropism.)

The researchers are teasing out genes for a variety of human disorders, from mental retardation and birth defects to cataracts. Their goal is to find new genetic targets for therapy.

"By exploiting evolution and looking at lower organisms that don't even have the organs we're looking for - blood vessels or even heads - but share some of the underlying molecular processes, we're able to discover genes relevant to human diseases," says Marcotte.

Marcotte admits it may seem odd to look for human disease genes in something like a plant or yeast, but that the information is proving to be extremely useful, if not surprising. "When we found the genes in plants responsible for Waardenberg syndrome in humans," he says, "we were screaming in the halls."

Marcotte, Wallingford and colleagues published their research in PNAS (Proceedings of the National Academy of Sciences). Marcotte and Wallingford are members of the Center for Systems and Synthetic Biology and the Institute for Cellular and Molecular Biology. Wallingford, associate professor of molecular cell and developmental biology, is a Howard Hughes Medical Institute Early Career Scientist. Co-authors Kriston McGary, Tae Joo Park, John Woods and Hye Ji Cha are graduate students at The University of Texas at Austin.

Brain Infection from Tapeworm "Serious Health Concern"

Increasing in Mexico and Bordering Southwestern States

MAYWOOD, Ill. -- Tapeworm infections of the brain, which can cause epileptic seizures, appear to be increasing in Mexico and bordering southwestern states, Loyola University Health System researchers report.

In Mexico, up to 10 percent of the population may have the infection, neurocysticercosis. While many people never develop symptoms, neurocysticercosis nevertheless "remains a serious health concern, especially among the poor," Loyola researchers wrote in the April issue of the journal Neurological Research.

Their article, "Management of Neurocysticercosis," is among several articles in the April issue of Neurological Research that describe neurological infections in Latin America. Guest editor is Dr. Jaime Belmares, assistant professor in the Division of Infectious Diseases, Loyola University Chicago Stritch School of Medicine.

Neurocysticercosis is caused by a tapeworm found in pigs called Taenia solium. A person can get infected with the parasite by eating undercooked pork. That person then can excrete tapeworm eggs. The contamination spreads through food, water or surfaces contaminated with feces. A person can become infected, for example, by drinking contaminated water or putting contaminated fingers in the mouth.

Neurocysticercosis is most common in poor rural communities in developing countries with poor sanitation and hygiene and where pigs are allowed to roam freely and eat human feces.

Once inside the stomach, the tapeworm egg hatches, travels through the bloodstream and ends up in the muscles, brain or eyes. The worm, which can grow to more than one-half inch long, becomes enveloped in a fluid-filled cyst. Cysts in the muscles generally don't cause symptoms. But cysts in the eyes can cause blurry vision, while cysts in the brain can cause headaches, encephalitis and seizures. Less common symptoms include confusion and difficulty with balance. Seizures occur in up to 70 percent of patients. "They're pretty dramatic," Belmares said. "Every seizure needs to be properly evaluated."

The article on neurocysticercosis was written by Dr. Adolfo Ramirez-Zamora, a former resident at Loyola now at the University of California at San Francisco and Tomas Alarcon, who did a rotation at Loyola during medical school.

Other articles in the April issue of Neurological Research describe other neurological infections in Latin America, including Chagas disease, hydatid disease of the central nervous system, neuroschistosomiasis, meningococcal disease and rabies.

People pick up pepper virus

Could a plant virus have found a way to infect humans? It has always been assumed that plant viruses cannot infect animals, and vice versa, but plant viruses are known to be abundant in human faeces.

Now Didier Raoult at the University of the Mediterranean in Marseille, France, and his team think a pepper virus is making people sick, too. They have found RNA from the pepper mild mottle virus in the faeces of 7 per cent of the 304 adults they tested. Those with the virus were more likely to report fever, abdominal pain and itching than those without it, his team found.

Not everyone is convinced, however. Because Raoult looked at many possible symptoms, he would be expected to find a few that randomly appear more common in virus-positive people, says Robert Garry, a virologist at Tulane University in New Orleans, Louisiana.

Moreover, in order to enter a cell and replicate, a virus must bind to a receptor on its surface, and a plant virus would be highly unlikely to recognise a receptor on a human cell, says Garry.

One possibility, Raoult says, is that the virus does not infect human cells directly. Instead, the naked viral RNA may alter the function of the cells through a mechanism similar to RNA interference, in which the presence of certain RNA sequences can turn genes on and off.

Raoult's team is now working to gather more direct evidence that the virus does infect humans.

Journal reference: PLoS One, DOI: 10.1371/journal.pone.0010041

Maternal Deaths Decline Sharply Across the Globe

By DENISE GRADY

For the first time in decades, researchers are reporting a significant drop worldwide in the number of women dying each year from pregnancy and childbirth, to about 342,900 in 2008 from 526,300 in 1980.

The findings, published in the medical journal The Lancet, challenge the prevailing view of maternal mortality as an intractable problem that has defied every effort to solve it. “The overall message, for the first time in a generation, is one of persistent and welcome progress,” the journal’s editor, Dr. Richard Horton, wrote in a comment accompanying the article, published online on Monday.

The study cited a number of reasons for the improvement: lower pregnancy rates in some countries; higher income, which improves nutrition and access to health care; more education for women; and the increasing availability of “skilled attendants” - people with some medical training - to help women give birth. Improvements in large countries like India and China helped to drive down the overall death rates.

But some advocates for women’s health tried to pressure The Lancet into delaying publication of the new findings, fearing that good news would detract from the urgency of their cause, Dr. Horton said in a telephone interview. “I think this is one of those instances when science and advocacy can conflict,” he said.

Dr. Horton said the advocates, whom he declined to name, wanted the new information held and released only after certain meetings about maternal and child health had already taken place.

He said the meetings included one at the United Nations this week, and another to be held in Washington in June, where advocates hope to win support for more foreign aid for maternal health from Secretary of State Hillary Rodham Clinton. Other meetings of concern to the advocates are the Pacific Health Summit in June, and the United Nations General Assembly meeting in December.

“People who have spent many years committed to the issue of maternal health were understandably worried that these figures could divert attention from an issue that they care passionately about,” Dr. Horton said. “But my feeling is that they are misguided in their view that this would be damaging. My view is that actually these numbers help their cause, not hinder it.”

He said the new study was based on more and better data, and more sophisticated statistical methods than were used in a previous analysis by a different research team that estimated more deaths, 535,900 in 2005. The authors of the earlier analysis, published in The Lancet, in 2007, included researchers from Unicef, Harvard, the World Bank, the World Health Organization and the Johns Hopkins School of Public Health. The World Health Organization still reports about half a million maternal deaths a year, but is expected to issue new statistics of its own this year.

The new report comes from the University of Washington and the University of Queensland in Brisbane, Australia, and was paid for by the Bill and Melinda Gates Foundation. A spokesman for Unicef said it had no comment on the new findings, and there was no response to messages that were left late Tuesday for W.H.O. officials.

Dr. Christopher J. L. Murray, the director of the institute for health metrics and evaluation at the University of Washington, in Seattle, and an author of the study, said, “There has been a perception of no progress.”

But, he said, “some of the policies and programs pursued may be having an effect, as opposed to all that effort with little to show for it. It really is an important positive finding for global health,” he said.

Dr. Murray said no one had approached him directly about delaying the release of his findings; he heard about those efforts from The Lancet, and described them as “disappointing.” He said, “We believe in the process of peer-reviewed science, and it’s the proper way to pursue these sorts of studies.”

The researchers analyzed maternal mortality in 181 countries from 1980 to 2008, using whatever information they could glean from each country: death records, censuses, surveys and published studies. They ultimately gathered about three times as much data as the previous researchers had found.

Among poor countries with longstanding high death rates, progress varied considerably. For instance, from 1990 to 2008, the maternal death rate dropped 8.8 percent a year in the Maldives, but rose 5.5 percent in Zimbabwe. Sub-Saharan Africa has the highest maternal death rates. Brazil improved more than Mexico, Egypt more than Turkey. Six countries accounted for more than half of all the maternal deaths in 2008: India, Nigeria, Pakistan, Afghanistan, Ethiopia and the Democratic Republic of Congo.

But India has made steady progress, and because its population is so large, its improvements have helped considerably to decrease the worldwide rate of maternal deaths. China has also made considerable progress. In India, there were 408 to 1,080 maternal deaths per 100,000 live births in 1980, and by 2008, there were 154 to 395, the new study found. In China, there were 144 to 187 deaths per 100,000 live births in 1980, and 35 to 46 in 2008.

Dr. Murray said the findings came as a surprise. What also surprised him and his colleagues, he said, was the number of pregnant women who died from AIDS: about 60,000. “Really to a large extent that’s why maternal mortality is rising in eastern and southern Africa,” Dr. Murray said. “It means, to us, that if you want to tackle maternal mortality in those regions, you need to pay attention to the management of H.I.V. in pregnant women. It’s not about emergency obstetrical care, but about access to antiretrovirals.”

Dr. Horton contended that the new data should encourage politicians to spend more on pregnancy-related health matters. The data dispelled the belief that the statistics had been stuck in one dismal place for decades, he said. So money allocated to women’s health is actually accomplishing something, he said, and governments are not throwing good money after bad.

An advocate for women’s health, Dr. Flavia Bustreo, director of the Partnership for Maternal, Newborn and Child Health, said the improvements described in the new report represented “hope at last.” She said her organization, affiliated with the World Health Organization, was not one of those that tried to delay release of the findings.

She said the report was well done and called The Lancet a “scrupulously” edited journal. She said the findings made sense and were consistent with other reports from large countries like India, which can drive global figures.

“For 20 years, the safe motherhood movement has been conveying an impression of no progress,” Dr. Bustreo said. “To hear confirmation of improvements is good news. To us, the good news will maintain the interest of investors. If you don’t show results, that’s the worst position you can be in. The evidence and scientific truths have to be put in the open and discussed.”

Her group issued its own report on Tuesday, noting improvements that were saving the lives of women during pregnancy and birth in various countries. For instance, India pays women to get prenatal care and skilled care for delivery. Nepal provides home visits for family planning. Malawi is training nonphysicians to perform emergency Caesarean sections. Brazil has set up a health system that provides free primary care and skilled attendance at birth for all.

Jackhammer 'superdrill' could speed mine rescues

14 April 2010 by Phil McKenna

FATAL coal mine accidents over the past month in West Virginia and China offer a grim reminder of how difficult it can be to reach workers underground when their usual route to the surface is cut off. In many such accidents, even the best rescue technology can fail to get to people quickly enough - so how could it be improved?

When people are trapped below ground, it can often be a race against time for the rescue teams above them to drill narrow boreholes through which they can lower food and water, blow in oxygen, or suck out dangerous gases such as methane or carbon monoxide.

Though no two mines are alike, it typically takes 10 hours to bore every 300 metres. Conventional rotary drills are limited in how fast they can cut, and they slow right down when drilling through granite or other hard rock. In 2007, a rescue effort at the Crandall Canyon mine in Utah failed after it took about 40 hours to drill 500 metres. Nine miners and rescue workers died.

A "superdrill" now under development could help. On 30 April, researchers at Sandia National Laboratories in New Mexico are due to deliver preliminary results to federal mine safety officials on a drill that can penetrate hard rock significantly faster than conventional drills. "It can go through granite like it's cutting butter," says Gerald Finfinger of The National Institute for Occupational Safety and Health (NIOSH), the US federal agency that is funding Sandia's research. "In a normal drill operation, you could sit there and read a book and barely see it penetrate."

In laboratory tests, Sandia's high-speed drill bored a hole 10 to 15 centimetres in diameter through 30 cm of granite in 6 seconds. This means it should be able to penetrate 300 metres of hard rock in under 2 hours.

Unlike the shearing or chipping employed by conventional rotary drills developed for the oil and gas industry, the new drill employs a high-powered pneumatic jackhammer with button-shaped tungsten carbide bits to fracture the rock and break it into a fine powder.

The drill could be available for mine rescues within two years. However, it wouldn't have significantly changed the outcome in West Virginia, where rescue teams were able to drill down in a relatively short time, or China, where many miners escaped through partially flooded mineshafts.

NIOSH has also commissioned Sandia to develop a robotic scout that rescue teams could send into a mine to check for survivors and assess whether it is safe to enter. The plan now is to test it under realistic conditions with a mine rescue team. Finfinger says that if it is to be of any use, "it has to make rescue faster or safer".

Ginkgo herbal medicines may increase seizures in people with epilepsy

Restrictions should be placed on the use of Ginkgo biloba (G. biloba) - a top-selling herbal remedy - because of growing scientific evidence that Ginkgo may increase the risk of seizures in people with epilepsy and could reduce the effectiveness of anti-seizure drugs, a new report concludes. The article appears in ACS' monthly Journal of Natural Products. It also suggests that Ginkgo may have harmful effects in other people after eating raw or roasted Ginkgo seed or drinking tea prepared from Ginkgo leaves.

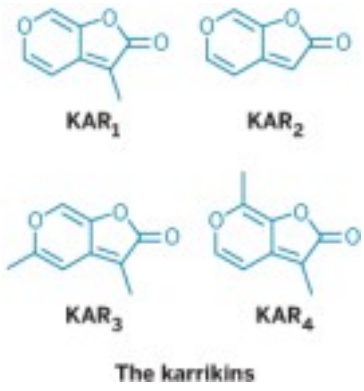
Eckhard Leistner and Christel Drewke note that consumers use pills, teas, and other products prepared from leaves of the Ginkgo tree to treat a wide array of health problems. Those include Alzheimer's disease and other memory loss, clinical depression, headache, irritable bladder, alcohol abuse, blockages in blood vessels, poor concentration, and dizziness. Scientific concern focuses mainly on one chemical compound in the herb. It is a potentially toxic material known as ginkgotoxin.

They reviewed scientific research on Ginkgo, and found 10 reports indicating that patients with epilepsy who take Ginkgo products face an increased risk of seizures. They note that laboratory studies explain how Ginkgo could have that unwanted effect. Ginkgotoxin seems to alter a chemical signaling pathway in ways that may trigger epileptic seizures. Further evidence showed that Ginkgo can interact with anti-seizure medications and reduce their effectiveness. "Contrary to our own previous assumption, we are now convinced, however, that G. biloba medications and other products can have a detrimental effect on a person's health condition," the report concludes. "It is therefore important that the large number of G. biloba product users and their health care providers be made aware of these risks, in order to enable them to make informed decisions about the use of these preparations."

Article *"Ginkgo biloba and Ginkgotoxin" http://pubs.acs.org/stoken/presspac/presspac/full/10.1021/np9005019*

Healing haze: Substances in smoke left over from forest fires speed plant growth

The hazy smoke lingering after forest fires contains chemicals that summon the forest back to life - and now are emerging as a potential new generation of agricultural chemicals that could boost food crop production and revitalize barren soil. Those biochemical signaling molecules, which stimulate the plant growth, are the topic of an article in the current issue of Chemical & Engineering News (C&EN), ACS' weekly newsmagazine.



The karrikins

C&EN Senior Editor Bethany Halford notes that smoke's ability to spur the growth of seeds after a forest fire first caught the attention of scientists 20 years ago. Scientists in Australia in 2004 finally identified the first smoke-derived chemicals responsible for promoting the germination of seeds. Named "karrikins," after the Aboriginal word for smoke, these substances trigger seed sprouting and foster seedling growth. They help explain the incredible ability of fire-ravaged landscapes to spring back to life.

Studies now show that karrikins speed the growth of corn, tomatoes, lettuce, and other food crops and help crops tolerate a wider range of temperatures. They have "tremendous" invigorating properties, enabling seeds stored for years to grow as if young. The article points out that scientists in Australia already are using karrikins on a limited basis to restore vegetation to land stripped bare during mining of aluminum ore. Wider use depends on development of ways of producing large amounts of karrikins at low cost, the article notes.

*ARTICLE "**Smoke Signals**" This story is available at* ***http://pubs.acs.org/cen/science/88/8815sci3.html***

Statins may slow progression of multiple sclerosis, new study finds

A UCSF-led study examining the impact of statins on the progression of multiple sclerosis found a lower incidence of new brain lesions in patients taking the cholesterol-lowering drug in the early stages of the disease as compared to a placebo. Study participants received an 80 milligram daily dose of atorvastatin, marketed by Pfizer Inc. as Lipitor.

Although the study was small with only 81 participants and its primary endpoint, designed to evaluate MS progression in patients following their first attack, was not met, the researchers found over the 12-month course that 55.3 percent of participants did not develop new brain lesions when administered statins compared with 27.6 percent of the placebo group.

Study findings were presented today (April 14, 2010) by University of California, San Francisco researchers during the annual American Academy of Neurology scientific meeting in Toronto.

The trial was a phase II, multi-center, randomized, placebo-controlled follow up to a landmark study published by principal investigator Scott S. Zamvil, MD, PhD, associate professor of neurology at UCSF (Youssef, et al., Nature 2002), after his laboratory first observed that statins cause T cell immune modulation that could be beneficial in multiple sclerosis and other autoimmune diseases.

Co-led by Zamvil and Emmanuelle Waubant, MD, PhD, associate professor of neurology at the UCSF MS Center, the study tested whether the drug could be used to prevent conversion to definite multiple sclerosis in individuals who have had a first attack.

"Our data is preliminary, and we need a larger study to confirm the effects of the drug and its magnitude. It is important that we understand how statins impact the progression of multiple sclerosis in order to better inform physicians and patients of their effect since these drugs are so broadly used throughout the United States and the world, and to learn whether a relatively inexpensive oral therapy can slow the course of disease," said Waubant.

MS is considered an autoimmune disease where immune cells attack the central nervous system. Nerves are made up of axons (nerve fibers) surrounded by a myelin sheath. MS occurs when the immune system attacks myelin, leaving scars or lesions in the demyelinated areas of the brain and spinal cord. Damage to myelin disrupts the ability of nerves to transmit information to nerve cells, resulting in neurological disability.
The team employed MRI to look at the activity of the medication on the disease course. More than 150 patients were originally intended, but enrollment was stopped due to slow recruitment after 81 patients were randomized. Each subject was asked to come in every three months (five scans over 12 months) for serial brain MRI evaluation. The subject pool was 76.5 percent female, 92.6 percent white, and ranged in age from 24 – 48 years.

Central MRI reading and coordinating was provided by Daniel Pelletier, MD, study author, associate professor of neurology and a member of the Multiple Sclerosis Research Group at UCSF.

"The exciting finding in this study is that reducing new brain MRI lesions should be meaningful for patients since new lesions are reliable correlates of future clinical attacks in MS," said Pelletier.

In addition to UCSF, the multi-center trial involved Oregon Health & Science University, The Cleveland Clinic, Virginia Mason MS Center, Washington University School of Medicine John L. Trotter MS Center, Montreal Neurological Institute, Barrow Neurological Institute, University of Texas Southwestern Medical Center, University of Rochester, The Multiple Sclerosis Comprehensive Care Center at USC Keck School of Medicine, Yale MS Research Center, Jacobs Neurological Institute, Johns Hopkins University, and Mount Sinai School of Medicine.

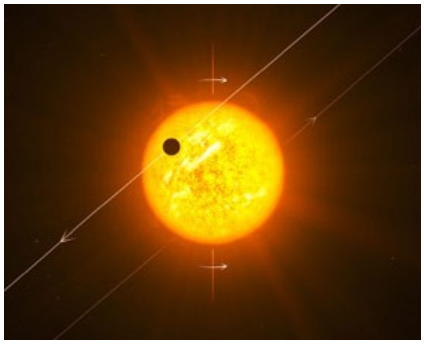
The research was performed as a project of the Immune Tolerance Network, a clinical research consortium headquartered at UCSF and sponsored by the National Institute of Allergy & Infectious Diseases. Atorvastatin, placebo and additional support were provided by Pfizer. Biogen-Idec provided Avonex, an immune system regulator drug (interferon beta-1a) for study participants who displayed disease activity while on placebo or atorvastatin. Additional funding was provided by the Nancy Davis Foundation and the Maisin Foundation.

News release for Zamvil 2002 Nature study: http://news.ucsf.edu/releases/cholesterol-drug-could-lead-to-new-therapy-for-multiple- sclerosis/ ***2002 Nature paper (Youssef, et al.)***

Exoplanets Orbit Stars in Reverse

These exoplanets are orbiting backwards, and they're turning theories of planet formation upside-down.

content **provided by Lisa Grossman**, Science News



***If these slanted orbits are common, it could be a death knell for the migration theory*. ESO**

THE GIST:

**** A bevy of exoplanets apparently are orbiting their stars backwards.***

**** The wrong-way planets could challenge theories of planet formation.***

**** These planets belong to a class of extrasolar planets called hot Jupiters.***

A bevy of backward-orbiting exoplanets could challenge theories of planet formation, new research suggests. The planets' wonky orbits might also rule out the presence of Earthlike bodies in some planetary systems.

The wrong-way planets got where they are by cartwheeling over their stars' heads, Andrew Collier Cameron of the University of St Andrews in Scotland proposed in an April 13 presentation at the Royal Astronomical Society's National Astronomy Meeting in Glasgow, Scotland.

Planets are thought to form from the disk of gas and dust that surrounds a young star. Because the star and the disk both coalesce from the same cloud of material, theory holds that both should spin in the same direction -- and so should any planets that arise. The "disk migration theory" posits that some planets should end up close to their stars by gently migrating inward over time, maintaining an orbital plane in line with the star's rotation.

Last summer, astronomers first discovered a handful of planets that threw that idea for a loop. These planets orbit backward, opposite to the direction of their stars' spin (SN: 9/12/09, p. 12). And other newly discovered planets that did have "forward" orbits were tilted 20 degrees or more with respect to the plane of the stellar disk where they were born.

These planets belong to a class of extrasolar planets called hot Jupiters -- giants that sit scorchingly close to their stars. "If I had to stick my neck out and make a prediction, it's probably not a good idea to go looking for terrestrial planets in systems that have hot Jupiters in them," Cameron says.

Cameron and his colleagues think a single mechanism pushed the tilted and backwards planets into their offbeat orbits and also drew them close to their stars. If these slanted orbits are common, it could be a death knell for the migration theory, says study coauthor Didier Queloz of the Geneva Observatory.

"Migration cannot produce misaligned systems," Queloz says. The new study brings the total number of planets for which astronomers have angle data up to 27. Of those many are misaligned, with half tilted at steep angles and six orbiting backwards. "Since most hot Jupiters are indeed misaligned, most cannot be formed by migrations," Queloz says. "We're kind of killing this first idea of migration."

The more likely explanation, the researchers say, is the Kozai mechanism. In this scenario, a second, distant large body like a planet or a companion star gravitationally perturbs a planet's orbit. The orbital plane can flip over the top of the star like a jump rope. When the orbit is flipped more than 90 degrees, the planet is orbiting backwards. At the same time, the shape of the orbit squishes and stretches like a rubber band. As the planet gets closer to the star, its orbit gets more circular, and the cartwheels become less dramatic. When the orbit finally settles into a circle near the star the tilt freezes.

Earlier research predicted that most orbits of giant planets perturbed by the Kozai mechanism should end up tilted around either 40 degrees -- a forward but slanted orbit -- or 140 degrees -- a backwards orbit.

"That looks very much like what we're now observing," Cameron says. "It looks almost too good to be true."

Some critics think he's right -- it is too good to be true. "I think they're eliminating the standard mechanism of disk migration prematurely," says Adam Burrows of Princeton University. Some combination of migration, scatter and the Kozai mechanism is still possible, he says. "Their data isn't that definitive to eliminate any other possibilities."

Astronomers had hoped that smaller, more Earthlike planets could be hiding in the neighborhoods of hot Jupiters, but the recent slug of orbital data suggests that may be unlikely. The giant planets' orbits can take hundreds of thousands of years to settle, "during which you have a rampaging Jupiter on a cometlike crazy tumbling orbit, which would simply fling any remaining debris out of the system," Cameron says.

Link between solar activity and the UK's cold winters

A link between low solar activity and jet streams over the Atlantic could explain why, despite global warming trends, people in regions North East of the Atlantic Ocean might need to brace themselves for more frequent cold winters in years to come. A new report published today, Thursday 15 April, in IOP Publishing's Environmental Research Letters describes how we are moving into an era of lower solar activity which is likely to result in UK winter temperatures more like those seen at the end of the seventeenth century.

Lead author Mike Lockwood of the University of Reading said: "This year's winter in the UK has been the 14th coldest in the last 160 years and yet the global average temperature for the same period has been the 5th highest. We have discovered that this kind of anomaly is significantly more common when solar activity is low."

The new paper, 'Are cold winters in Europe associated with low solar activity?', differs from previous efforts to explain the UK's recent cold winters by comparing the most comprehensive, but regionally specific, temperature dataset available (the Central England Temperature dataset) to the long-term behaviour of the Sun's magnetic field, and to trends across the entire Northern Hemisphere.

The paper is being published now as the researchers have just had the opportunity to put this year's data to the test and found that this year's results fit well with the trends they have discovered.

The researchers suggest that the anomaly in Northern Europe's winter temperatures could be to do with a phenomenon called 'blocking'.

'Blocking' is related to the jet stream which brings winds from the west, over the Atlantic, and into Northern Europe but, over the past couple of winters, could have lost its way, for weeks at a time, in an 'anticyclone' before it reaches Europe.

The researchers have found strong correlations between weak solar activity and the occurrences of 'blocking'. As the temperature is affected by a weak Sun so the wind's patterns also change and, as the warmer westerly winds fail to arrive, the UK is hit by north-easterlies from the Arctic.

The researchers, from the Department of Meteorology at the University of Reading, the Science and Technology Facilities Council Space Science and Technology Department, and the Max-Planck Institute for Solar System Research in Katlenburg-Lindau, Germany, are keen to stress the regional and seasonal (European and winter) nature of their research.

Professor Mike Lockwood has explained that the trends do not guarantee colder winters but they do suggest that colder winters will become more frequent. He said: "If we look at the last period of very low solar activity at the end of the seventeenth century, we find the coldest winter on record in 1684 but, for example, the very next year, when solar activity was still low, saw the third warmest winter in the entire 350-year record. "The results do show however that there are a greater number of cold UK winters when solar activity is low."

The paper can be found in IOP Publishing's open-access journal Environmental Research Letters at http://stacks.iop.org/1748-9326/5/024001 from Thursday 15 April.

Slobbery kisses from 'man's best friend' aid cancer research

TGen and VARI study cancer in dogs to find new treatments for humans

PHOENIX, Ariz. - Fido's wet licks might hold more than love. They could provide the DNA keys to findings new treatments for rare cancers and other diseases in both dogs and human patients.

The Translational Genomics Research Institute (TGen) and the Van Andel Research Institute (VARI) have created the Canine Hereditary Cancer Consortium, a program designed to study naturally occurring cancers in dogs to better understand why both pets and people get sick.

"Rare diseases in humans also show up in dogs. By studying the DNA of canines, we expect to more quickly discover the genomic causes of disease and more quickly find ways to better treat dogs, and people," said Dr. Mark Neff, director of the new TGen-VARI Program for Canine Health and Performance.

Using voluntarily donated saliva, blood and tumor samples from many breeds of privately owned dogs, researchers hope that by studying canine cancers they can pinpoint the causes of human cancers. The goal is to translate that knowledge into therapeutics useful to both veterinarians and clinical oncologists.

No dogs will be harmed and many should be helped. Nearly half of all dogs 10 years and older die from cancer. Dogs will be treated as patients at veterinary clinics nationwide. The research is endorsed by the American Kennel Club and by the Morris Animal Foundation. Samples will be gathered with the consent of owners and veterinarians. In addition to cancer, TGen and VARI eventually will study neurological and behavioral disorders as well as hearing loss and other debilitative conditions in dogs that could relate to people.

The cancer research will be supported by the recent approval of a 2-year, $4.3 million federal stimulus grant to the Canine Hereditary Cancer Consortium, which includes TGen and VARI in partnership with the National Cancer Institute (NCI), the University of Pennsylvania, Michigan State University, dog breeders and veterinarians. The public-private program also is funded by $1 million in grants from businesses involved in pet care - $500,000 from PetSmart, and $500,000 from Hill's Pet Nutrition.

"We're proud to be part of such an innovative approach that fully supports our mission of providing total lifetime care for pets, and one that will offer hope to people and dogs who are suffering from these illnesses," said Phil Francis, Executive Chairman of PetSmart.

Neil Thompson, President and CEO of Hill's Pet Nutrition, said support of cancer research in dogs "goes hand-in-hand with the company's mission of enriching and lengthening the special relationships between people and their pets. Maintaining the health of dogs goes beyond good nutrition. We support this research and the hope it provides, which will ultimately benefit dogs and dog lovers everywhere."

Through the federal grant, researchers also will draw on experts at the National Cancer Institute's Pediatric and Genetics Branches and Comparative Oncology program, including Dr. Paul Meltzer, Chief of NCI's Genetics Branch. Dr. Meltzer and his colleagues will use gene expression profiling to identify genes involved in osteosarcoma to determine if the same genetic markers, alterations, and targets found are also found in human osteosarcoma, and in dogs. Comparing data between humans and dogs has the potential to significantly advance understanding of this cancer.

Dr. Meltzer indicated he is hopeful the study will pinpoint the genetic causes of osteosarcoma, as well as identify individualized treatment options.

The program's "bark-to-bedside" approach represents an unprecedented alliance of veterinarians, basic scientists and private practice clinicians, non-profit research institutes, universities, industry and government. The project also will involve TGen Drug Development Services (TD2), a subsidiary of TGen, which will seek partnerships with pharmaceutical companies.

Why study dogs?

Dr. Jeffrey Trent, President and Research Director for TGen and VARI, said that it is difficult to study rare cancers in people, because there is insufficient data. But by studying similar types of cancers more prevalent in dogs, researchers should be better able to help those who currently have little hope.

"There's no question that you are doubly-cursed if you get a rare cancer. You may have a very difficult disease course, and you have very little information about how to guide the physician, and what treatment would be best. For some of these rare cancers, we don't even have consensus on what the best treatments might be," Dr. Trent said.

For example, children with osteosarcoma, a rare bone cancer, still often results in the loss of limbs.

"Many rare human cancers are very common in dogs. We're excited about the idea that we may be able to identify areas that could be mutually beneficial - that could help the canine patient and can help the human patient with these various cancers," Dr. Trent said. "The unique and exciting aspect of this is that it's a rare occasion where industry, academia, government and the private sector are joined together in a common goal of obtaining information to advance both pet and human health."

Study will investigate many diseases

The study is focused on sarcomas, those cancers that originate in the connective tissues such as bone, cartilage and fat. "The sad reality of sarcoma, because it is such a rare human disease, is that very few scientists take the time to do any research on it because it is not possible to get the number of samples you need for those kinds of studies," said Dr. Nick Duesbery, co-director of VARI's Center for Comparative Biology and Genetics.

The project began with the study of hemangiosarcoma - angiosarcoma in humans - a cancer for which there are currently no effective treatments. These tumors start in the lining of blood vessels and in the spleen. They are highly malignant and can be found most anywhere in the body.

Although rare in humans, these tumors are relatively common in certain breeds of dogs, such as Golden Retrievers, German Shepherds and Clumber Spaniels. After as many as 150 years of breeding, there are few genetic variations in these dogs, making it easier to identify the few genetic differences that can affect cancer susceptibility and response to drugs.

Study initiated by VARI

With the support of the American Kennel Club and the Clumber Spaniel Health Foundation, VARI in February 2008 began to study hemangiosarcoma in Clumber Spaniels. Researchers are using new genetic technologies developed at VARI to create genetic screens, diagnostic tests and treatments for hereditary canine cancers. VARI is analyzing the DNA and RNA of Clumber Spaniels, looking for genetic patterns that eventually could indicate if a particular dog is a carrier of a defective gene that could cause cancer.

With the addition of TGen and federal and private funding, the program is expanding to study four other cancers among as many as 20 breeds of dogs.

In the first two years, the project also will study osteosarcoma, oral melanoma, malignant histiocytosis, and non-Hodgkin lymphoma. Information from these studies will be used to develop diagnostic DNA tests for larger groups of dogs, enabling researchers to look for genes that influence cancer.

"We've got an incredible advantage here with the dogs, because these diseases are much more common in dogs than they are in humans. We can get some insight into the biology. Our strongest hope and desire is that we can translate that into therapies we can use for people," Dr. Duesbery said.

Study compared to the Human Genome Project

Dr. Trent drew a parallel between the Human Genome Project and the new study of dogs, predicting that new and useful information will soon become available to aid human health.

"The Human Genome Project provided a new playbook for biomedical research and patient care," Dr. Trent said. "As we begin to catalog the dog genome, we have the opportunity to really understand a number of the problems that afflict the dog, but also a number of possible health solutions for people."

Health worries over antibacterial soap additive

THE safety of antimicrobial soaps and toothpastes is under review following concerns that they could interfere with hormones in the body.

Last week, the US Food and Drug Administration said it will re-evaluate the safety of triclosan, which is added to plastics, soaps and toothpastes to kill bacteria and fungi. The agency is not yet recommending that consumers avoid such products.

Over the next year, the FDA will look at evidence that triclosan might affect the development of the nervous system, in which thyroid hormones play a key role, or the reproductive system. One recent study showed that triclosan lowers levels of thyroid hormones in rats, while a 2008 report found that it boosts the effects of oestrogen and testosterone.

Sarah Janssen of the Natural Resources Defense Council, a US environmental advocacy group, says the announcement is "long overdue".

When a Volcano Kills Quietly

By Michael Reilly

Ruapehu In June of 1996 New Zealand's Mt. Ruapehu erupted with violence. Its ash cloud blotted out the sun for miles, climbing almost 30,000 feet into the atmosphere. In all, some 7 million tons of rock and ash were ejected.

Yet no one was killed. At least, not within 60 miles of the volcano.

But in the cities of Auckland and Hamilton, hundreds of miles from Ruapehu, something strange happened. No warnings were sounded, and the skies appeared normal to the naked eye. But more people than usual started showing up at hospitals, many of them later dying of aggravated respiratory diseases.

Some 69 people in the two cities died from "unexplained" respiratory illness that July, according to health statistics. It could have been undiagnosed flu, or something else; there are myriad diseases that attack our lungs. But a new paper in the journal Atmospheric Environment puts forth another theory: invisible particles of acid-coated volcanic ash wafted into the cities.

A city of 1.3 million people, Auckland is 175 miles from the volcano -- that would seem to be a safe distance. But respiratory deaths there and in Hamilton were higher in 1996 than any other time that decade.

That's exactly the researchers' point. The scientists point out that all sorts of eruptions -- from Mt. St. Helens in 1980 to the epic Laki fissure eruption of 1783 in Iceland -- throw out loads of microscopic particles that are much more dangerous to people's lungs than the bits of ash we can see.

In fact, people further away from volcanoes may suffer worse exposure than those living right next to it, because small particles will initially go thousands of feet in the air and get carted away by wind.

If you're one of the 500 million people on Earth living with a 60-mile bulls eye of an active volcano, then you know you have a problem. What this research is saying is that if you live much further away, you may not be still be in trouble -- maybe worse trouble, because no one sees it coming. They write:

...the long-distance dispersal of diffuse fine volcanic ash and gaseous aerosols may pose a far more extensive health hazard than is generally perceived by medical and civic authorities. If so, people in many large cities, with limited or no awareness of this threat and no effective emergency procedures, may be at risk.

Weizmann scientists developed an electronic 'nose' that can predict the pleasantness of novel odors

These findings have implications for automated environmental toxicity monitoring and transmitting scent digitally

Weizmann Institute scientists have 'trained' an electronic system to be able to predict the pleasantness of novel odors, just like a human would perceive them – turning the popular notion that smell is completely personal and culture-specific on its head. In research published in PLoS Computational Biology, the scientists argue that the perception of an odor's pleasantness is innately hard-wired to its molecular structure, and it is only within specific contexts that personal or cultural differences are made apparent.

These findings have important implications for automated environmental toxicity and malodor monitoring, fast odor screening in the perfume industry, and provide a critical building block for the Holy Grail of sense technology – transmitting scent digitally.

Over the last decade, electronic devices, commonly known as electronic noses or 'eNoses,' have been developed to be able to detect and recognize odors. The main component of an eNose is an array of chemical sensors. As an odor passes through the eNose, its molecular features stimulate the sensors in such a way as to produce a unique electrical pattern – an 'odor fingerprint' – that characterizes that specific odor. Like a sniffer dog, an eNose first needs to be trained with odor samples so as to build a database of reference. Then the instrument can recognize new samples of those odors by comparing the odor's fingerprint to those contained in its database.

But unlike humans, if eNoses are presented with a novel odor whose fingerprint has not already been recorded in their database, they are unable to classify or recognize it.

So a team of Weizmann scientists, led by Dr. Rafi Haddad, then a graduate student of Prof. Noam Sobel of the Neurobiology Department and co-supervisor Prof. David Harel of the Computer Science and Applied

Mathematics Department, together with their colleague Abebe Medhanie of the Neurobiology Department, and Dr. Yehudah Roth of the Edith Wolfson Medical Center, Holon, decided to approach this issue from a different perspective. Rather than train an eNose to recognize a particular odor, they trained it to estimate the odor along a particular perceptual axis. The axis they chose was odorant pleasantness. In other words, they trained their eNose to predict whether an odor would be perceived as pleasant or unpleasant, or anywhere in between.

To achieve this, the scientists first asked a group of native Israelis to rate the pleasantness of a selection of odors according to a 30-point scale ranging from 'very pleasant' to 'very unpleasant.' From this dataset, they developed an 'odor pleasantness' algorithm, which they then programmed into the eNose. The scientists then got the eNose to predict the pleasantness of a completely new set of odors not contained in their database against the ratings provided by a completely different group of native Israelis. The scientists found that the eNose was able to generalize and rate the pleasantness of novel odors it never smelled before, and these ratings were about 80% similar to those of naive human raters who had not participated in the eNose training phase. Moreover, if the odors were simply categorized as either 'pleasant' or 'unpleasant,' as opposed to being rated on a scale, it achieved an accuracy of 99%.

But these findings still don't determine whether olfactory perception is culture-specific or not. With this in mind, the scientists decided to test eNose predictions against a group of recent immigrants to Israel from Ethiopia. The results showed that the eNose's ability to predict the pleasantness of novel odors against the native Ethipoians' ratings was just as good, even though it was 'tuned' to the pleasantness of odors as perceived by native Israelis. In other words, even though different odors have different meanings across cultures, the eNose performed equally well across these populations. This suggests a fundamental cross-cultural similarity in odorant pleasantness.

Sobel: 'Being able to predict whether a person who we never tested before would like a specific odorant, no matter their cultural background, provides evidence that odor pleasantness is a fundamental biological property, and that certain aspects of molecular structure are what determine whether an odor is pleasant or not.' So how are cultural differences accounted for? 'We believe that culture influences the perception of olfactory pleasantness mostly in particular contexts. To stress this point, many may wonder how the French can like the smell of their cheese, when most find the smell quite repulsive. We believe that it is not that the French think the smell is pleasant per se, they merely think it is a sign of good cheese. However, if the smell was presented out of context in a jar, then the French would probably rate the odor just as unpleasant as anyone else would.'

The scientists' findings that odor perception is hard-wired to molecular structure and their design of an eNose that is able to classify new odors could provide new methods for odor screening and environmental monitoring, and may, in the future, allow for the digital transmission of smell to scent-enable movies, games and music to provide a more immersive and captivating experience.

Prof. Noam Sobel's research is supported by the Nella and Leon Benoziyo Center for Neurosciences; the J&R Foundation; and Regina Wachter, New York. This research was funded by an FP7 grant from the European Research Council awarded to Noam Sobel.

Lung virus taking its toll on young lives, study finds

A common virus that causes wheezing and pneumonia claims the lives of up to two hundred thousand children worldwide each year, a study has found. The research, conducted by the University of Edinburgh, also showed that about 3.4 million children require hospital treatment for severe lung infection caused by the bug – respiratory syncytial virus (RSV). RSV – which infects most children before the age of two – usually causes mild cold-like symptoms, but can lead to serious illness in babies who are born prematurely or who have congenital heart disease.

The study, published in the Lancet journal, confirms that RSV is the single largest cause of lung infection in children. It is the first time that the numbers of children dying globally from RSV before the age of five has been quantified.

The international team analysed unpublished data from developing countries as well as all the published medical research on RSV infection. They found that about 33.8m children become infected with RSV each year and that 99 per cent of RSV-related deaths occur in developing countries.

The team hopes that by identifying the numbers affected by the virus, they may contribute to the development of a vaccine against the infection. Dr Harish Nair, of the University of Edinburgh's Department of Population Health Studies, said: "Our greatest hope of fighting this virus is to develop a vaccine, but before we can implement an immunisation programme, we need to understand exactly how big a problem RSV poses.

"This is the first time we have gathered information on such a global scale and is the best estimate we have for the number of children dying each year from this preventable illness."

City in Oregon Considers Beacon for 'the Big One'

By WILLIAM YARDLEY

CANNON BEACH, Ore. - Well before recent earthquakes shook Haiti, Chile and the California border with Mexico, this corner of the West Coast was trying harder than many places to prepare for the Big One. It has upgraded its warning signs and sirens, refined evacuation routes and reassessed bridges and buildings.

Now, as anxiety has increased, Cannon Beach, a tourist-friendly curve on the rocky Oregon coast, wants to be the first community in the United States to build a seismically sound evacuation tower, a $4 million escape from earthquakes' deadly ocean offspring, tsunamis.

"It's going to be distinctive," said Jay Raskin, a former mayor and an architect who is leading the effort to get the tower built. "So people will know what it's for."

California is often perceived as the epicenter for earthquakes in the United States. Yet new scientific studies show that the Pacific Northwest - Oregon, Washington and parts of Northern California, British Columbia and Alaska - is at a greater risk of experiencing a catastrophic "great earthquake," a giant rupture in the Cascadia Subduction Zone that could set the region shaking for as long as five minutes, from the sea to Seattle.

The new studies add to fears that increased after the 2004 earthquake and tsunami in Indonesia, and the 2008 earthquake in China's Sichuan Province. The region has taken several steps to prepare, including allocating $15 million this year to strengthen school buildings in Oregon and a plan to upgrade fire stations and scores of other buildings in Seattle.

On the southwest coast of Washington, that state is considering building 25-foot-high berms to which people could evacuate; the berms would be intended to withstand the 18-foot waves a tsunami could generate.

Yet whether all the work will get done in time is unclear. No one knows the deadline.

"If it happens tomorrow, it's going to be a disaster, no doubt," Chris Goldfinger, who heads the Active Tectonics and Seafloor Mapping Laboratory at Oregon State University and was the lead author of a recent study, said of a potential earthquake. "But if it happens 20 or 40 or 50 years from now it might not have to be that way, if we have enough knowledge and will to take action."

Mr. Goldfinger and his colleagues recently projected that the southern part of the Cascadia zone, off the Northwest coast, has a 37 percent probability of causing an earthquake with a magnitude of 8 or higher in the next 50 years, a significant rise in the risk rate compared with earlier studies. The last major earthquake occurred about 1700. Mr. Goldfinger said new data showed that 80 percent of earthquakes here over the past 10,000 years had occurred within 360 years of each other. Big cities like Seattle are also believed to be at a greater risk than previously thought, with some buildings built as recently as the 1990s in danger of collapse. Infrastructure like water pipes and sewer pipes also are at risk.

In 2001, the Puget Sound area experienced damage but no deaths in the Nisqually earthquake, a magnitude 6.8 quake centered about 50 miles southwest of Seattle. But experts say future quakes could be far larger. The same is true for tsunamis, which have struck the coast here before. In 1964, a tsunami set off by an earthquake in Alaska killed 11 people in Crescent City, Calif., just south of the Oregon border.

That wave also knocked out the main bridge north of Cannon Beach. Experts say the current bridge, over Ecola Creek, would not survive an earthquake or a tsunami, and local officials are discussing whether to try to strengthen it or build something new.

Cannon Beach Elementary and its 120 students are just south of the bridge, in the heart of what scientists say would be the inundation zone in a tsunami. The school district is considering moving the school and two others in nearby towns to higher ground.

Awareness seems to be on the rise everywhere here. Color-coded evacuation instructions are posted by the beach and breakfast joints: "Drop, cover and hold. Move immediately inland to higher ground. Do not wait for an official warning."

Cleve Rooper, the local fire chief, explained the range of risk. "In the best case, we'll have a few hours' warning from an earthquake that happened somewhere far away in the Pacific Basin," said Mr. Rooper, who has worked in the fire department for 40 years. "In the worst case, we'll have 10 to 20 minutes after the ground stops shaking here to try to get to high ground."

Yet the variables do not stop there. A quake could register a magnitude of 7, or of 9 or even higher. A tsunami could hit on a weekday in winter, when Cannon Beach is largely left to its year-round residents, about 1,700 people. It could also strike on a Saturday in August, when the population swells significantly.

"Cannon Beach has been thought of as a leader on this stuff on the coast and maybe we are, but I still don't feel like we're prepared," said Rich Mays, the city manager. "It's a tourist destination. What are we going to do if there are 15,000 people in town when it happens?"

If the earthquake is nearby, Cannon Beach, hemmed in by the Coast Mountains and the coast itself, could have a hard time finding help if the rest of the region is devastated. Nearby towns like Seaside and Manzanita face similar risks, as do Indian tribes on the Olympic Peninsula in Washington.

The proposed evacuation tower, based on those built in Japan, could hold up to about 1,000 people, possibly more, but far from all who might need help. Mr. Raskin, who is part of a group that submitted a federal financing request for the project through Oregon's Congressional delegation, has proposed replacing City Hall with the new structure, though other sites are also being considered.

The tower, like the berms being considered in Washington, is based on new guidelines for vertical evacuation from tsunamis by the Federal Emergency Management Agency, and the proposal for financing is thick with structural diagrams and data from soil scours.

Some considerations are based on more local preferences, however. A rendering by Mr. Raskin includes cedar shingles that he designed to echo, perhaps as much as a tsunami evacuation tower can, the windswept houses here. "I knew that you have to kind of engage the locals and their ideas about the town," Mr. Raskin said. "That's why I put the shingles on it."

Pitt Dental School researchers find susceptibility for caries, gum disease in genes

PITTSBURGH – Certain genetic variations may be linked to higher rates of tooth decay and aggressive periodontitis, according to two recently published papers by researchers at the University of Pittsburgh School of Dental Medicine and their collaborators.

Alexandre R. Vieira, D.D. S., Ph.D., senior author of both papers and an assistant professor of oral biology, and his colleagues at the School of Dental Medicine found that the rate of dental caries was influenced by individual variations, or polymorphisms, in a gene called beta defensin 1(DEFB1), which plays a key role in the first-line immune response against invading germs. The findings are available online in the Journal of Dental Research.

"We were able to use data gathered from our Dental Registry and DNA Repository, the only one of its kind in the world, to see if certain polymorphisms were associated with the development of caries," Dr. Vieira said. "This could help us find new ways to treat people who are particularly susceptible to tooth decay, a problem that afflicts millions of Americans."

For the study, the researchers analyzed nearly 300 anonymous dental records and accompanying saliva samples from the registry, assigning each case a DMFT score based on the presence of decayed teeth, missing teeth due to caries, and tooth fillings, as well as a DMFS score, based on decayed teeth, missing teeth, and filled surface of a tooth. In general, individuals with fewer caries have lower DMFT and DMFS scores.

Saliva samples contained one of three variants, dubbed G-20A, G-52A and C-44G, of the DEFB1 gene. Individuals who carried a G-20A copy had DMFT and DMFS scores that were five-times higher than for people who had other variants. The G-52A polymorphism was associated with lower DMFT scores.

"It's possible that these variations lead to differences in beta defensin's ability to inhibit bacterial colonization," Dr. Vieira said. "In the future, we might be able to test for these polymorphisms as clinical markers for caries risk."

In a second paper, published last week in PLoS One, Dr. Vieira, colleagues at Pitt and collaborators in Brazil studied saliva samples of 389 people in 55 families to look for genetic links to aggressive periodontitis, which is rapid and severe destruction of the gums and bone that starts at a young age and is thought to be more common in Africans and those of African descent. Brazil's population is composed primarily of Caucasians of Portuguese ancestry, Africans and native Indians.

They found hints of an association between the disease and the FAM5C gene. While further testing did not find any mutations or polymorphisms that bore out a relationship, other experiments showed elevated levels of FAM5C expression, or activation, in areas of diseased periodontal tissue compared to healthy tissue.

"The FAM5C gene recently was implicated in cardiovascular disease, in which inflammation plays a role, just as in periodontitis," Dr. Vieira said. "More research is needed to see if variation in the gene is associated with different activity profiles."

Ayla Ozturk, D.D.S., Ph.D., and Pouran Famili, D.D.S., Ph.D., Pitt School of Dental Medicine, co-authored the Journal of Dental Research paper, which was funded by the School of Dental Medicine.

Co-authors of the PLoS One paper included researchers at Pitt, the Federal University of Rio de Janeiro, Rio de Janeiro State University, Sao Paulo University and other universities in Brazil. The study was funded by the Pitt School of Dental Medicine and Brazilian funding agencies.

Low vitamin D levels associated with more asthma symptoms and medication use

Low levels of vitamin D are associated with lower lung function and greater medication use in children with asthma, according to researchers at National Jewish Health. In a paper published online this week in the Journal

of Allergy & Clinical Immunology, Daniel Searing, MD, and his colleagues also reported that vitamin D enhances the activity of corticosteroids, the most effective controller medication for asthma.

"Asthmatic children in our study who had low levels of vitamin D were more allergic, had poorer lung function and used more medications," said Dr. Searing. "Conversely, our findings suggest that vitamin D supplementation may help reverse steroid resistance in asthmatic children and reduce the effective dose of steroids needed for our patients."

The researchers examined electronic medical records of 100 pediatric asthma patients referred to National Jewish Health. Overall, 47 percent of them had vitamin D levels considered insufficient, below 30 nanograms per milliliter of blood (ng/mL). Seventeen percent of the patients had levels below 20 ng/mL, which is considered deficient. These levels were similar to vitamin D levels found in the general population.

Patients low in vitamin D generally had higher levels of IgE, a marker of allergy, and responded positively to more allergens in a skin prick test. Allergies to the specific indoor allergens, dog and house dust mite, were higher in patients with low vitamin D levels. Low vitamin D also correlated with low FEV1, the amount of air a person can exhale in one second, and lower FEV1/FVC, another measure of lung function. Use of inhaled steroids, oral steroids and long-acting beta agonists were all higher in patients low in vitamin D.

"Our findings suggest two possible explanations," said senior author Donald Leung, MD, PhD. "It could be that lower vitamin D levels contribute to increasing asthma severity, which requires more corticosteroid therapy. Or, it may be that vitamin D directly affects steroid activity, and that low levels of vitamin D make the steroids less effective, thus requiring more medication for the same effect."

The researchers performed a series of laboratory experiments that indicated vitamin D enhances the action of corticosteroids. They cultured some immune cells with the corticosteroid dexamethasone alone and others with vitamin D first, then dexamethasone. The vitamin D significantly increased the effectiveness of dexamethasone. In one experiment vitamin D and dexamethasone together were more effective than 10 times as much dexamethasone alone. The researchers also incubated immune-system cells for 72 hours with a staphylococcal toxin to induce corticosteroid resistance. Vitamin D restored the activity of dexamethasone.

"Our work suggests that vitamin D enhances the anti-inflammatory function of corticosteroids,' said Dr. Leung. "If future studies confirm these findings vitamin D may help asthma patients achieve better control of their respiratory symptoms with less medication."

This study comes on the heels of another paper by National Jewish Health faculty, which showed that low levels of vitamin D in adult asthma patients are associated with lower lung function and reduced responsiveness to corticosteroids.

Texas Children's Cancer Center First in Texas to Magnetically Lengthen Nine-Year-Old's Leg as She Grows

HOUSTON – Nine-year-old Morgan LaRue is the first cancer patient in Texas to benefit from a groundbreaking procedure that will magnetically lengthen her leg, sparing her the possibility of up to 10 future surgeries as her body grows. The implant and extension took place at Texas Children's Cancer Center in Houston, Texas. Click here to watch the procedure. Or learn more about Texas Children's Cancer Center or the device.

On March 29, 2010, Morgan lost a portion of the bone in her upper leg to osteosarcoma (bone cancer) and was facing the potential of numerous surgeries in order to keep her left leg even with her right, as she grows into adulthood. In her initial surgery two weeks ago, Dr. Rex Marco, an oncologic orthopedic surgeon at Texas Children's Hospital and the University of Texas Health Science Center at Houston, implanted a prosthetic device that saved Morgan from a lower limb amputation and allowed her cancerous bone to be replaced with a metal implant. The device, a Stanmore Implants Extendable Distal Femoral Replacement, can be extended as Morgan grows, saving her from ongoing invasive procedures.

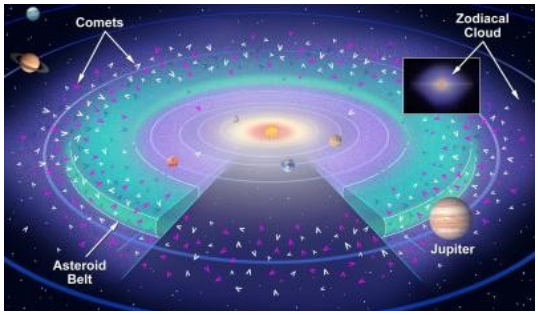
This week at Texas Children's Cancer Center, Morgan underwent her first outpatient procedure to magnetically extend her leg. By placing her leg into a magnetized "donut" in the outpatient clinic, doctors were able to extend the implanted prosthesis without having to do any surgery. The magnet extender, manufactured by Stanmore Implants, is a reversible extender that is the first and only device of its kind to be used in Texas.

"The difference this device makes for Morgan is incredible," said Dr. Marco. "Her quality of life is so much higher than it would be if she were constantly undergoing surgery."

While the device has been approved and is regularly being used in Europe, it is still pending U. S. Food and Drug Administration approval and has only been used for approximately 15 patients in this country. Dr. Wang, pediatric oncologist at Texas Children's Cancer Center and Assistant Professor, Department of Pediatrics, Section of Hematology/Oncology, Baylor College of Medicine, and Dr. Marco, advocated for and received a "compassionate use" exception for the young girl, in order to implant the groundbreaking device.

"Morgan has already been through a lot of treatment for her cancer," said Dr. Wang, Morgan's oncologist, "and this will prevent her from future uncomfortable surgeries."

Source of zodiac glow identified



The eerie glow that straddles the night time zodiac in the eastern sky is no longer a mystery. First explained by Joshua Childrey in 1661 as sunlight scattered in our direction by dust particles in the solar system, the source of that dust was long debated. In a paper to appear in the April 20 issue of The Astrophysical Journal, David Nesvorny and Peter Jenniskens put the stake in asteroids. More than 85 percent of the dust, they conclude, originated from Jupiter Family comets, not asteroids.

"This is the first fully dynamical model of the zodiacal cloud," says planetary scientist Nesvorny of the Southwest Research Institute in Boulder, Colo. "We find that the dust of asteroids is not stirred up enough over its lifetime to make the zodiacal dust cloud as thick as observed. Only the dust of short-period comets is scattered enough by Jupiter to do so."

This result confirms what meteor astronomer Jenniskens of the SETI Institute in Mountain View, Calif., had long suspected. An expert on meteor showers, he had noticed that most consist of dust moving in orbits similar to those of Jupiter Family comets, but without having active dust-oozing comets associated with them.

The dust between the planets, that scatters sunlight our way, is not from the asteroid belt (depicted here in green), but from periodically disrupting comets that spend much of their time near the orbit of Jupiter, according to calculations by Nesvorny and Jenniskens. **Southwest Research Institute**

Instead, Jenniskens discovered a dormant comet in the Quadrantid meteor shower in 2003 and has since identified a number of other such parent bodies. While most are inactive in their present orbit around the Sun, all have in common that they broke apart violently at some point in time in the past few thousand years, creating dust streams that now have migrated into Earth's path.

Nesvorny and Jenniskens, with the help of Harold Levison and William Bottke of the Southwest Research Institute, David Vokrouhlicky of the Institute of Astronomy at Charles University in Prague, and Matthieu Gounelle of the Natural History Museum in Paris, demonstrated that these comet disruptions can account for the observed thickness of the dust layer in the zodiacal cloud.

In doing so, they solved another mystery. It was long known that snow in Antarctica is laced with micro-meteorites, some 80 to 90 percent of which have a peculiar primitive composition, rare among the larger meteorites that we know originated from asteroids. Instead, Nesvorny and Jenniskens suggest that most Antarctic micro-meteorites are pieces of comets. According to their calculations, cometary grains dive into Earth's atmosphere at entry speeds low enough for them to survive, reach the ground, and be picked up later by a curious micro-meteorite hunter.

This work was funded by the NASA Planetary Geology and Geophysics Program and the NASA Planetary Astronomy programs.

Appalachian professor's research finds no evidence of cannibalism at Donner Party campsite

BOONE – Research conducted by Dr. Gwen Robbins, an assistant professor of biological anthropology at Appalachian State University, finds there is no evidence of cannibalism among the 84 members of the Donner Party who were trapped by a snowstorm in the Sierra Nevada Mountains in the mid-1840s.

Remains from the Donner party's Alder Creek campsite were excavated by a team of archaeologists from the University of Montana and the University of Oregon Museum. A sample of bones from the campsite hearth was analyzed by Robbins and Kelsey Gray, an Appalachian graduate. They will present the results of this project this week at the annual meeting of the American Association of Physical Anthropologists in Albuquerque, N.M.

James F. Reed and his wife, Margret W. Keyes Reed, seen in this file photo taken in the 1850s, were survivors of the tragic Donner Party. **AP Photo**

During the excavation of the Donner Party's campsite, 16,000 burned, fragmented bones were found. Many of the bones also had butchery and boiling marks. Robbins, an osteologist who specializes in bone biology and microstructure, examined the bones with three questions in mind: Are there any human bones in the hearth, which would provide material evidence for cannibalism? What kinds of other animals are present in the assemblage of bone fragments? and, What did the starvation diet look like?

The Donner Party has long been infamous for reportedly resorting to cannibalism after becoming trapped in the Sierra Nevada Mountains of California for months during the winter of 1846-1847. The party, originally 84 men, women and children, became stranded after a series of bad decisions and misfortunes caused numerous

delays on their westward migration route and left them attempting to cross the mountains into California just as the first snows were falling in early October 1846.
In 2003, archaeologists Kelly Dixon (University of Montana) and Julie Schablitsky (then of the University of Oregon Museum) uncovered a hearth during the excavation of the Donner family's campsite. Within the hearth, they found thousands of tiny burned fragments of bone, most measuring less than a quarter inch in diameter.

In 2004, Robbins, who was then a graduate student completing her PhD at the University of Oregon, was asked to determine whether the bones were human. A preliminary analysis of the bones was completed in 2006, after Robbins returned to the United States from dissertation research in India. This early analysis of 30 specimens indicated that there were no human bones from the hearth.

Upon joining the faculty at Appalachian, Robbins continued her research on the remains. With a team of undergraduate students, she pored through the tiny fragments looking for remains that could withstand further testing. The majority of bone fragments were so small and so delicate that they would crumble if subjected to thin sectioning, but there were about 250 larger, sturdier pieces of bone that showed evidence of cutting, chopping and boiling. Of these, 55 additional fragments were studied.

The team produced thin sections from these specimens and examined them using a microscope, measuring each basic structural unit and characterizing the tissue types. From this work, they determined that humans were not among the food refuse examined. A power analysis indicated that, statistically, Robbins and Gray can be 70 percent confident that if cannibalism made up a small fraction of the diet (less than 1 percent) at the site in the last few weeks of occupation, and if humans were processed in the same way animals were processed, at least one of the 85 bone fragments examined would be human.

So, what did the Donner family eat during that winter? Robbins' team identified the remains as cattle, deer, horse and dog. While the historical record had indicated that cattle were the principle means of subsistence during that winter, there was previously no record that the Donner family also successfully hunted deer despite the 20 to 30 feet of snow on the ground that winter. The historical record does indicate that relief parties in February brought horses to the camps and that a few were left behind. There was no record of the horses being consumed and no mention of eating dog.

The legend of the Donner party was primarily created by print journalists, who embellished the tales based on their own Victorian macabre sensibilities and their desire to sell more newspapers. In all, 47 people lived to tell the tale: 11 men and 36 women and children. The survivors fiercely denied allegations of cannibalism and one man even filed a defamation suit immediately upon reaching Sutter's Fort near Sacramento. Although the court ruled in his favor, he was forever known to local residents as Keseberg the Cannibal. The voices of the survivors of the Donner Party ordeal have long been overwhelmed by the spectacular imagery of a legend that swiftly took on a life of its own. Their descendants are still today affected by the stigma of this tale.

The archaeological record provides a new picture of the party's activities. In the trash and debris left around the hearth in the spring of 1847, archaeologists found pieces of slate and shards of broken china. These pieces of slate and crockery around the hearth suggest an attempt to maintain a sense of a "normal life," a family intent on maintaining a routine of lessons, to preserve the dignified manners from another time and place, a refusal to accept the harsh reality of the moment, and a hope that the future was coming.

Robbins' research will be published in the July issue of the journal American Antiquity. The archaeology team also is finishing a book manuscript for University of Oklahoma Press to be released in 2011.

Nose-dwelling leech species found

A new species of leech, discovered by an international team of scientists, has a preference for living up noses.

Researchers say the leech can enter the body orifices of people and animals to attach itself to mucous membranes. They have called the new blood-sucking species Tyrannobdella rex which means tyrant leech king.

The creature was first discovered in 2007 in Peru when a specimen was plucked from the nose of a girl who had been bathing in a river. The creature lives in the remote parts of the Upper Amazon and has a "particularly unpleasant habit of infesting humans", the scientists say. Studies also revealed that it had "a preference for living up noses". The research published their findings in the online scientific journal PLoS One.

The leech was discovered when one was plucked from the nose of a young girl

Dr. Renzo Arauco-Brown, from the School of Medicine at the Universidad Peruana Cayetano Heredia in Lima, was the medical doctor who extracted the leech and preserved sent it a zoologist in the US. The zoologist, from the American Museum of Natural History in New York, was quick to recognise it as a new species. He

said it had some very unusual features, including just one single jaw, eight very large teeth and extremely small genitalia.

Dr Siddall then brought together a team of researchers who studied the leech's features and DNA.

Anna Phillips, a graduate student affiliated with the museum, led the study. She said: "We think that Tyrannobdella rex is most closely related to another leech that gets into the mouths of livestock in Mexico.

"The leech could feed on aquatic mammals, from their noses and mouths for example, where they could stay for weeks at a time."

The DNA analysis also revealed "evolutionary relationships" between leeches that now inhabit distant regions. This suggested that a common ancestor of this group may have lived when the continents were pressed together into a single land mass or supercontinent called Pangaea.

Dr Siddall explained: "The earliest species in this family of leeches no doubt shared an environment with dinosaurs about 200 million years ago. "Some ancestor of our T. rex may have been up that other T. rex's nose."

Although around 600 to 700 species leeches have been described, scientists believe there could be as many as 10,000 species throughout the world in marine, terrestrial and fresh water environments.

Drug shared by addicts seems to protect against HIV brain dementia

To their surprise, researchers at Georgetown University Medical Center (GUMC) have discovered that morphine (a derivate of the opium poppy that is similar to heroin) protects rat neurons against HIV toxicity - a finding they say might help in the design of new neuroprotective therapies for patients with the infection.

The discovery, being presented at the annual meeting of the Society of NeuroImmune Pharmacology, also helps explain why a subset of people who are heroin abusers and become infected with HIV through needle sharing don't develop HIV brain dementia. This brain disorder includes cognitive and motor abnormalities, anxiety and depression.

"We believe that morphine may be neuroprotective in a subset of people infected with HIV," says the study's lead investigator, Italo Mocchetti, PhD, Professor of neuroscience at GUMC. "That is not to say that people should use heroin to protect themselves - that makes no medical sense at all - but our findings gives us ideas about designing drugs that could be of benefit.

"Needless to say we were very surprised at the findings," he added. "We started with the opposite hypothesis - that heroin was going to destroy neurons in the brain and lead to HIV dementia."

The researchers conducted the study because they knew that a number of HIV-positive people are also heroin abusers, and because of that, some are at high risk of developing neurological complications from the infection. Others, however, never develop these cognitive problems, Mocchetti says.

Because little is known about the molecular mechanisms linking opiates and HIV neurotoxicity, Mocchetti and his team conducted experiments in rats. They found that in the brain, morphine inhibited the toxic property of the HIV protein gp120 that mediates the infection of immune cells. With further investigation, they concluded that morphine induces production of the protein CCL5, which they discovered is released by astrocytes, a type of brain cell. CCL5 is known to activate factors that suppress HIV infection of human immune cells. "It is known to be important in blood, but we didn't know it is secreted in the brain," says Mocchetti. "Our hypothesis is that it is in the brain to prevent neurons from dying."

They say morphine blocked HIV from binding to CCR5 receptors it typically uses to enter and infect cells. The researchers believe CCL5 itself attached to those receptors, preventing the virus from using it. In this way, it prevented HIV-associated dementia. This effect, however, only worked in the M-trophic strain of HIV, the strain that most people are first infected with. It did not work with the second T-trophic strain that often infects patients later.

"Ideally we can use this information to develop a morphine-like compound that does not have the typical dependency and tolerance issues that morphine has," says Mocchetti.

Provided by Georgetown University Medical Center (news : web)

First evidence that chitosan could repair spinal damage

Chitosan offers hope for spinal injury patients

Richard Borgens and his colleagues from the Center for Paralysis Research at the Purdue School of Veterinary Medicine have a strong record of inventing therapies for treating nerve damage. From Ampyra, which improves walking in multiple sclerosis patients to a spinal cord simulator for spinal injury victims, Borgens has had a hand in developing therapies that directly impact patients and their quality of life. Another therapy that is currently undergoing testing is the use of polyethylene glycol (PEG) to seal and repair damaged spinal cord nerve cells. By repairing the damaged membranes of nerve cells, Borgens and his team can restore the spinal cord's ability to transmit signals to the brain. However, there is one possible clinical drawback: PEG's breakdown products are potentially toxic. Is there a biodegradable non-toxic compound that is equally effective

at targeting and repairing damaged nerve membranes? Borgens teamed up with physiologist Riyi Shi and chemist Youngnam Cho, who pointed out that some sugars are capable of targeting damaged membranes.

Could they find a sugar that restored spinal cord activity as effectively as PEG? Borgens and his team publish their discovery that chitosan can repair damaged nerve cell membranes in The Journal of Experimental Biology on 16 April 2010 at http://jeb.biologists.org.

Having initially tested mannose and found that it did not repair spinal cord nerve membranes, Cho decided to test a modified form of chitin, one of the most common sugars that is found in crustacean shells. Converting chitin into chitosan, Cho isolated a segment of guinea pig spinal cord, compressed a section, applied the modified chitin and then added a fluorescent dye that could only enter the cells through damaged membranes. If the chitosan repaired the crushed membranes then the spinal cord tissue would be unstained, but if the chitosan had failed, the spinal cord neurons would be flooded with the fluorescent dye. Viewing a section of the spinal cord under the microscope, Cho was amazed to see that the spinal cord was completely dark. None of the dye had entered the nerve cells. Chitosan had repaired the damaged cell membranes.

Next Cho tested whether a dose of chitosan could prevent large molecules from leaking from damaged spinal cord cells. Testing for the presence of the colossal enzyme lactate dehydrogenase (LDH), Borgens admits he was amazed to see that levels of LDH leakage from chitosan treated spinal cord were lower than from undamaged spinal cords. Not only had the sugar repaired membranes at the compression site but also at other sites where the cell membranes were broken due to handling. And when the duo tested for the presence of harmful reactive oxygen species (ROS), released when ATP generating mitochondria are damaged, they found that ROS levels also fell after applying chitosan to the damaged tissue: chitosan probably repairs mitochondrial membranes as well as the nerve cell membranes.

But could chitosan restore the spinal cord's ability to transmit electrical signals to the brain through a damaged region? Measuring the brain's response to nerve signals generated in a guinea pig's hind leg, the duo saw that the signals were unable to reach the brain through a damaged spinal cord. However, 30·min after injecting chitosan into the rodents, the signals miraculously returned to the animals' brains. Chitosan was able to repair the damaged spinal cord so that it could carry signals from the animal's body to its brain.

Borgens is extremely excited by this discovery that chitosan is able to locate and repair damaged spinal cord tissue and is even more enthusiastic by the prospect that nanoparticles of chitosan could also target delivery of neuroprotective drugs directly to the site of injury 'giving us a dual bang for our buck,' says Borgens.

REFERENCE: *Cho, Y., Shi, R. and Borgens, R. B. (2010). Chitosan produces potent neuroprotection and physiological recovery following traumatic spinal cord injury. J. Exp. Biol. 213, 1513-1520. http://jeb.biologists.org*

Discovery could help diabetics and others with slow-to-heal wounds

MAYWOOD, Ill. -- A new discovery about the wound-healing process could lead to better treatments for diabetics and other patients who have wounds that are slow to heal.

Loyola University Health System researchers found that certain immune system cells slow the wound-healing process. Thus, it might be possible to improve healing by inactivating these immune system cells, said Elizabeth Kovacs, PhD, who heads the laboratory team that made the discovery. The findings by Kovacs and colleagues are reported online, in advance of print, in the Journal of Surgical Research.

In the study, the immune system cells that impeded the healing process are called natural killer T (NKT) cells. NKT cells perform beneficial functions such as killing tumor cells and virus-infected cells. However, researchers discovered that NKT cells also migrate to wound sites and impede the healing process.

Kovacs and colleagues used an animal model to examine the effects of NKT cells on healing. Healing was significantly slower in normal mice that had NKT cells than it was in a special breed of mice that lacked NKT cells. "We demonstrated that early wound closure was accelerated in the absence of NKT cells," Kovacs and colleagues wrote. "Importantly, we also made the novel observation that NKT cells themselves are a constituent of the early wound inflammatory infiltrate."

Certain conditions, such as diabetes and infections, can slow or prevent wounds from healing. The study found that NKT cells may be at least partially to blame. Researchers don't know how NKT cells slow healing. But they believe they may be able to inactivate NKT cells using an antibody. They are testing this prediction in a follow-up study.

Kovacs is a professor and vice chair of research in the Department of Surgery at Loyola University Chicago Stritch School of Medicine. She also is director of research of Loyola's Burn & Shock Trauma Institute.

Co-authors of the study are Jessica Palmer, Julia Tulley, Dr. John Speicher, Douglas Faunce, PhD, first author Dr. David Schneider and Dr. Richard Gamelli. Schneider is a resident at Loyola and Gamelli is dean of the Stritch School of Medicine and director of the Burn & Shock Trauma Institute.

The study was supported by the National Institutes of Health (NIH) and by the Ralph and Marion C. Falk Medical Research Trust.

Scott Somers, Ph.D., who manages wound healing research and training grants supported by the NIH's National Institute of General Medical Sciences, said, "Beyond the novel finding of a fundamental mechanism controlling wound healing, this work also highlights the contributions of physician-scientists like Dr. Schneider, a surgical resident who is training to do hypothesis-based, cutting-edge scientific investigation."

Lunar polar craters may be electrified

As the solar wind flows over natural obstructions on the moon, it may charge polar lunar craters to hundreds of volts, according to new calculations by NASA's Lunar Science Institute team.

Polar lunar craters are of interest because of resources, including water ice, which exist there. The moon's orientation to the sun keeps the bottoms of polar craters in permanent shadow, allowing temperatures there to plunge below minus 400 degrees Fahrenheit, cold enough to store volatile material like water for billions of years. "However, our research suggests that, in addition to the wicked cold, explorers and robots at the bottoms of polar lunar craters may have to contend with a complex electrical environment as well, which can affect surface chemistry, static discharge, and dust cling," said William Farrell of NASA's Goddard Space Flight Center, Greenbelt, Md. Farrell is lead author of a paper on this research published March 24 in the Journal of Geophysical Research. The research is part of the Lunar Science Institute's Dynamic Response of the Environment at the moon (DREAM) project.

"This important work by Dr. Farrell and his team is further evidence that our view on the moon has changed dramatically in recent years," said Gregory Schmidt, deputy director of the NASA Lunar Science Institute at NASA's Ames Research Center, Moffett Field, Calif. "It has a dynamic and fascinating environment that we are only beginning to understand."

New research from NASA's Lunar Science Institute indicates that the solar wind may be charging certain regions at the lunar poles to hundreds of volts. In this short video Dr. Bill Farrell discusses this research and what it means for future exploration of the moon's poles. **NASA/Goddard Space Flight Center**

Solar wind inflow into craters can erode the surface, which affects recently discovered water molecules. Static discharge could short out sensitive equipment, while the sticky and extremely abrasive lunar dust could wear out spacesuits and may be hazardous if tracked inside spacecraft and inhaled over long periods.

The solar wind is a thin gas of electrically charged components of atoms -- negatively charged electrons and positively charged ions -- that is constantly blowing from the surface of the sun into space. Since the moon is only slightly tilted compared to the sun, the solar wind flows almost horizontally over the lunar surface at the poles and along the region where day transitions to night, called the terminator.

The researchers created computer simulations to discover what happens when the solar wind flows over the rims of polar craters. They discovered that in some ways, the solar wind behaves like wind on Earth -- flowing into deep polar valleys and crater floors. Unlike wind on Earth, the dual electron-ion composition of the solar wind may create an unusual electric charge on the side of the mountain or crater wall; that is, on the inside of the rim directly below the solar wind flow.

Since electrons are over 1,000 times lighter than ions, the lighter electrons in the solar wind rush into a lunar crater or valley ahead of the heavy ions, creating a negatively charged region inside the crater. The ions eventually catch up, but rain into the crater at consistently lower concentrations than that of the electrons. This imbalance in the crater makes the inside walls and floor acquire a negative electric charge. The calculations reveal that the electron/ion separation effect is most extreme on a crater's leeward edge – along the inside crater wall and at the crater floor nearest the solar wind flow. Along this inner edge, the heavy ions have the greatest difficulty getting to the surface. Compared to the electrons, they act like a tractor-trailer struggling to follow a motorcycle; they just can't make as sharp a turn over the mountain top as the electrons. "The electrons build up an electron cloud on this leeward edge of the crater wall and floor, which can create an unusually large negative charge of a few hundred Volts relative to the dense solar wind flowing over the top," says Farrell.

The negative charge along this leeward edge won't build up indefinitely. Eventually, the attraction between the negatively charged region and positive ions in the solar wind will cause some other unusual electric current to flow. The team believes one possible source for this current could be negatively charged dust that is repelled by the negatively charged surface, gets levitated and flows away from this highly charged region. "The Apollo astronauts in the orbiting Command Module saw faint rays on the lunar horizon during sunrise that might have been scattered light from electrically lofted dust," said Farrell. "Additionally, the Apollo 17 mission landed at a site similar to a crater environment – the Taurus-Littrow valley. The Lunar Ejecta and Meteorite Experiment

left by the Apollo 17 astronauts detected impacts from dust at terminator crossings where the solar wind is nearly-horizontal flowing, similar to the situation over polar craters."

Next steps for the team include more complex computer models. "We want to develop a fully three-dimensional model to examine the effects of solar wind expansion around the edges of a mountain. We now examine the vertical expansion, but we want to also know what happens horizontally," said Farrell. As early as 2012, NASA will launch the Lunar Atmosphere and Dust Environment Explorer (LADEE) mission that will orbit the moon and could look for the dust flows predicted by the team's research.

This work was enabled by support from NASA Goddard's Internal Research and Development program and NASA's Lunar Science Institute. The team includes researchers from NASA Goddard, the University of California, Berkeley, and the University of Maryland, Baltimore County.

Is Estrogen the New Ritalin?

The sex hormone boosts thinking in some women, impairs it in others

By Erik Vance

Big test coming up? Having trouble concentrating? Try a little estrogen.

Neuroscientists at the University of California, Berkeley, report in a recent study that hormone fluctuations during a woman's menstrual cycle may affect the brain as much as do substances such as caffeine, methamphetamines or the popular attention drug Ritalin.

Scientists have known for decades that working memory (short-term information processing) is dependent on the chemical dopamine. In fact, drugs like Ritalin mimic dopamine to help people concentrate. Researchers have also had evidence that in rats, estrogen seems to trigger a release of dopamine. The new study from Berkeley, however, is the first to show that cognition is tied to estrogen levels in people—explaining why some women have better or worse cognitive abilities at varying points in their menstrual cycles.

The Berkeley team examined 24 healthy women, some of whom had naturally high levels of dopamine and some of whom had low levels, as indicated by genetic testing. As expected, those with the lower levels struggled with complicated working memory tasks, such as repeating a series of five numbers in reverse order. When the test was repeated during ovulation, however, when estrogen levels are highest (usually 10 to 12 days after menstruation), these women fared markedly better, improving their performance by about 10 percent. Surprisingly, those with naturally high dopamine levels took a nosedive in their ability to do complicated mental tasks at that point in their cycle.

According to Ph.D. student Emily Jacobs, who conducted the study, dopamine in the brain is a "classic Goldilocks scenario." For women with the lowest levels—about 25 percent of the general population—increased dopamine during ovulation will sharpen cognitive functions, whereas for the 25 percent of women with the highest levels, ovulation seems to take them beyond a threshold and to impair thinking. The remaining half of women fall somewhere in between and were not a part of the study.

The work has broad implications. Jacobs says it may mean that caffeine, which triggers a dopamine release, and Ritalin-like drugs are less effective—or even detrimental—at certain times of the month for some women, when estrogen is spiking. More broadly, she hopes to remind scientists studying brain disease that women's and men's brains, though equal in aptitude, are not the same.

"There are pretty important differences," Jacobs says. "And until we figure out how they differ in a normal state, we can't predict how they differ in a diseased state***."***

[For more on sex hormones in the brain, see "Different Shades of Blue".]

A brain-recording device that melts into place

Scientists have developed a brain implant that essentially melts into place, snugly fitting to the brain's surface. The technology could pave the way for better devices to monitor and control seizures, and to transmit signals from the brain past damaged parts of the spinal cord.

"These implants have the potential to maximize the contact between electrodes and brain tissue, while minimizing damage to the brain. They could provide a platform for a range of devices with applications in epilepsy, spinal cord injuries and other neurological disorders," said Walter Koroshetz, M.D., deputy director of the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health.

The study, published in Nature Materials, shows that the ultrathin flexible implants, made partly from silk, can record brain activity more faithfully than thicker implants embedded with similar electronics.

The simplest devices for recording from the brain are needle-like electrodes that can penetrate deep into brain tissue. More state-of-the-art devices, called micro-electrode arrays, consist of dozens of semi-flexible wire electrodes, usually fixed to rigid silicon grids that do not conform to the brain's shape.

In people with epilepsy, the arrays could be used to detect when seizures first begin, and deliver pulses to shut the seizures down. In people with spinal cord injuries, the technology has promise for reading complex signals in the brain that direct movement, and routing those signals to healthy muscles or prosthetic devices.

"The focus of our study was to make ultrathin arrays that conform to the complex shape of the brain, and limit the amount of tissue damage and inflammation," said Brian Litt, M.D., an author on the study and an associate professor of neurology at the University of Pennsylvania School of Medicine in Philadelphia. The silk-based implants developed by Dr. Litt and his colleagues can hug the brain like shrink wrap, collapsing into its grooves and stretching over its rounded surfaces.

The implants contain metal electrodes that are 500 microns thick, or about five times the thickness of a human hair. The absence of sharp electrodes and rigid surfaces should improve safety, with less damage to brain tissue. Also, the implants' ability to mold to the brain's surface could provide better stability; the brain sometimes shifts in the skull and the implant could move with it. Finally, by spreading across the brain, the implants have the potential to capture the activity of large networks of brain cells, Dr. Litt said.

Neural electrode array wrapped onto a model of the brain. The wrapping process occurs spontaneously, driven by dissolution of a thin, supporting base of silk. **C. Conway and J. Rogers, Beckman Institute**

Besides its flexibility, silk was chosen as the base material because it is durable enough to undergo patterning of thin metal traces for electrodes and other electronics. It can also be engineered to avoid inflammatory reactions, and to dissolve at controlled time points, from almost immediately after implantation to years later. The electrode arrays can be printed onto layers of polyimide (a type of plastic) and silk, which can then be positioned on the brain.

To make and test the silk-based implants, Dr. Litt collaborated with scientists at the University of Illinois in Urbana-Champaign and at Tufts University outside Boston. John Rogers, Ph.D., a professor of materials science and engineering at the University of Illinois, invented the flexible electronics. David Kaplan, Ph.D., and Fiorenzo Omenetto, Ph.D., professors of biomedical engineering at Tufts, engineered the tissue-compatible silk. Dr. Litt used the electronics and silk technology to design the implants, which were fabricated at the University of Illinoisecently, the team described a flexible silicon device for recording from the heart and detecting an abnormal heartbeat. In the current study, the researchers approached the design of a brain implant by first optimizing the mechanics of silk films and their ability to hug the brain. They tested electrode arrays of varying thickness on complex objects, brain models and ultimately in the brains of living, anesthetized animals.

The arrays consisted of 30 electrodes in a 5x6 pattern on an ultrathin layer of polyimide – with or without a silk base. These experiments led to the development of an array with a mesh base of polyimide and silk that dissolves once it makes contact with the brain – so that the array ends up tightly hugging the brain.

Next, they tested the ability of these implants to record the animals' brain activity. By recording signals from the brain's visual center in response to visual stimulation, they found that the ultrathin polyimide-silk arrays captured more robust signals compared to thicker implants.

In the future, the researchers hope to design implants that are more densely packed with electrodes to achieve higher resolution recordings.

"It may also be possible to compress the silk-based implants and deliver them to the brain, through a catheter, in forms that are instrumented with a range of high performance, active electronic components," Dr. Rogers said.

The study received support from NINDS, NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB), the U.S. Department of Energy's Division of Materials Sciences, the U.S. Army, the Defense Advanced Research Projects Agency (DARPA), and the Klingenstein Foundation.

Reference: Kim et al. "Dissolvable Films of Silk Fibroin for Ultrathin Conformal Bio-Integrated Electronics." Nature Materials, published online April 18, 2010.

Mat of microbes the size of Greece discovered on seafloor

By Katherine Harmon

Gargantuan whales and hefty cephalopods are typically thought of as the classic marine mammoths, but they might have to make way for the mighty microbes, which constitute 50 to 90 percent of the oceans' total biomass, according to newly released data.

These tiny creatures can join together to create some of the largest masses of life on the planet, and researchers working on the decade-long Census of Marine Life project found one such seafloor mat off the Pacific coast of South America that is roughly the size of Greece.

A single liter of seawater, once thought to contain about 100,000 microbes, can actually hold more than one billion microorganisms, the census scientists reported. But these small creatures don't just live in the water column or on the seafloor. Large communities of microscopic animals have even been discovered more than one thousand meters beneath the seafloor. Some of these deep burrowers, such as loriciferans, are only a quarter of a millimeter long.

"Far from being a lifeless desert, the deep sea rivals such highly diverse ecosystems as tropical rainforests and coral reefs," Pedro Martinez Arbizu, of the German Center for Marine Biodiversity Research and leader of the Census of the Diversity of Abyssal Marine Life, said in a prepared statement.

Thanks to high-throughput DNA sequencing, researchers have been able to vastly expand their catalogue of marine microbes. "Scientists are discovering and describing an astonishing new world of marine microbial diversity and abundance," Mitch Sogin, of the Marine Biological Laboratory in Woods Hole and leader of the International Census of Marine Microbes, said in a prepared statement.

Image of loricciferan Culexiregiloricus tricchisccalida, which was discovered off the coast of Africa some 4,100 meters below the surface last year through the census. **Gad/Marco Buntzow/German Center for Marine Biodiversity Research/Census of Marine Life**

This genetic data has revealed that there might be as many as 100 times more microbe genera than researchers had assumed. One study conducted in the English Channel landed 7,000 new genera alone.

Current estimates place the number of marine microbial species at about a billion, according to a prepared statement by John Baross of the University of Washington and chair of the International Census of Marine Microbes's scientific advisory council.

And research has yet to plumb the guts and surfaces of more macro ocean life, which, like humans, can play host to billions of microbial cells. The species living on and in "marine animals alone may account for hundreds of millions of microbial species," Baross said. "This is a huge frontier for the next decade."

Despite their small individual size, microbes play a big role in the oceans—and the planet overall. Microbes help to turn atmospheric carbon dioxide into usable carbon, completing about 95 percent of all respiration in the Earth's oceans. Even those deep in the seafloor, such as the deep-sea burrowers, "help oxygenate sediments and interact with microbes to cycle nutrients and carbon on the ocean floor." Arbizu said. But little is known about these creatures' susceptibility to the changes in ocean temperatures, dissolved gasses and acid levels that are predicted to occur with climate change.

"Tracking and visualizing such complex populations was impossible 10 years ago," Baross said. "Sequencing allows us to give the equivalent of an Internet URL to millions of microbes, to which we can attach all kinds of other information, like their favorite temperature and amount of salt and light."

The full findings of the census will be presented in October in London. For the coming decade Baross suggests a survey of marine viruses.