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Uninsured adolescents and young adults more likely to be diagnosed with advanced cancer

Study shows way forward for age group that has benefited least from cancer progress

ATLANTA –A new American Cancer Society study shows that uninsured adolescents and young adults were far more likely to be diagnosed with late-stage cancer, which is more difficult and expensive to treat and more deadly, compared to young patients with health insurance. The study, published early online, will appear in the March issue of the journal *CANCER*.

The study's authors says their data suggest a way forward for cancer control efforts in the adolescent and young adult (AYA) population, a group that has benefited the least from recent progress in cancer. "The findings suggest that policies such as the Affordable Care Act that increase the number of people in America with health coverage will result in fewer late-stage cancer diagnoses and save lives." For their study, researchers led by Anthony Robbins, M.D., Ph.D., American Cancer Society director of health services research, analyzed data from nearly 260,000 cancer patients ages 15 to 39 in the National Cancer Database.

After adjusting for age, race/ethnicity, facility type, ZIP code-based income and education levels, and U.S. Census region, it was found that uninsured males were 1.51 times more likely to be diagnosed at a distant stage of disease compared with patients with private insurance. Among females, the effect of insurance was even stronger, with uninsured patients found to be 1.86 times more likely to be diagnosed at a distant stage.

Uninsured patients were younger, more likely to be male, more likely to be black or Hispanic, more likely to reside in the South, more likely to be treated in teaching/research facilities, and less likely to be treated in NCI-designated facilities. Uninsured patients were also more likely to reside in ZIP codes with the lowest median income, as well as in ZIP codes with the highest percentage of residents without a high school diploma.

"We believe that this observation holds the promise of improved cancer control efforts in the AYA population, after decades in which AYA patients have experienced far less victory in the War on Cancer than their younger and older counterparts," conclude the authors. "However, the success of these efforts may be directly tied to the fate of the Medicaid expansion component of the Patient Protection and Affordable Care Act, which, at the time of this writing, remains quite unclear."

Article: Robbins, A. S., Lerro, C. C. and Barr, R. D. (2014), Insurance status and distant-stage disease at diagnosis among adolescent and young adult patients with cancer aged 15 to 39 years: National Cancer Data Base, 2004 through 2010. Cancer. doi: 10.1002/encr.28568 <http://onlinelibrary.wiley.com/doi/10.1002/encr.28568/abstract>

<http://www.bbc.co.uk/news/uk-scotland-glasgow-west-26322310>

Medics hail 'kidney swap' scheme after Scots success

Medics in Scotland have hailed the success of a kidney pairing scheme which allowed a gravely-ill woman to receive a transplant.

Sue Heathcote, 55, from Ayr, underwent the procedure to help her sister-in-law Claire, 41, to receive a new kidney. Under the scheme, kidneys are swapped between one incompatible donor and recipient and another mismatched pair. Transplant surgeon Marc Clancy said this was "extremely welcome" when there was a shortage of organs available. Mother-of-two, Claire Heathcote, has suffered from a form of kidney failure since birth. After a period of deteriorating health, she was told that a replacement kidney was the only option open to her.

'Altruistic donor'

Despite family members offering to help, no matches were found until Sue Heathcote registered for the kidney pairing scheme. Sue Heathcote said: "We did not get a match in our first run in October, or January or April 2013. "However, in July last year Claire got a call to say that we had matched. An altruistic donor had kindly donated to the pairing pool and their kidney matched with Claire. "I still had to agree to donate my kidney as the altruistic kidney was in the pool and therefore someone would still need mine."

The operation went ahead at the Western Infirmary in Glasgow on 27 September last year and both women are now back at work. Mrs Heathcote added: "It's made such a difference to Claire's life and I was so happy to do this as she is the type of person who would have done it for me."

Mr Clancy, who is lead clinician for transplant at NHS Greater Glasgow and Clyde, said the kidney pairing service was a welcome development when people were dying due to a lack of available organs.

He said: "Paired donation is when a donor and recipient are incompatible or mismatched with each other, either by blood group or by tissue type, it may be possible for them to be matched with another donor and recipient pair in the same situation and for the kidneys to be exchanged or swapped. "The benefit of this type of donation is that each recipient receives a transplant that they would otherwise not have."

<http://phys.org/news/2014-02-neanderthals-extinction-modern-humans-emerged.html>

Neanderthals may have faced extinction long before modern humans emerged

Western European Neanderthals were on the verge of extinction long before modern humans showed up
Western Europe has long been held to be the "cradle" of Neanderthal evolution, and anthropologists have theorized that climatic factors or competition from modern humans were the likely causes when Neanderthals started disappearing around 30,000 years ago. But new research suggests that Western European Neanderthals were on the verge of extinction long before modern humans showed up.

This perspective comes from a study of ancient DNA carried out by an international research team. Rolf Quam, a Binghamton University anthropologist, was a co-author of the study led by Anders Götherström at Uppsala University and Love Dalén at the Swedish Museum of Natural History, and published in the journal *Molecular Biology and Evolution*.

"The Neanderthals are our closest fossil relatives and abundant evidence of their lifeways and skeletal remains has been found at many sites across Europe and western Asia," said Quam, assistant professor of anthropology. "Until modern humans arrived on the scene, it was widely thought that Europe had been populated by a relatively stable Neanderthal population for hundreds of thousands of years. Our research suggests otherwise and, in light of these new results, this long-held theory now faces scrutiny."



Range of *Homo neanderthalensis*. Eastern and northern ranges may extend to include Okladnikov in Altai and Mamotnaia in Ural

Focusing on mitochondrial DNA sequences from 13 Neanderthal individuals, including a new sequence from the site of Valdegoba cave in northern Spain, the research team found some surprising results. When they started looking at the DNA, a clear pattern emerged. Neanderthal individuals from Western Europe that were older than 50,000 years and individuals from sites in western Asia and the Middle East showed a high degree of genetic variation, on par with what might be expected from a species that had been abundant in an area for a long period of time. In fact, the amount of genetic variation was similar to what characterizes modern humans as a species. In contrast, Neanderthal individuals from Western Europe that were younger than 50,000 years show an extremely reduced amount of genetic variation, less even than the present-day population of remote Iceland.

These results suggest that Western European Neanderthals went through a demographic crisis, a population bottleneck that severely reduced their numbers, leaving Western Europe largely empty of humans for a period of time. The demographic crisis seems to coincide with a period of extreme cold in Western Europe. Subsequently, this region was repopulated by a small group of individuals from a surrounding area. The geographic origin of this source population is not clear, but it may be possible to pinpoint it further with additional study.

"The fact that Neanderthals in Western Europe were nearly extinct, but then recovered long before they came into contact with modern humans came as a complete surprise to us," said Dalén, associate professor at the Swedish Museum of Natural History in Stockholm. "This indicates that the Neanderthals may have been more sensitive to the dramatic climate changes that took place in the last Ice Age than was previously thought." Quam concurs and suggests that this discovery calls for a major rethinking of the idea of cold adaptation in Neanderthals.

"At the very least, this tells us that without the aid of material culture or technology, there is a limit to our biological adaptation," Quam said. "It may very well have been the case that the European Neanderthal populations were already demographically stressed when modern humans showed up on the scene."

The results presented in the study are based entirely on degraded ancient DNA, and the analyses have therefore required advanced laboratory and computational methods. The research team includes statisticians, experts on modern DNA sequencing and paleoanthropologists from Sweden, Denmark, Spain and the United States.

"This is just the latest example of how studies of ancient DNA are providing new insights into an important and previously unknown part of Neanderthal history," Quam said. "Ancient DNA is complementary to anthropological studies focusing on the bony anatomy of the skeleton, and these kinds of results are only possible with ancient DNA studies. It's exciting to think about what will turn up next."

*More information: Love Dalén, Ludovic Orlando, Beth Shapiro, Mikael Brandström Durling, Rolf Quam, M. Thomas P. Gilbert, J. Carlos Díez Fernández-Lomana, Eske Willerslev, Juan Luis Arsuaga, and Anders Götherström. "Partial genetic turnover in neandertals: continuity in the east and population replacement in the west." *Mol Biol Evol.* first published online February 23, 2012 DOI: 10.1093/molbev/mss074*

http://www.eurekalert.org/pub_releases/2014-02/hfhs-mhc022414.php

Mental health conditions in most suicide victims left undiagnosed at doctor visits

Mental health condition of most people who commit suicide remain undiagnosed though many visit a primary care provider or medical specialist in the year before they die

DETROIT – The mental health conditions of most people who commit suicide remain undiagnosed, even though many visit a primary care provider or medical specialist in the year before they die, according to a national study led by Henry Ford Health System with the Mental Health Research Network.

Among those in the study, 83 percent received health care treatment in the year prior to dying, and they used medical and primary care services more frequently than any other health service. However, a mental health diagnosis was made in less than half (45 percent) of these cases. To help prevent suicides, health care providers should therefore become more attuned to their patients' mental health state and possible suicidal thoughts, concluded the study led by Brian K. Ahmedani, Ph.D., assistant scientist in the Center for Health Policy and Health Services Research at Henry Ford Health System in Detroit.

"Many suicides might be prevented, and a national suicide reduction goal may be met, if more primary care doctors and specialists receive and use training to identify and treat patients most at risk," says Dr. Ahmedani.

The study is published online in the Journal of General Internal Medicine.



VIDEO: The mental health conditions of most people who commit suicide remain undiagnosed, even though many visit a primary care provider or medical specialist in the year before they die, according to a national study led by Henry Ford Health System with the Mental Health Research Network. Among those in the study, 83 percent received health care treatment in the year prior to dying, and they used medical and primary care services more frequently than any other health service. However, a mental health diagnosis was made in less than half (45 percent) of these cases.

Henry Ford Health System

Suicide is the 10th leading cause of death in the U.S. and the No. 1 cause of injury-related death, recently topping motor vehicle deaths. It accounts for the loss of nearly 37,000 American lives each year, according to the Centers for Disease Control and Prevention. While previous research suggested that more suicides could be prevented, this study is currently the largest investigation of suicide and health services use.

Ahmedani and colleagues in the Mental Health Research Network studied the medical records of 5,894 health plan members in eight states who committed suicide between 2000 and 2010. This methodology provided data on the health care received by people who commit suicide prior to their deaths.

Of those seeking medical attention in the four weeks before they died, 25 percent were diagnosed with a mental health condition; one in every five people who committed suicide made a health care visit in the week before they died. In comparison, only 5 percent of people who committed suicide received psychiatric hospitalization, and 15 percent received such treatment in the year prior to committing suicide.

The largest number of suicides occurred among men. Among all suicides, 79 percent were by violent methods: 48.6 percent firearms; 22 percent hanging; 3.6 percent jumping; 2 percent sharp or blunt objects; 1.6 percent drowning; and 1.5 percent by other means. The remaining suicides studied were by non-violent means: 20.2 percent poisoning and 0.6 percent by other means.

Drilling deeper into the data, the researchers found that only about 25 percent of the suicides had a mental health diagnosis within a month of their deaths, and those most likely to seek medical treatment during the year before their suicides were women, ages 65 or older, and those who died by non-violent means.

Ahmedani says this study provides important information to help target future prevention in order to achieve the goals set forth in 2012 by the U.S. Surgeon General and the National Action Alliance for Suicide Prevention to reduce American suicides by 20 percent in five years.

"The data clearly told us that although a large proportion of those who committed suicide had health system contact in the year before their death, a mental health diagnosis was commonly absent," Dr. Ahmedani explains.

"Greater efforts need to be made to assess mental health and suicide risk."

"And because most visits occurred in primary care or medical specialty settings, suicide prevention in these clinics would likely reach the largest number of individuals."

Funding: National Institute of Mental Health; U19MH092201.

Participating members of the Mental Health Research Network included: Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit; Group Health Cooperative, Group Health Research Institute, Seattle; Kaiser Permanente Colorado, Institute for Health Research, Denver; Kaiser Permanente Hawaii, Center for Health Research, Honolulu; HealthPartners, Institute for Education and Research, Minneapolis; Kaiser Permanente Northwest, Center for Health Research, Portland; Kaiser Permanente Georgia, Center for Health Research, Atlanta; Kaiser Permanente Northern California, Division of Research, Oakland; Department of Psychiatry, Henry Ford Health System, Detroit.

http://www.eurekalert.org/pub_releases/2014-02/ru-ahp022414.php

Acupuncture holds promise for treating inflammatory disease

Rutgers-led study suggests pathways to alleviating inflammation in disorders such as sepsis, arthritis

When acupuncture first became popular in the western hemisphere it had its doubters. It still does. But over time, through detailed observation, scientists have produced real evidence that ancient Chinese practitioners of the medical arts were onto something.

Now new research documents a direct connection between the use of acupuncture and physical processes that could alleviate sepsis, a condition that often develops in hospital intensive care units, springs from infection and inflammation, and takes an estimated 250,000 lives in the United States every year.

"Sepsis is the major cause of death in the hospital," says Luis Ulloa, an immunologist at Rutgers New Jersey Medical School who led the study, which has been published by the journal *Nature Medicine*. "But in many cases patients don't die because of the infection. They die because of the inflammatory disorder they develop after the infection. So we hoped to study how to control the inflammatory disorder."

The researchers already knew that stimulation of one of the body's major nerves, the vagus nerve, triggers processes in the body that reduce inflammation, so they set out to see whether a form of acupuncture that sends a small electric current through that and other nerves could reduce inflammation and organ injury in septic mice. Ulloa explains that increasing the current magnifies the effect of needle placement, and notes that electrification is already FDA-approved for treating pain in human patients.

When the electroacupuncture was applied to mice with sepsis, molecules called cytokines that help limit inflammation were stimulated as predicted, and half of those mice survived for at least a week. There was zero survival among mice that did not receive acupuncture.

Ulloa and his team then probed further, to figure out exactly why the acupuncture treatments had succeeded. And they made a discovery that, on its face, was very disappointing. They found that when they removed adrenal glands – which produce hormones in the body – the electroacupuncture stopped working. That discovery, on its face, presented a big roadblock to use of acupuncture for sepsis in humans, because most human cases of sepsis include sharply reduced adrenal function. In theory, electroacupuncture might still help a minority of patients whose adrenal glands work well, but not many others.

So the researchers dug even deeper – to find the specific anatomical changes that occurred when electroacupuncture was performed with functioning adrenal glands. Those changes included increased levels of dopamine, a substance that has important functions within the immune system. But they found that adding dopamine by itself did not curb the inflammation. They then substituted a drug called fenoldopam that mimics some of dopamine's most positive effects, and even without acupuncture they succeeded in reducing sepsis-related deaths by 40 percent.

Ulloa considers the results a double triumph.

On the one hand, he says, this research shows physical evidence of acupuncture's value beyond any that has been demonstrated before. His results show potential benefits, he adds, not just for sepsis, but treating other inflammatory diseases such as rheumatoid arthritis, osteoarthritis and Crohn's disease.

On the other hand, by also establishing that a drug reduced sepsis deaths in mice, he has provided an innovative roadmap toward developing potential drugs for people. That roadmap may be crucial, because no FDA-approved drug to treat sepsis now exists. "I don't even know whether in the future the best solution for sepsis will be electroacupuncture or some medicine that will mimic electroacupuncture," Ulloa concludes. The bottom line, he says, is that this research has opened the door to both.

Funding sources included the National Institutes of Health (grant RO1-GM084125) and the Mexican National Council for Science and Technology.

http://www.eurekalert.org/pub_releases/2014-02/wch-por022414.php

Preventive oophorectomy reduces risk of death by 77 percent for women with BRCA mutation

Women who carry a BRCA gene mutation and opt for preventive ovary removal surgery, have a 77 per cent lower risk of death than those who do not

TORONTO, ON - Women who carry a BRCA gene mutation and opt for a preventive oophorectomy, or ovary removal surgery, have a 77 per cent lower risk of death than those who do not, according to a new study led by Women's College Hospital's Amy Finch and Dr. Steven Narod.

Research has long shown that preventive oophorectomy reduces the risks of ovarian and breast cancers in women with a BRCA gene mutation, but the best age for women to have the surgery and its impact on mortality has not been well studied. The findings by Finch and colleagues, published today in the *Journal of Clinical*

Oncology, are the first to look at these effects among a large cohort of women over a nearly six-year followup period.

"Scientific evidence clearly shows removal of a woman's ovaries and fallopian tubes is very effective in preventing both breast and ovarian cancer in women with a BRCA mutation," said Finch, a researcher at Women's College Research Institute and the study's lead author. "But the real question has been at what age these women should have the surgery to best diminish their chance of developing cancer."

In the study, researchers evaluated the effect of a preventive oophorectomy in reducing death and the risk of ovarian, fallopian tube or peritoneal cancer in 5,783 women with a BRCA gene mutation. They found the surgery was associated with:

An 80 per cent reduction in the risk of ovarian, fallopian and peritoneal cancer

A 77 per cent lower risk of death from all causes and

A 68 per cent lower risk of death from all causes in women who previously had breast cancer

"Our study supports the notion that women who carry a BRCA gene mutation will have a much lower risk of developing or dying from cancer if they have an oophorectomy at age 35," said Dr. Steven Narod, a co-author of the study and senior scientist at Women's College Research Institute. "If a woman with a BRCA1 mutation opts to delay the surgery until age 40 or 50, her chance of developing ovarian, fallopian tube or peritoneal cancers jumps to 4 and 14.2 per cent, respectively."

While oophorectomy is a safe procedure, it can carry some complications, including premature menopause.

"After an oophorectomy, the long-term effects on a woman's cardiovascular health and her bone health are less well known, and further research is needed," Finch added.

Finch and Dr. Narod, along and colleagues from Women's College Hospital and the University Health Network, are now examining these potential impacts in a new study to gain a better understanding of the risks of a preventive oophorectomy for women with a BRCA mutation.

While the decision to undergo oophorectomy is life altering, particularly for young women, these findings showing the clear benefit of this surgery on cancer risk and mortality and will strengthen the recommendation for this surgery, the researchers said.

http://www.eurekalert.org/pub_releases/2014-02/d-ssa022014.php

Study shows association between diabetes and stroke in women but not men

Research shows that diabetes in women is associated with an increased risk of stroke, whereas the data do not show the same association among men

New research published in *Diabetologia* (the journal of the European Association for the Study of Diabetes) shows that diabetes in women is associated with an increased risk of stroke, whereas the data do not show the same association among men. The research is by Dr Wenhui Zhao (the first author), Dr Gang Hu and colleagues at the Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.

Differences in incidence and mortality between sexes have been reported for various conditions, including stroke. More women than men tend to die from stroke in developed countries. For example, in the USA, 77,109 women and 52,367 men died from stroke in 2010. Women accounted for almost 60% of US stroke deaths in 2010. In the UK, 32,828 women and 20,358 men died from stroke in 2007.

The authors prospectively investigated the sex-specific association of different levels of HbA1c with incident stroke risk among 10,876 male and 19,278 female patients with type 2 diabetes in the Louisiana State University Hospital-Based Longitudinal Study (LSUHLS). During a mean follow up of 6.7 years, 2,949 incident cases of stroke were identified. The authors calculated the risk of stroke associated with different levels of HbA1c at baseline (<6.0%, 6.0- 6.9% [reference group, considered normal blood sugar control], 7.0-7.9%, 8.0- 8.9%, 9.0-9.9%, and $\geq 10.0\%$). Among men, although there was a trend towards increased risk of stroke as HbA1c increased, this increased risk was not statistically significant. Among women, however, those with HbA1c of 8.0-8.9% were 19% more likely to have a stroke than the normal blood sugar reference group women; those with 9.0-9.9% HbA1c were 32% more likely to have a stroke, and those above 10% HbA1c were 42% more likely to have a stroke, with each of these associations statistically significant.

Even when the data were adjusted by race, and whether or not anti-diabetic drugs were used by the women, this graded association of HbA1c with stroke in women was still present. When adjusted by age, the researchers found the risk of stroke among diabetic women was substantially raised for women aged 55 years and over compared with younger women.

Worldwide, stroke is more common among men, but women with stroke appear to become more severely ill following a stroke. These sex differences have profound implications for effective prevention and treatment of stroke. Thus the increased knowledge of stroke risk factors in the population, such as that provided by this study, may lead to improved prevention of stroke.

"Several mechanisms could explain why diabetes has a greater adverse effect in women than in men. In the general population, higher numbers of strokes occurring among women than men is at least partly attributed to the longer life expectancy of women," explains Dr Zhao. "Some studies have suggested that the sex difference in cardiovascular risk is mediated in large part by differences in the levels of cardiovascular risk factors because women with diabetes have significantly higher levels of blood pressure and lipids than men with diabetes. Others suggested that the greater risk associated with diabetes seen in women may reflect a treatment bias that favours men. Recent studies found that men with diabetes or established cardiovascular disease are more likely to receive aspirin, statins, or antihypertensive drugs than women."

Referring to the increased risk of stroke in diabetic women aged 55 years and over, Dr Hu says: "This might suggest that poor blood glucose control is more harmful in elderly women than in younger ones. The possible explanation may point to the role for oestrogen. After onset of menopause, when oestrogen levels decline, the incidence of cerebrovascular disease in women increases. Pre-clinical (animal) studies have indicated that oestrogen is neuroprotective and reduces stroke infarct volume, but clinical trials failed to show the benefit. There is a need for more research to clarify this association." He also adds that the lack of an association between HbA1c and stroke risk in men with type 2 diabetes in the present study could be due to men with higher HbA1c values dying from coronary heart disease, rather than having a stroke.

Dr Hu concludes: "Diabetes poses a substantially greater increase in the risk of stroke among women than among men which merits further investigation. This graded positive association was more significant in women 55 years and older than in women younger than 55 years. Females with type 2 diabetes, especially postmenopausal females, are at high risk for stroke. More aggressive blood sugar treatments and better control of other risk factor levels in women with diabetes are likely to substantially reduce stroke in this subgroup."

http://www.eurekalert.org/pub_releases/2014-02/miot-apd022414.php

A paper diagnostic for cancer

Simple, cheap, paper test could improve diagnosis rates and help people get treated earlier

CAMBRIDGE, MA -- Cancer rates in developing nations have climbed sharply in recent years, and now account for 70 percent of cancer mortality worldwide. Early detection has been proven to improve outcomes, but screening approaches such as mammograms and colonoscopy, used in the developed world, are too costly to be implemented in settings with little medical infrastructure.

To address this gap, MIT engineers have developed a simple, cheap, paper test that could improve diagnosis rates and help people get treated earlier. The diagnostic, which works much like a pregnancy test, could reveal within minutes, based on a urine sample, whether a person has cancer. This approach has helped detect infectious diseases, and the new technology allows noncommunicable diseases to be detected using the same strategy.

The technology, developed by MIT professor and Howard Hughes Medical Institute investigator Sangeeta Bhatia, relies on nanoparticles that interact with tumor proteins called proteases, each of which can trigger release of hundreds of biomarkers that are then easily detectable in a patient's urine.

"When we invented this new class of synthetic biomarker, we used a highly specialized instrument to do the analysis," says Bhatia, the John and Dorothy Wilson Professor of Health Sciences and Technology and Electrical Engineering and Computer Science. "For the developing world, we thought it would be exciting to adapt it instead to a paper test that could be performed on unprocessed samples in a rural setting, without the need for any specialized equipment. The simple readout could even be transmitted to a remote caregiver by a picture on a mobile phone."

Bhatia, who is also a member of MIT's Koch Institute for Integrative Cancer Research and Institute for Medical Engineering and Science, is the senior author of a paper describing the particles in the Proceedings of the National Academy of Sciences the week of Feb. 24. The paper's lead authors are graduate student Andrew Warren, postdoc Gabriel Kwong, and former postdoc David Wood.

Amplifying cancer signals

In 2012, Bhatia and colleagues introduced the concept of a synthetic biomarker technology to amplify signals from tumor proteins that would be hard to detect on their own. These proteins, known as matrix metalloproteinases (MMPs), help cancer cells escape their original locations by cutting through proteins of the extracellular matrix, which normally holds cells in place.

The MIT nanoparticles are coated with peptides (short protein fragments) targeted by different MMPs. These particles congregate at tumor sites, where MMPs cleave hundreds of peptides, which accumulate in the kidneys and are excreted in the urine.

In the original version of the technology, these peptides were detected using an instrument called a mass spectrometer, which analyzes the molecular makeup of a sample. However, these instruments are not readily available in the developing world, so the researchers adapted the particles so they could be analyzed on paper, using an approach known as a lateral flow assay - the same technology used in pregnancy tests.

To create the test strips, the researchers first coated nitrocellulose paper with antibodies that can capture the peptides. Once the peptides are captured, they flow along the strip and are exposed to several invisible test lines made of other antibodies specific to different tags attached to the peptides. If one of these lines becomes visible, it means the target peptide is present in the sample. The technology can also easily be modified to detect multiple types of peptides released by different types or stages of disease.

In tests in mice, the researchers were able to accurately identify colon tumors, as well as blood clots. Bhatia says these tests represent the first step toward a diagnostic device that could someday be useful in human patients. "This is a new idea - to create an excreted biomarker instead of relying on what the body gives you," she says. "To prove this approach is really going to be a useful diagnostic, the next step is to test it in patient populations."

Developing diagnostics

To help make that happen, the research team recently won a grant from MIT's Deshpande Center for Technological Innovation to develop a business plan for a startup that could work on commercializing the technology and performing clinical trials. Bhatia says the technology would likely first be applied to high-risk populations, such as people who have had cancer previously, or had a family member with the disease. Eventually, she would like to see it used for early detection throughout developing nations.

Such technology might also prove useful in the United States, and other countries where more advanced diagnostics are available, as a simple and inexpensive alternative to imaging. "I think it would be great to bring it back to this setting, where point-of-care, image-free cancer detection, whether it's in your home or in a pharmacy clinic, could really be transformative," Bhatia says.

With the current version of the technology, patients would first receive an injection of the nanoparticles, then urinate onto the paper test strip. To make the process more convenient, the researchers are now working on a nanoparticle formulation that could be implanted under the skin for longer-term monitoring.

The team is also working to identify signatures of MMPs that could be exploited as biomarkers for other types of cancer, as well as for tumors that have metastasized.

The research was funded by a National Science Foundation Graduate Research Fellowship, a Mazumdar-Shaw International Oncology Fellowship, the Ruth L. Kirschstein National Research Service Award from the National Institutes of Health, the Burroughs Wellcome Fund, the National Cancer Institute, and the Howard Hughes Medical Institute.

http://www.eurekalert.org/pub_releases/2014-02/cifa-mac022314.php

Marine algae can sense the rainbow

Study shows that algae can detect a wide spectrum of colors to adapt to their environments

A new study published in Proceedings of the National Academy of Sciences has shown for the first time that several types of aquatic algae can detect orange, green and blue light.

Land plants have receptors to detect light on the red and far red of the spectrum, which are the common wavelengths in the air. These plants sense the light to move and grow as their environment changes, for example when another plant shades them from the sun. But in the ocean, the water absorbs red wavelengths, instead reflecting colours such as blue and green. As part of the study, a team of researchers including Canadian Institute for Advanced Research (CIFAR) Senior Fellow Alexandra Worden sequenced about 20 different marine algae and found they were capable of detecting not only red light, but also many other colours. Collaborators in the lab of J. Clark Lagarias performed the biochemical analyses that established the wavelength detection.

"It's an amazing innovation of these algae to sense the whole rainbow," says Dr. Worden, who leads a microbial ecology research group at Monterey Bay Aquarium Research Institute in California. She is a member of CIFAR's Integrated Microbial Biodiversity program, which uses interdisciplinary research to study how a diversity of microbial life shapes all ecosystems. Her lab selected and grew the algae for sequencing in a collaborative effort with CIFAR Fellow Adrián Reyes-Prieto, who she first met at the Institute's program meetings. They specifically targeted diverse but largely unstudied organisms that might reveal new evolutionary insights into photosynthetic organisms. The Gordon and Betty Moore Foundation accepted sequencing nominations from Dr. Worden and provided sequencing funds in support of understanding eukaryotic algae.

"The phytoplankton in the oceans are, of course, really important to regulating our climate, and we just never knew that they were able to sense our environment in this way," she says.

Dr. Worden says her collaborators are interested in understanding the origins of photosynthetic life, in part because it played a crucial role in allowing other life forms, including humans, to exist. The research could also help with food production by teaching us ways to engineer crops so they will grow in many light conditions.

This article will be available at: <http://www.pnas.org/cgi/doi/10.1073/pnas.1401871111>.

Authors on this paper include Nathan C. Rockwell, Deqiang Duanmu, Shelley S. Martin, Charles Bachy, Dana C. Price, Debashish Bhattacharya, Alexandra Z. Worden, and J. Clark Lagarias.

<http://arstechnica.com/science/2014/02/artificial-muscles-made-with-fishing-line/>

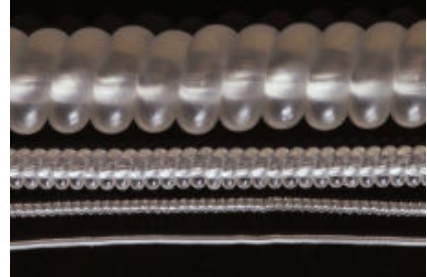
Artificial muscles made with fishing line

With the proper treatment, common materials contract with heat treatment.

by Yogi Patel Feb 25 2014, 2:10am TST

Take a rubber band and twist it. Keep twisting it until it starts to collapse onto itself and form larger loops - it's something you can do with almost any strand-like structure. Now, scientists from the University of Texas at Dallas in Richardson are taking advantage of this property in everyday materials such as fishing line and sewing thread and using it to make artificial muscles.

The scientists took pieces of fiber that were a few hundred micrometers long and twisted them until they began to coil. As the pieces coiled, the twisted fibers became shorter and thicker; once tightly coiled, the scientists heat-treated them to prevent the fibers from unfolding. If heat is applied to the finished coil after this procedure, the individual fibers try to untwist. The untwisting causes the coils to expand in volume as they shorten in length, just like a muscle.



Fishing line of different diameters, formed into the coiled-coils used in these experiments. Science/AAAS

The researchers found that if they made the fiber form larger coils in the same direction as the initial twists, the fibers contracted. If the fibers were made to coil in the opposite direction from the twist, the fibers expanded. By combining large quantities of these twisted fibers, the team could produce artificial muscles with above-average characteristics.

Fishing line muscles in action.

In their study, the scientists compared their artificial muscles to natural ones. Biological muscles contract to only about 20 percent of their length, while these artificial muscles contract to over 50 percent of their length. In addition, the synthetic versions can lift loads over 100 times heavier than human muscles of the same length and weight can handle. The twisted fibers can generate over 5 kilowatts of mechanical work per kilogram of muscle weight, which is similar to the output of a jet engine.

These are not the first artificial muscles to have been created, but they are among the first that are inexpensive and store large amounts of energy. The team that developed them believes the heat-dependent contraction, low cost, and the ability to store large amounts of energy make these fibers ideal candidates for a huge range of applications, including medical devices, clothing, prosthetic limbs, and even home automation. Some day, your blinds may open and close on their own as coiled fibers respond to the weather.

Science, 2014. DOI: 10.1126/science.1246906 (About DOIs).

<http://bit.ly/1o2NKrO>

Toilet? Planter? Urinal uses bamboo to deal with waste

Uses biofilters – plants in a growing medium – to treat urine

18:20 24 February 2014 by Christopher Weber

It is almost impossible to find a public toilet in the US – and that creates problems. When desperate people pee in doorways and alleys, it offends residents and drives customers away from local businesses.

Enter the PPlanter, a public urinal with an ecological twist. It uses biofilters – plants in a growing medium – to treat urine. Easy to move, it consumes less water than the average toilet and sink, while avoiding the harsh chemicals of conventional portable toilets. On top of all of that, its inventors claim it is odour-free.

The small booth of the PPlanter is not just for men: disposable funnels allow women to use the PPlanter standing up. The treatment process begins once the user washes their hands at a built-in sink. A foot pump pushes clean water through a faucet. The rinse water does double duty by flushing the urinal.

The water and urine empty into an air-tight tank; without exposure to air, urine does not produce malodorous ammonia. The liquids are pumped into a pallet-sized biofilter that is lightweight and movable, containing bamboo, wood chips, straw, rock and pectin-coated styrofoam. The bamboo takes up the water as well as nutrients in the urine, including nitrogen and phosphorus. Bacteria break down protein and carbohydrates. That leaves only salts.

Unconventional relief

The PPlanter was designed and built by the Hyphae Design Laboratory of Oakland, California. The idea was to reduce public urination while challenging people to rethink conventional plumbing. "Our goal is to refocus attention to developing ecological sanitation, making it aesthetically pleasing, clean, functional, and cool," says lab founder Brent Bucknum.

Last year, Bucknum and his staff tested the PPlanter in a crowded San Francisco neighbourhood. It stood up well to heavy use and has relieved as many as 300 people over an 8-hour period. Now the city has ordered a permanent one with two urinals and a composting toilet. With proper maintenance, it should last 10-15 years. Additionally, Bucknum plans to rent PPlanters for festivals and events. Bucknum hopes that international development agencies will be interested in installing PPlanters in nations lacking sewer infrastructure. But there is also a potential market close at hand, in dense neighbourhoods like those of San Francisco.

"The PPlanter is lower cost and lower maintenance than any other kind of toilet," says Darryl Smith, co-director of the Luggage Store Gallery in the city's Tenderloin neighbourhood. An outdoor portion of the gallery hosted a PPlanter for three months during testing, and he hopes to get one permanently. "The openness of the design keeps people from taking over these toilets to do drugs or other unhealthy things. It makes it safer."

<http://www.medscape.com/viewarticle/821006?src=rss>

Prenatal Acetaminophen Linked to Behavioral Problems in Kids

Prenatal exposure to acetaminophen — a drug considered safe in pregnancy — may raise the risk for behavioral problems in children, including attention-deficit/hyperactivity disorder (ADHD) and hyperkinetic disorder (HKD), a severe form of ADHD, new research suggests.

Megan Brooks

"Because the exposure and outcomes are frequent, these results are of public health relevance," the investigators write. The findings "should inspire much more research and a cautious use of these drugs during pregnancy; they should only be taken when they are really needed," study investigator Jørn Olsen, MD, PhD, of the Institute of Public Health, University of Aarhus, Denmark, told Medscape Medical News. The study was published online February 24 in JAMA Pediatrics.

Hormone Disrupter?

The premise of the study was that acetaminophen may act as a hormone disrupter and thus alter fetal brain development. Dr. Olsen and colleagues analyzed data on 64,322 children and their mothers enrolled in the Danish National Birth Cohort (1996 - 2002). Acetaminophen use during pregnancy was assessed during pregnancy and 6 months after childbirth.

More than half of the women (56%) reporting using acetaminophen during pregnancy. Children with prenatal exposure to acetaminophen were at higher risk of being diagnosed with HKDs, using ADHD medications, or having ADHD-like behaviors.

For all outcomes, stronger effects were seen among children exposed to acetaminophen during more than 1 trimester and among those exposed for a greater number of weeks (P trend < .001).

Outcome	Hazard Ratio	95% CI
<i>HKD</i>	<i>1.37</i>	<i>1.19 - 1.59</i>
<i>ADHD medication use</i>	<i>1.29</i>	<i>1.15 - 1.44</i>
<i>ADHD-like behavior</i>	<i>1.13</i>	<i>1.01 - 1.27</i>
CI, confidence interval		

The results did not appear to be confounded by maternal inflammation or infection during pregnancy, mother's mental health problems, or any of a number of other factors evaluated, the investigators report. However, they add that they cannot rule out residual confounding by genetic factors, unmeasured maternal psychopathology, exposure to other medications, or indication for drug use.

Interpret With Caution

Acetaminophen can cross the placenta barrier, and recent studies have suggested that maternal use of acetaminophen increases the risk for cryptorchidism in boys, owing to its endocrine-disrupting properties, the investigators note in their article.

"Maternal hormones, such as sex hormones and thyroid hormones, play critical roles in regulating fetal brain development, and it is possible that acetaminophen may interrupt brain development by interfering with maternal hormones or via neurotoxicity such as the induction of oxidative stress that can cause neuronal death," the researchers write.

If the current observations reflect causal associations, "acetaminophen should no longer be considered a safe drug for use in pregnancy," Dr. Olsen and colleagues conclude.

But the authors of an editorial published with the study emphasize that "causation cannot be inferred from the present observed associations" and that a replication study is needed.

For now, these "interesting" observations "should be interpreted cautiously and should not change practice," write Miriam Cooper, MRCPsych, of the Institute of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, United Kingdom, and coauthors.

The findings "underline the importance of not taking a drug's safety during pregnancy for granted, and they provide a platform from which to conduct further related analyses exploring a potential relationship between acetaminophen use and altered neurodevelopment," they write.

The study was supported by the Danish Medical Research Council. One author on the study who contributed to the study when she was at University of Arizona currently works at Novartis Farmaceutica SA, Barcelona, Spain. No other disclosures were reported. *JAMA Pediatr.* Published online February 24, 2014.

<http://news.discovery.com/space/alien-life-exoplanets/advanced-exoplanet-hunter-images-alien-worlds-140224.htm#mkcpgn=rssnws1>

Advanced Exoplanet Hunter Images Alien Worlds

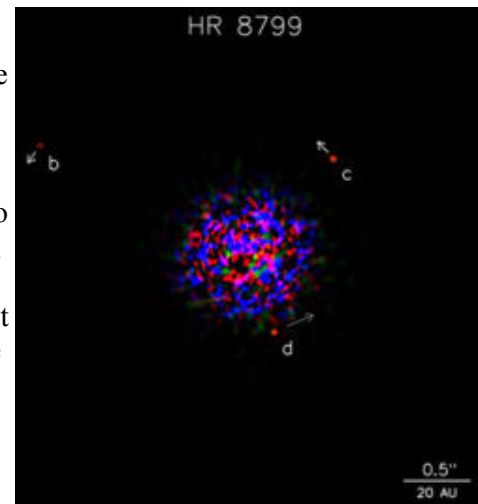
A planet-hunting project is snapping pictures of alien worlds and other objects orbiting nearby stars in an effort to give scientists a better understanding of these intriguing exoplanets.

Feb 24, 2014 04:04 PM ET // by Miriam Kramer, SPACE.com

Project 1640 is designed to probe the atmospheres of exoplanets to create new, low-resolution images of the planets and their stars. By understanding the atmosphere of the planets and the composition of the stars, scientists working with the project could potentially learn more about how they formed.

Scientists working with Project 1640 - an imaging system at the Palomar Observatory in California - are using the specialized system to survey about 200 stars looking for a range of planets and other objects, project scientist Ben Oppenheimer said at the American Museum of Natural History event on Feb. 5. According to AMNH officials, Project 1640 is "the most advanced and highest contrast imaging system in the world."

"The planets of our own solar system, of course, are planets in and of themselves and in order to understand them - and indeed this planet - I think we need to study other planets," Oppenheimer said. "If you just look at the planets of our own solar system, they're really complicated."



This image shows the star HR8799 in infrared light, along with three of its four alien planets larger than Jupiter. The star is 127 light-years from Earth. Christian Marois and Bruce Macintosh

The project is designed to help space scientists get a better sense of the diversity of planets that exist in the universe. Scientists are also looking for mysterious cosmic objects known as brown dwarfs that are too large to be considered a planet, but too small to produce fusion in their cores.

Different chemicals, like carbon dioxide, absorb light differently, allowing scientists working with Project 1640 to take measurements and see where various signatures fall on the spectra.

Oppenheimer and his colleagues using Project 1640 have already peered into the atmospheres of four cloud-covered alien planets around the star HR 8799, 127 light-years from Earth. All four of the planets are more massive than Jupiter and display some odd characteristics. "These warm, red planets are unlike any other known object in our universe," Oppenheimer said in a statement announcing the discovery in 2013. "All four planets have different spectra, and all four are peculiar. The theorists have a lot of work to do now."

The scientists found that all four of the planets' atmospheres had either ammonia or methane, but not both. This is odd because the alien worlds are somewhat warm at about 1340 degrees Fahrenheit (727 degrees Celsius).

With that temperature, scientist would expect to see both methane and ammonia mingling in their atmospheres. Project 1640 observations are ongoing and are expected to last for three years.

<http://www.bbc.co.uk/news/health-26323720>

Cooking meat 'may be dementia risk'

Browning meat in the oven, grill or frying pan produces chemicals which may increase the risk of developing dementia, US researchers suggest.

Advanced glycation end (AGE) products have been linked to diseases such as type-2 diabetes. Mice fed a high-AGEs diet had a build-up of dangerous proteins in the brain and impaired cognitive function. Experts said the results were "compelling" but did not provide "definitive answers". AGEs are formed when proteins or fats react with sugar. This can happen naturally and during the cooking process. Researchers at the Icahn school of medicine at Mount Sinai, in New York, tested the effect of AGEs on mice and people.

The animal experiments, published in Proceedings of the National Academy of Sciences, showed that a diet rich in AGEs affects the chemistry of the brain. It leads to a build-up of defective beta amyloid protein - a hallmark of Alzheimer's disease. The mice eating a low-AGEs diet were able to prevent the production of damaged amyloid. The mice performed less well in physical and thinking tasks after their AGEs-rich diet. A short-term analysis of people over 60 suggested a link between high levels of AGEs in the blood and cognitive decline.

'Effective treatment'

The study concluded: "We report that age-related dementia may be causally linked to high levels of food advanced glycation end products. "Importantly, reduction of food-derived AGEs is feasible and may provide an effective treatment strategy."

Derek Hill, a professor of medical imaging sciences at University College London, commented: "The results are compelling. "Because cures for Alzheimer's disease remain a distant hope, efforts to prevent it are extremely important, but this study should be seen as encouraging further work, rather than as providing definitive answers. "But it is grounds for optimism - this paper adds to the body of evidence suggesting that using preventative strategies might reduce the prevalence of Alzheimer's disease and other dementias in society and that could have very positive impact on us all."

Dr Simon Ridley, from the charity Alzheimer's Research UK, said: "Diabetes has previously been linked to an increased risk of dementia, and this small study provides some new insight into some of the possible molecular processes that may link the two conditions. "It's important to note that the people in this study did not have dementia. This subject has so far not been well studied in people, and we don't yet know whether the amount of AGEs in our diet might affect our risk of dementia."

http://www.eurekalert.org/pub_releases/2014-02/asfm-mvw022014.php

MERS virus widespread in Saudi Arabian camels

Coronavirus has been infecting the animals for at least 20 years

The coronavirus responsible for Middle East Respiratory Syndrome (MERS) is prevalent in camels throughout Saudi Arabia and has been around for at least 20 years, according to a study to be published on February 25 in mBio®, the online open-access journal of the American Society for Microbiology.

"Our study shows the MERS coronavirus (MERS-CoV) is widespread," says senior study author W. Ian Lipkin of Columbia University, New York. "Adult camels were more likely to have antibodies to the virus while juveniles were more likely to have active virus. This indicates that infection in camels typically occurs in early life, and that if people get the virus from camels the most likely source is young camels."

MERS, a serious viral respiratory illness, has been identified in 182 people from 2012 through Feb. 7, according to the World Health Organization; 79 people have died from the condition. While most infections have occurred in Saudi Arabia, the origin of disease, in most cases, has remained unknown. Efforts to identify an animal source of infection have focused on bats and camels. The first known case of MERS was in a Saudi Arabian man who had four pet camels.

In the study, investigators from the United States and Saudi Arabia conducted a comprehensive survey of dromedary camels throughout Saudi Arabia. They collected blood samples and rectal and nasal swabs from camels, sheep and goats in November and December of 2013. Using mobile laboratory equipment, they tested blood samples for antibodies reactive with MERS-CoV, and the swabs and blood for active virus. They also analyzed archived blood samples from dromedary camels taken from 1992 through 2010.

Overall, 74% of camels sampled countrywide had antibodies to MERS-CoV. More than 80% of adult camels throughout the country had antibodies to the virus, while in camels age two or younger the prevalence ranged from 90% in the east to 5% in the southwest. Antibodies to the virus were seen in camel serum samples dating back to 1992, which strongly suggests that either MERS-CoV or a closely related virus has been circulating in the Saudi Arabian animals for at least two decades.

The researchers also found that active virus was frequently detected in nasal swabs in 35% of young camels and 15% of adult camels countrywide. It was less frequently found in rectal swabs and not in blood, indicating that the virus most likely is spread by respiratory secretions.

While they speculate that camels are potential reservoirs for human transmission, the authors say the current study does not prove that. "Our findings suggest that continuous, longer-term surveillance will be necessary to determine the dynamics of virus circulation in dromedary camel populations."

Lead authors for the paper were Abdulaziz Alagaili of King Saud University and the Saudi Wildlife Authority in Riyadh and Thomas Briese of Columbia University.

http://www.eurekalert.org/pub_releases/2014-02/wuso-sff022414.php

Stand-alone facility for organ retrieval is more efficient, less costly than hospital

Retrieving organs from brain-dead donors is logistically challenging and time consuming in hospitals.

Multiple surgical teams often fly to a donor's hospital but frequently face delays in retrieving organs due to crowded operating-room schedules. However, a new study shows that moving organ donors from hospitals to a regional stand-alone facility with a designated operating room for retrieving organs is more efficient and lowers costs considerably, according to new research by transplant surgeons at Washington University School of Medicine in St. Louis. The research is published Feb. 25 in the American Journal of Transplantation.

"The magnitude of these changes has been transformative, with no negative effects on the organ donation process," said the study's first author, M.B. Majella Doyle, MD, a Washington University liver transplant surgeon at Barnes-Jewish Hospital, who also directs the adult liver transplant program. "This approach of moving organ donors to a free-standing organ recovery center is one that we believe has great merit and could be implemented more broadly."

Historically, transplant teams have traveled to donors' hospitals, often at night, when operating rooms are more likely to be available, to perform time-sensitive surgeries. And typically they are assisted by local staff who are not always familiar with organ donation procedures.

To improve the organ donation process, Mid-America Transplant Services in 2001 built the nation's first stand-alone organ retrieval facility in St. Louis, a few miles from transplant centers at Washington University School of Medicine and Saint Louis University. The nonprofit organization coordinates organ donations and retrievals for eastern Missouri, southern Illinois and northeast Arkansas.

After patients are declared brain dead and families consent to organ donation, donors in areas covered by Mid-America Transplant are transported to the stand-alone facility either by ambulance, if the hospitals are within an 80-mile radius, or by air. The organization owns an airplane that can accommodate mechanical ventilators and other equipment needed to keep donors' bodies stable.

Surgical teams still must travel to the facility to retrieve donor organs, but they do not need to scramble for an open operating room. The operating room at the facility, which is primarily used by Washington University and Saint Louis University surgeons, can be scheduled as soon as a donor is available, so surgeons and patients' families all know what to expect.

"Organ donors often are given low priority in hospitals because of scheduled surgeries or emergency cases," explained the study's senior author, William C. Chapman, MD, the Eugene M. Bricker Chair of Surgery and surgical director of the Washington University transplant center at Barnes-Jewish Hospital. "In addition to the cost savings, we rarely encounter delays anymore, making organ donation easier on families who have lost loved ones and on transplant teams because we can know when donors' surgeries will take place." The facility also is staffed by critical care nurses and other personnel who have expertise and training in organ donation. As part of the study, the researchers analyzed 915 liver transplants performed at Barnes-Jewish Hospital during a 10-year period from 2001 through 2011, looking at where the organs were procured. In the first year, 36 percent (9/25) were retrieved at Mid-America Transplant Services, gradually increasing to 93 percent (56/60) during the last year of the analysis.

By 2011, the average cost of retrieving a liver had dropped 37 percent, from nearly \$8,000 to just under \$5,000, largely due to a reduction in costs at the facility compared with hospital costs. Donors' families do not pay for any costs associated with organ retrieval, and any cost savings realized by moving donors to the Mid-America Transplant facility are passed directly to patients receiving the donors' organs.

During the time period covered by the study, surgeons' average round trip travel and retrieval time was reduced from 8 to 2.7 hours, which also meant that recovered organs more quickly could be transplanted into people on waiting lists.

The researchers also found no difference in the quality of livers procured at the stand-alone facility, compared with the hospital. In addition to having its own operating room, Mid-America Transplant also has state-of-the-art imaging equipment and technology to evaluate organs for transplant.

Donors' families have embraced the concept of moving their loved ones to St. Louis.

"We thought moving the donors might be a major obstacle but that has turned out not to be the case," explained Chapman, a liver transplant surgeon. "We think this is because the donation process is much more controlled, and the families can reliably know how long the surgery will take and when their loved ones will be returned to them."

Doyle MBM, Vachharajani N, Wellen JR, Lowell JA, Shenoy S, Ridolfi G, Jendrisak MD, Coleman J, Maher M, Brockmeier D, Kappel D, Chapman WC. A novel organ donor facility: A decade of experience with liver donors. American Journal of Transplantation. Feb. 25, 2014.

http://www.eurekalert.org/pub_releases/2014-02/sp-tot022514.php

The only top 10 cancer where survival rates are falling

We really need to talk about bladder cancer

Of the top 10 cancers in the UK, bladder cancer is only one where survival rates have been shown to be getting worse. New figures published this month in the Journal of Clinical Urology confirm in a study of cases of bladder cancer in England over a 19 year period (from 1990 until 2009) that survival rates here in the UK are falling and are worse than in other European countries with similar incidence rates. Shockingly, bladder cancer isn't a rare cancer that only affects a few people every year. In fact, bladder cancer is our 7th most common cancer (the 4th most common for men) with over 10,000 people diagnosed with it every year in the UK alone. Over 5,000 people in this country lose their lives to this little discussed disease every year.

That's more people than are affected by many well known cancers, including leukaemia, kidney cancer, ovarian cancer, liver cancer, pancreatic cancer, cervical cancer and brain tumours. Each year more people die in the UK from bladder cancer than die in road accidents. Yet, it is still a cancer that is hardly ever talked about.

Bladder cancer is generally easily diagnosed by urologists, but unfortunately most people are not aware of the key symptoms, so they don't go and see their GP as quickly as they should. In addition, some of the main symptoms of bladder cancer are also linked with other medical problems, resulting in GPs delaying the referral of patients on to urology specialists. This is a particular problem for women, who experience a greater amount of delayed diagnosis than men. There is also a common misconception that bladder cancer only affects older men which means that GPs often believe that the symptoms are not symptomatic of a cancer and instead diagnose problems such as recurring urinary tract infections when they occur in women, younger men and children.

Historically, there has been very little research into the causes and treatment of bladder cancer, with treatment of the disease hardly changing in the last 30 years. Despite being so common, bladder cancer receives just 0.6% of cancer research spend. This is for a cancer that is the most expensive for the NHS to treat and has the highest recurrence rate of any cancer. Simple evidence that the current treatments just aren't working as well as they should. Very few members of the public will know that smoking is believed to be the main cause of about half of the cases of bladder cancer, or that others cases can stem from exposure to industrial chemicals and dyes. However, for many bladder cancer patients, the medical profession still cannot find a reason why they have succumbed to this disease.

The most common symptom of bladder cancer is blood in your wee. Sometimes this is clearly visible, but in many cases it can only be picked up when tested by your doctor. There are no accepted screening tests for bladder cancer, so it is really important that awareness of all the causes and symptoms are better known. If caught early, the 5 years survival rates for bladder cancer can be as high as 80%, but if treatment is delayed this can drop to as low as 15% or less for advanced cases.

This new research paper has also highlighted the need for a greater equality in treatment, regardless of age, gender, socio-economic status and which part of the country you live in. It also calls for improved, more radical treatment for some of the early stage cancers, to prevent them spreading further into the bladder and then into other parts of the body (which is when survival rates suddenly get worse). The study authors highlight lack of awareness of the causes and symptoms amongst the general public and within primary care as a major problem, resulting in late diagnosis which, in turn, dramatically affects survival rates. Every day, 28 people are diagnosed and 14 people will die of bladder cancer in the UK alone. Those affected, and their families, are demanding that money needs to be spent to reverse this fall in survival rates and to find new and improved treatments.

Background Information:

Andrew Winterbottom is the Founder and Director of Fight Bladder Cancer, the only patient led bladder cancer charity in the UK. Andrew was diagnosed in 2009 with a Stage 4 aggressive bladder cancer. Having survived surgery, he found that there was no dedicated charity or organisation to support people affected by bladder cancer or to provide information about treatment and aftercare. To change this, Andrew, with his wife and close friends, started a local support group which has now grown into Fight Bladder Cancer, a national charity to support those affected by the disease. As well as offering a confidential online support forum, they also run a dedicated website for people affected by bladder cancer. The charity's main aims are to support people affected by bladder cancer, campaign for greater awareness both in the general public and amongst the medical profession, and to support research into the causes, treatment and after care of bladder cancer.

<http://www.fightbladdercancer.co.uk>

One of the authors of this recent study is Hugh Mostafid who is Chairman of Action on Bladder Cancer, a charity that was founded in 2010 by UK healthcare professionals with a special interest in bladder cancer. Their objectives are to improve public awareness and understanding of the causes and symptoms of bladder cancer, improve medical knowledge to avoid mis- or late diagnosis and ensure swift referrals and improve the priority of bladder cancer on the UK health agenda.

<http://www.actiononbladdercancer.org>

The two charities are working closely on promoting research into bladder cancer and to ensure greater awareness in order to promote earlier diagnosis and thus better survival rates.

http://www.eurekalert.org/pub_releases/2014-02/tjn-mv1022014.php

MMR vaccine linked to lower rate of infection-related hospital admissions

Receipt of the live measles, mumps, and rubella vaccine was associated with a lower rate of hospital admissions for any infections,

In a nationwide group of Danish children, receipt of the live measles, mumps, and rubella (MMR) vaccine on schedule after vaccination for other common infections was associated with a lower rate of hospital admissions for any infections, but particularly for lower respiratory tract infections, according to a study in the February 26 issue of JAMA.

Childhood vaccines are recommended worldwide, based on their protective effect against the targeted diseases. However, studies from low-income countries show that vaccines may have nonspecific effects that reduce illness and death from non-targeted diseases, according to background information in the study. Such nonspecific effects of vaccines might also be important for the health of children in high-income settings. Signe Sorup, Ph.D., of the Statens Serum Institut, Copenhagen, Denmark, and colleagues examined whether the live MMR vaccine was associated with lower rates of hospital admissions for infections among children in a higher-income setting (Denmark). The study included children 495,987 born 1997-2006 and followed from ages 11 months to 2 years. The recommended vaccination schedule was inactivated vaccine against diphtheria, tetanus, pertussis, polio, and Haemophilus influenzae type b (DTaP-IPV-Hib) administered at ages 3, 5, and 12 months; and MMR at age 15 months.

There were 56,889 hospital admissions for any type of infection among the children in the study. The researchers found that receiving the live MMR vaccine after the inactivated DTaP-IPV-Hib vaccine was associated with a lower rate of hospital admissions for any infection. The association was particularly strong for lower respiratory tract infections and for longer hospital admissions. Children who received DTaP-IPV-Hib after MMR had a higher rate of infectious disease admission.

"The coverage with MMR is suboptimal in many high-income countries; in the present study, about 50 percent of children were not vaccinated on time. Physicians should encourage parents to have children vaccinated on time with MMR and avoid giving vaccinations out of sequence, because the present study suggests that timely MMR vaccination averted a considerable number of hospital admissions for any infection between ages 16 and 24 months," the authors write.

(doi:10.1001/jama.2014.470; Available pre-embargo to the media at <http://media.jamanetwork.com>)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Nonspecific Effects of Vaccines

In an accompanying editorial, David Goldblatt, M.B.Ch.B., Ph.D., of the UCL Institute of Child Health and Great Ormond Street Children's Hospital, London, and Elizabeth Miller, F.R.C.Path., of Public Health England, London, write that the WHO Strategic Advisory Group of Experts recently decided to revisit the issue of nonspecific effects of vaccines as part of its continued appraisal of important issues that could be relevant to inform global immunization policy.

"Systematic reviews of all available epidemiologic and immunologic evidence relevant to the issue of the nonspecific effects of vaccines on childhood mortality will be undertaken to decide whether current evidence is sufficient to lead to adjustments in policy recommendations or to warrant further scientific investigation. The study by Sorup et al is a further contribution to this body of literature. Although reanalysis of the available evidence is important, the ability to properly control for bias and confounding [factors that can influence outcomes] in observational studies is often limited, and without randomized controlled trials specifically designed to test the hypothesis, the issue of nonspecific effects of vaccines may remain subject to continuing debate."

(doi:10.1001/jama.2014.471; Available pre-embargo to the media at <http://media.jamanetwork.com>)

Editor's Note: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Goldblatt reported receiving grants from, and serving on advisory boards for, GlaxoSmithKline, Sanofi Pasteur, Merck, and Novartis and serving on an advisory board for Pfizer. No other disclosures were reported.

http://www.eurekalert.org/pub_releases/2014-02/uol-pso022514.php

Psychological side-effects of anti-depressants worse than thought

A University of Liverpool researcher has shown that thoughts of suicide, sexual difficulties and emotional numbness as a result of anti-depressants may be more widespread than previously thought.

LIVERPOOL, UK - In a survey of 1,829 people who had been prescribed anti-depressants, the researchers found large numbers of people – over half in some cases – reporting on psychological problems due to their medication, which has led to growing concerns about the scale of the problem of over-prescription of these drugs. Psychologist and lead researcher, Professor John Read from the University's Institute of Psychology,

Health and Society, said: "The medicalisation of sadness and distress has reached bizarre levels. One in ten people in some countries are now prescribed antidepressants each year. "While the biological side-effects of antidepressants, such as weight gain and nausea, are well documented, the psychological and interpersonal effects have been largely ignored or denied. They appear to be alarmingly common."

Each person completed an online questionnaire which asked about twenty adverse effects. The study was carried out in New Zealand and all of the participants had been on anti-depressants in the last five years. The survey factored in people's levels of depression and asked them to report on how they had felt while taking the medication.

Over half of people aged 18 to 25 in the study reported suicidal feelings and in the total sample there were large percentages of people suffering from 'sexual difficulties' (62%) and 'feeling emotionally numb' (60%).

Percentages for other effects included: 'feeling not like myself' (52%), 'reduction in positive feelings' (42%), 'caring less about others' (39%) and 'withdrawal effects' (55%). However, 82% reported that the drugs had helped alleviate their depression.

Professor Read concluded: "While the biological side-effects of antidepressants, such as weight gain and nausea, are well documented, psychological and interpersonal issues have been largely ignored or denied. They appear to be alarmingly common." "Effects such as feeling emotionally numb and caring less about other people are of major concern. Our study also found that people are not being told about this when prescribed the drugs.

"Our finding that over a third of respondents reported suicidality 'as a result of taking the antidepressants' suggests that earlier studies may have underestimated the problem."

http://www.eurekalert.org/pub_releases/2014-02/usmc-rgn022514.php

Researchers generate new neurons in brains, spinal cords of living adult mammals

Southwestern Medical Center researchers created new nerve cells in the brains and spinal cords of living mammals without the need for stem cell transplants to replenish lost cells.

DALLAS - Although the research indicates it may someday be possible to regenerate neurons from the body's own cells to repair traumatic brain injury or spinal cord damage or to treat conditions such as Alzheimer's disease, the researchers stressed that it is too soon to know whether the neurons created in these initial studies resulted in any functional improvements, a goal for future research.

Spinal cord injuries can lead to an irreversible loss of neurons, and along with scarring, can ultimately lead to impaired motor and sensory functions. Scientists are hopeful that regenerating cells can be an avenue to repair damage, but adult spinal cords have limited ability to produce new neurons. Biomedical scientists have transplanted stem cells to replace neurons, but have faced other hurdles, underscoring the need for new methods of replenishing lost cells.

Scientists in UT Southwestern's Department of Molecular Biology first successfully turned astrocytes – the most common non-neuronal brain cells – into neurons that formed networks in mice. They now successfully turned scar-forming astrocytes in the spinal cords of adult mice into neurons. The latest findings are published today in Nature Communications and follow previous findings published in Nature Cell Biology.

"Our earlier work was the first to clearly show in vivo (in a living animal) that mature astrocytes can be reprogrammed to become functional neurons without the need of cell transplantation. The current study did something similar in the spine, turning scar-forming astrocytes into progenitor cells called neuroblasts that regenerated into neurons," said Dr. Chun-Li Zhang, assistant professor of molecular biology at UT Southwestern and senior author of both studies.

"Astrocytes are abundant and widely distributed both in the brain and in the spinal cord. In response to injury, these cells proliferate and contribute to scar formation. Once a scar has formed, it seals the injured area and creates a mechanical and biochemical barrier to neural regeneration," Dr. Zhang explained. "Our results indicate that the astrocytes may be ideal targets for in vivo reprogramming."

The scientists' two-step approach first introduces a biological substance that regulates the expression of genes, called a transcription factor, into areas of the brain or spinal cord where that factor is not highly expressed in adult mice. Of 12 transcription factors tested, only SOX2 switched fully differentiated, adult astrocytes to an earlier neuronal precursor, or neuroblast, stage of development, Dr. Zhang said.

In the second step, the researchers gave the mice a drug called valproic acid (VPA) that encouraged the survival of the neuroblasts and their maturation (differentiation) into neurons. VPA has been used to treat epilepsy for more than half a century and also is prescribed to treat bipolar disorder and to prevent migraine headaches, he said.

The current study reports neurogenesis (neuron creation) occurred in the spinal cords of both adult and aged (over one-year old) mice of both sexes, although the response was much weaker in the aged mice, Dr. Zhang

said. Researchers now are searching for ways to boost the number and speed of neuron creation. Neuroblasts took four weeks to form and eight weeks to mature into neurons, slower than neurogenesis reported in lab dish experiments, so researchers plan to conduct experiments to determine if the slower pace helps the newly generated neurons properly integrate into their environment.

In the spinal cord study, SOX2-induced mature neurons created from reprogramming of astrocytes persisted for 210 days after the start of the experiment, the longest time the researchers examined, he added.

Because tumor growth is a concern when cells are reprogrammed to an earlier stage of development, the researchers followed the mice in the Nature Cell Biology study for nearly a year to look for signs of tumor formation and reported finding none.

Dr. Zhida Su, a UT Southwestern visiting instructor of molecular biology from the Second Military Medical University in Shanghai, China, was lead author on the current study. Co-authors included: Dr. Wenze Niu, instructor; Dr. Meng-Lu Liu, postdoctoral researcher; and Yuhua Zou, research scientist, all from UT Southwestern's Department of Molecular Biology. Co-authors of the Nature Cell Biology study include lead author Dr. Niu, Ms. Zou, and postdoctoral researcher Dr. Tong Zang, all of the Department of Molecular Biology, as well as former postdoctoral researcher Dr. Sanhua Fang, now a lecturer at Zhejiang University in China; Dr. Robert Bachoo, an assistant professor of neurology and neurotherapeutics, and internal medicine, at UT Southwestern; and Derek Smith, a graduate student of neuroscience and molecular biology.

Both studies received support from the American Heart Association, the Welch Foundation, the Ellison Medical Foundation, and the National Institutes of Health. The Nature Cell Biology study also received support from an NIH Director's New Innovator Award and from the Whitehall Foundation.

http://www.eurekalert.org/pub_releases/2014-02/bu-a3y022514.php

Analysis: 32 years of US filicide arrests

Paper provides the first comprehensive statistical analysis of filicide in the United States

PROVIDENCE, R.I. [Brown University] - Instances in which parents kill their children may seem so horrifying and tragic that they defy explanation. Published scientific and medical research, meanwhile, doesn't offer much epidemiological context to help people understand patterns among such heinous crimes. A paper in the March edition of the journal Forensic Science International provides the first comprehensive statistical analysis of filicide in the United States, drawing on 32 years of data on more than 94,000 arrests. The study also explores possible underlying psychiatric and biological underpinnings of filicide.

The research could help identify valid patterns among filicide cases, said lead author Dr. Timothy Mariano, a third-year psychiatry resident in the Alpert Medical School of Brown University, which could in turn aid in studying the causes of filicide.

"To know more about the epidemiology of this crime will hopefully help medical practitioners to identify people who are at risk for committing such crimes and that will help us with prevention, which is the ultimate goal of this research," Mariano said.

A broad understanding of filicide, for instance, can help disabuse professionals and members of the public of certain myths and stereotypes about the crime, said senior author Dr. Wade Myers, professor of psychiatry and human behavior at Brown and a forensic psychiatrist at Rhode Island Hospital. For example, the data show that men are about as likely as women to kill infants. Stepchildren are not more likely than biological children to die at their parents' hands, and nearly one in five filicides (18 percent) are killings of adult children, suggesting filicide is a lifetime risk.

Statistical context

The data in the study, first published online last month, come from the U.S. Federal Bureau of Investigation's Supplementary Homicide Reports (SHR) database. Mariano, Myers, and co-author Heng Choon Chan looked at 632,017 arrests between 1976 and 2007, finding that 94,146 cases (14.9 percent) were filicides. The database includes information on the ages, genders, and races of the victims and alleged offenders, as well as the means employed to commit the murder.

Over time, the total number of cases in the country has remained relatively stable at around 3,000 a year. There may be some good news, however. Not only has the number drifted somewhat downward since the early 1990s, but also the numbers did not climb with population growth over the last three decades.

Close to three-quarters (72 percent) of the children killed were age 6 or younger. One-third were infants (children less than 1 year of age). Only about 10 percent of children killed were between ages 7 and 18. Adult offspring were the balance of the victims. Male children were more likely to be killed (58.3 percent) than female children. About 11 percent of victims were stepchildren, which is on the low end of the estimated proportion of U.S. children (10-20 percent) who live with a stepparent.

Among offenders, while fathers were about equally likely to kill an infant, they were more likely to be the alleged murderer of children older than a year, especially when the children were adults (fathers were the offenders in 78.3 percent of those cases). Overall, fathers were the accused murderer 57.4 percent of the time.

The data allowed the researchers to determine the most common filicide scenarios. A father killing a son was the most likely (29.5 percent of cases), a mother killing a son (22.1 percent) follows. A mother was slightly more likely to kill a daughter (19.7 percent of cases) than a father was (18.1 percent). The rarest instances were stepmothers killing either a stepson (0.5 percent) or a stepdaughter (0.3 percent).

The researchers found that the most common method of killing was with "personal weapons," such as by the beating, choking, or drowning of victims. Parents used these means in 69 percent of murders of infants. As victims aged, firearms were more common, becoming the weapon used in 72.3 percent of the cases in which the victim as an adult. Men were much more likely to use guns than women. Across the board, parents rarely used contact weapons (such as a bat) or edged weapons (such as a knife). While stepparents weren't overrepresented in the study, they were twice as likely as biological parents to use guns to (40 percent vs. 21 percent).

Biological underpinnings

Before Mariano worked with Myers and Chan to analyze the Supplementary Homicide Reports data, he had begun studying filicide while on a psychiatry rotation in medical school at Case Western Reserve University. There he had been reviewing the scientific literature on animal models of filicide. That published work, combined with studies of people and trends in the arrest statistics, offers a way for mental health professionals to develop hypotheses about the causes of filicide, he said.

In the current paper, Mariano synthesizes three main hypotheses about these underlying motives. One is that at least some parents who commit filicide have mental illness that derives from low levels of the neurotransmitter serotonin. Not only is that borne out in some animal studies, but the most typical ages of filicidal parents in the SHR data (18-30 years) are also the age at which many serotonin-related illnesses occur, like depression and schizophrenia.

Looking at the substantial differences that gender appears to make in the SHR data, a second hypothesis focuses on sex hormones. High levels of testosterone appear to coincide with higher rates of filicide in animal studies, for example, and in the crime statistics men were more likely to commit filicide, especially after victims were older than a year.

The final hypothetical motive category pertains mostly to those youngest of victims, "the unwanted child." This evolutionarily motivated idea, also informed by other studies, suggests that parents, particularly young mothers, may kill young children who are sick or for whom they feel they cannot provide care.

Neither the statistics nor the hypotheses definitively explain filicide, but they provide researchers with a basis to focus their inquiries, Mariano and Myers said.

"Hopefully future research will continue to improve society's ability to identify, manage, and treat populations at risk," they conclude.

The research was partially funded by a grant from the National Institutes of Health (grant: T32GM007250).

http://www.eurekalert.org/pub_releases/2014-02/esoa-ocr022514.php

Ordinary conditioner removes head lice eggs as effectively as special products

New research shows that ordinary hair conditioner is just as effective as commercial as nit-removal products

Eggs from head lice, also called nits, are incredibly difficult to remove. Female lice lay eggs directly onto strands of hair, and they cement them in place with a glue-like substance, making them hard to get rid of. In fact, the eggs are glued down so strongly that they will stay in place even after hair has been treated with pediculicides -- substances used to kill lice.

Some shampoos and conditioners that contain chemicals or special oils are marketed as nit-removal products. However, new research just published in the Journal of Medical Entomology shows that ordinary hair conditioner is just as effective. In an article called "Efficacy of Products to Remove Eggs of *Pediculus humanus capitis* (Phthiraptera: Pediculidae) From the Human Hair," (DOI: <http://dx.doi.org/10.1603/ME13106>) scientists from Belgium gathered 605 hairs from six different children. Each hair had a single nit attached to it.

Approximately 14% of the eggshells contained a dead egg, whereas the rest were empty.

They then tried to remove the eggs and tested the amount of force needed to do so. They found that nits on the hairs that were left completely untreated were the most difficult to remove. Eggs on hairs that had been soaked in deionized water were much easier to remove, as were the eggs on hairs that had been treated with ordinary hair conditioner and with products specifically marketed for the purpose of nit removal.

However, they found no significant differences between the ordinary conditioners and the special nit-removal products. In all cases, less force was required to remove the nits after the hair had been treated, but the effectiveness of the products was essentially the same. "There were no significant differences in measured forces between the ordinary conditioner and the commercial nit removal product," the authors write. "The commercial nit removal products tested in the current study do not seem to have an additional effect."

The authors hypothesize that the deionized water was effective because it acts as a lubricant, so less friction is needed to remove the nits from the hairs. The same goes for the conditioners. "Treatment with conditioner reduces the coefficient of friction of undamaged and damaged hair," they write. "As a consequence, conditioners will facilitate nit removal."

The fast-tracked article is available now at <http://tinyurl.com/qy2dpzn>. In the future it will available at <http://dx.doi.org/10.1603/ME13106>.

http://www.eurekalert.org/pub_releases/2014-02/osu-bba022514.php

Breast-feeding benefits appear to be overstated, according to study of siblings

Advantages of women who choose breast-feeding likely bias findings in previous research

COLUMBUS, Ohio – A new study comparing siblings who were fed differently during infancy suggests that breast-feeding might be no more beneficial than bottle-feeding for 10 of 11 long-term health and well-being outcomes in children age 4 to 14.

The outlier was asthma, which was associated more with breast-feeding than with bottle-feeding.

The study also included an analysis of outcomes across families of different races and socioeconomic circumstances for comparison purposes, and those results matched other studies suggesting that breast-feeding's benefits to children outweigh bottle-feeding. The lead researcher noted that there is a clear reason for that.

"Many previous studies suffer from selection bias. They either do not or cannot statistically control for factors such as race, age, family income, mother's employment – things we know that can affect both breast-feeding and health outcomes," said Cynthia Colen, assistant professor of sociology at The Ohio State University and lead author of the study. "Moms with more resources, with higher levels of education and higher levels of income, and more flexibility in their daily schedules are more likely to breast-feed their children and do so for longer periods of time."

Previous research has identified clear patterns of racial and socioeconomic disparities between women who breast-feed and those who don't, complicating an already demanding choice for women who work outside the home at jobs with little flexibility and limited maternity leave.

Colen's study is also rare for its look at health and education benefits of infant feeding practices for children age 4 to 14 years, beyond the more typical investigation of breast-feeding's effects on infants and toddlers.

Federal health officials have declared breast-feeding for at least six months a national priority, which could end up stigmatizing women who can't opt to nurse their babies, Colen said.

"I'm not saying breast-feeding is not beneficial, especially for boosting nutrition and immunity in newborns," Colen said. "But if we really want to improve maternal and child health in this country, let's also focus on things that can really do that in the long term – like subsidized day care, better maternity leave policies and more employment opportunities for low-income mothers that pay a living wage, for example."

The study is published in the journal *Social Science & Medicine*.

Demographic differences across families that can bias studies in favor of breast-feeding include parental race, age, marital status, family income, insurance coverage, the mother's education and employment, and whether a woman smokes or drinks during pregnancy. "When we get more advantaged moms selecting into breast-feeding and we know those traits also will affect the health outcomes, it's not clear what's affecting an outcome like obesity – is it breast-feeding itself or those other background characteristics?" Colen said.

Colen used data from the 1979 cohort of the National Longitudinal Survey of Youth (NLSY), a nationally representative sample of young men and women who were between ages 14 and 22 in 1979, as well as results from NLSY surveys between 1986 and 2010 of children born to women in the 1979 cohort. The children were between ages 4 and 14 during the time period studied. The NLSY79 is conducted by Ohio State's Center for Human Resource Research for the U.S. Bureau of Labor Statistics.

Colen analyzed three samples: 8,237 children, 7,319 siblings and 1,773 "discordant" sibling pairs, or children from 665 surveyed families in which at least one child was breast-fed and at least one other child was bottle-fed. The children who were differently fed in the same family represented about 25 percent of the siblings in the data. For each sample, the researchers sought answers to two basic questions: Was at least one child breast-fed and, if so, what was the duration of breast-feeding?

The study measured 11 outcomes that are common to other studies of breast-feeding's effects: body mass index (BMI), obesity, asthma, hyperactivity, parental attachment (secure emotional relationships between parents and child) and behavior compliance, as well as scores predicting academic achievement in vocabulary, reading recognition, math ability, intelligence and scholastic competence. Colen constructed statistical models for the analysis.

As expected, the analyses of the samples of adults and their children across families suggested that breast-feeding resulted in better outcomes than bottle-feeding in a number of measures: BMI, hyperactivity, math skills, reading recognition, vocabulary word identification, digit recollection, scholastic competence and obesity. When the sample was restricted to siblings who were differently fed within the same families, however, scores reflecting breast-feeding's positive effects on 10 of the 11 indicators of child health and well-being were closer to zero and not statistically significant – meaning any differences could have occurred by chance alone.

The outlying outcome in this study was asthma; in all samples, children who were breast-fed were at higher risk for asthma, which could relate to data generated by self-reports instead of actual diagnoses.

Some examples of differing benefits: Breast-feeding's beneficial influence on BMI decreased by 66 percent between siblings across families and siblings within families. The magnitude of the beneficial effects of breast-feeding for math, reading, vocabulary and intelligence declined by between 69 and 29 percent, respectively, when comparing data across families to data from within families.

"Instead of comparing across families we are comparing within families, completely taking into account all of those characteristics – both measured and unmeasured – that differ by family, such as parental education, household income and race/ethnicity," Colen explained. These same differences between samples were found in the analysis of the effects of the duration of breastfeeding.

These findings have implications for health policy, she noted. "If breast-feeding doesn't have the impact that we think it will have on long-term childhood outcomes, then even though it is very important in the short-term we really need to focus on other things," she said. "We need to look at school quality, adequate housing and the type of employment parents have when their kids are growing up.

"We need to take a much more careful look at what happens past that first year of life and understand that breast-feeding might be very difficult, even untenable, for certain groups of women. Rather than placing the blame at their feet, let's be more realistic about what breast-feeding does and doesn't do."

Colen co-authored the study with David Ramey, a Ph.D. candidate in sociology at Ohio State.

This work is supported by a grant from the Eunice Kennedy Shriver National Institute of Child Health & Human Development awarded to the Ohio State University Institute for Population Research.

<http://www.bbc.co.uk/news/science-environment-26343894>

Chile's stunning fossil whale graveyard explained

It is one of the most astonishing fossil discoveries of recent years - a graveyard of whales found beside the Pan-American Highway in Chile.

By Jonathan Amos Science correspondent, BBC News

And now scientists think they can explain how so many of the animals came to be preserved in one location more than five million years ago. It was the result of not one but four separate mass strandings, they report in a Royal Society journal. The evidence strongly suggests the whales all ingested toxic algae. The dead and dying mammals were then washed into an estuary and on to flat sands where they became buried over time.



The Smithsonian has produced tools to allow the public to tour and investigate Cerro Ballena

It was well known that this area in Chile's Atacama Desert preserved whale fossils. Their bones could be seen sticking out of rock faces, and the spot acquired the name Cerro Ballena ("whale hill") as a result. But it was only when a cutting was made to widen the Pan-American Highway that US and Chilean researchers got an opportunity to fully study the fossil beds.

They were given just two weeks to complete their field work before the heavy plant returned to complete construction of the new road. The team set about recording as much detail as possible, including making 3D digital models of the skeletal remains in situ and then removing bones for further study in the lab.

Identified in the beds were over 40 individual rorquals - the type of large cetacean that includes the modern blue, fin and minke whales. Among them were other important marine predators and grazers.

"We found extinct creatures such as walrus whales - dolphins that evolved a walrus-like face. And then there were these bizarre aquatic sloths," recalls Nicholas Pyenson, a palaeontologist at the Smithsonian's National Museum of Natural History. "To me, it's amazing that in 240m of road-cut, we managed to sample all the superstars of the fossil marine-mammal world in South America in the Late Miocene. Just an incredibly dense accumulation of species," he told BBC News.

The team immediately noticed that the skeletons were nearly all complete, and that their death poses had clear commonalities. Many had come to rest facing in the same direction and upside down, for example.

This all pointed to the creatures succumbing to the same, sudden catastrophe; only, the different fossils levels indicated it was not one event but four separate episodes spread over a period of several thousand years.

The best explanation is that these animals were all poisoned by the toxins that can be generated in some algal blooms. Such blooms are one of the prevalent causes for repeated mass strandings seen in today's marine animals. If large quantities of contaminated prey are consumed, or the algae are simply inhaled - death can be rapid. "All the creatures we found - whether whales, seals or billfishes - fed high up in marine food webs and that would have made them very susceptible to harmful algal blooms," said Dr Pyenson.



Hundreds of fossils await unearthing and description at Cerro Ballena

The researchers believe the then configuration of the coastline at Cerro Ballena in the late Miocene Epoch worked to funnel carcasses into a restricted area where they were lifted on to sand flats just above high tide, perhaps by storm waves. This would have put the bodies beyond marine scavengers. And, being a desert region, there would have been very few land creatures about to steal bones either. A lot of the fossils at Cerro Ballena are perfect but for a few nicks inflicted by foraging crabs.

The researchers are not in a position to say for sure that harmful algal blooms were responsible for the mass strandings. There were no distinct algal cell fragments in the sediments; such a presence could have amounted to a "smoking gun". What the team did find, however, were multiple grains encrusted in iron oxides that could hint at past algal activity.

"There are tiny spheres about 20 microns across - that's exactly the right size to be dinoflagellate cysts," said Dr Pyenson. "They're found in algal-like mats all around the site. We can't say whether those were the killer algae, but they do not falsify the argument for harmful algal blooms being the cause in the way that the sedimentology falsifies tsunami being a potential cause."

Cerro Ballena is now regarded as one of the densest fossil sites in the world - certainly for whales and other extinct marine mammals. The scientists calculate there could be hundreds of specimens in the area still waiting to be unearthed and investigated.

The University of Chile in Santiago is currently working to establish a research station to carry this into effect. To coincide with the publication of a scholarly paper in Proceedings B of the Royal Society, the Smithsonian has put much of its digital data, including 3D scans and maps, online at cerroballena.si.edu.

http://www.eurekalert.org/pub_releases/2014-02/ehs-nsp022514.php

New study presents evidence that blood pressure should be measured in both arms *Difference in interarm blood pressure linked to greater risk of future cardiovascular events, reports The American Journal of Medicine*

Philadelphia, PA - As heart disease continues to be one of the leading causes of death in the United States, practitioners and patients alike are looking for ways to cut risk factors and identify new clues to assist with early detection. New research published in the March issue of The American Journal of Medicine suggests that there is an association between a difference in interarm systolic blood pressure and a significant increased risk for future cardiovascular events, leading researchers to recommend expanded clinical use of interarm blood pressure measurement.

While blood pressure is a widely used medical metric, most measurements are taken only using one arm. Measuring interarm blood pressure involves taking two readings, one for each arm. Increased interarm systolic blood pressure differences are defined as 10 mmHg or greater, and while a link between interarm blood pressure and cardiovascular risk was suspected, little data existed to support the hypothesis until now.

This new study examined 3,390 participants aged 40 years and older from the Framingham Heart Study. All subjects were free of cardiovascular disease at baseline, but investigators found that participants with higher interarm systolic blood pressure differences were at a much higher risk for future cardiovascular events than those with less than a 10 mm Hg difference between arms.

"In this large prospective, community based cohort of middle-age men and women free of cardiovascular disease, an increased interarm systolic blood pressure difference was found to be present in nearly 10% of individuals and is associated with increased levels of traditional cardiovascular risk factors," explains lead investigator Ido Weinberg, MD, Institute for Heart Vascular and Stroke Care, Massachusetts General Hospital, Boston. "Furthermore, an increased interarm systolic blood pressure difference is associated with an increased risk for incident cardiovascular events, independent of traditional cardiovascular risk factors."

Researchers also found that participants with elevated interarm blood pressure difference were older, had a greater prevalence of diabetes mellitus, higher systolic blood pressure, and a higher total cholesterol level. According to these findings, investigators suggest practitioners should consider including blood pressure readings in both arms in order to get the most accurate readings possible and detect any differences in interarm

blood pressure. "Even modest differences in clinically-measured systolic blood pressures in the upper extremities reflect an increase in cardiovascular risk," says Weinberg. "This study supports the potential value of identifying the interarm systolic blood pressure difference as a simple clinical indicator of increased cardiovascular risk."

http://www.eurekalert.org/pub_releases/2014-02/iocr-scr022514.php

Skin cancer risk may have driven evolution of black skin

Early humans may have evolved black skin to protect against a very high risk of dying from ultraviolet light (UV)-induced skin cancer, a new analysis concludes.

Skin cancer has usually been rejected as the most likely selective pressure for the development of black skin because of a belief that it is only rarely fatal at ages young enough to affect reproduction.

But a new paper, published in Proceedings of the Royal Society B, cites evidence that black people with albinism from parts of Africa with the highest UV radiation exposure, and where humans first evolved, almost all die of skin cancer at a young age. The paper, by Professor Mel Greaves at The Institute of Cancer Research, London, cites studies showing that 80 per cent or more of people with albinism from African equatorial countries such as Tanzania and Nigeria develop lethal skin cancers before the age of 30.

Albinism is also linked to skin cancer in indigenous populations of other tropical countries with high, year-round UV exposure such as Panama. Professor Greaves argues that the fact that people with albinism, which is caused by genetic changes that prevent the production of melanin, develop cancer at reproductive ages is indirect but persuasive evidence that early, pale-skinned humans were under strong evolutionary pressure to develop melanin-rich skin in order to avoid lethal skin cancer.

Genetic evidence suggests that the evolution of skin rich in eumelanin, which is brown-black in colour, occurred in early humans between 1.2 and 1.8 million years ago in the East African Savannah. Early humans having lost most of their body hair (probably to facilitate heat loss) probably had pale skin containing pheomelanin - like our nearest surviving relatives, chimpanzees. Pheomelanin, characteristic of white skin, is red-yellow and packaged into smaller stores under the skin than eumelanin, characteristic of black skin.

Eumelanin provides a much more effective barrier against the DNA damage that causes skin cancers, providing almost complete protection. Most scientists agree the development of black skin occurred in early humans primarily because of the ability of eumelanin to effectively absorb ultraviolet radiation, but they have debated exactly how this could have protected early humans against lethal diseases.

As well as affecting skin cancer risk, increased black melanin production could have given other benefits that helped individuals to pass on their genes to the next generation, such as preventing damage to sweat glands or the destruction of folate, which is important in foetal development. While there could have been many benefits of having black skin in Africa (and retaining it in New Guinea), Professor Greaves argues that individuals with albinism and no protective benefit from melanin almost all die young from cancer.

Professor Greaves is Director of the new Centre for Evolution and Cancer at The Institute of Cancer Research (ICR). The Centre aims to gain new insights into how individual cancers evolve – the process behind the development of drug resistance, and the often extraordinary genetic diversity within single tumours – and to uncover clues in our evolutionary history that could help us understand why human cancers develop.

Professor Mel Greaves, Director of the Centre for Evolution and Cancer at The Institute of Cancer Research, London, said: "Charles Darwin thought variation in skin colour was of no adaptive value and other investigators have dismissed cancer as a selective force in evolution. But the clinical data on people with albinism, particularly in Africa, provide a strong argument that lethal cancers may well have played a major role in early human evolution as an important factor in the development of skin rich in dark pigmentation - in eumelanin."

<http://arstechnica.com/science/2014/02/open-access-science-publisher-demands-full-availability-of-data/>

Open access science publisher demands full availability of data

If you publish in PLoS, be prepared to share all the underlying data.

by John Timmer - Feb 26 2014, 8:34am TST

Yesterday, the open access publisher Public Library of Science announced a change to its data sharing requirements. Previously, anyone publishing in one of its journals (including PLoS One, the largest scientific journal around) implicitly agreed to make the data that they used in the paper available to other researchers, which typically meant that the other researchers had to make a formal request for it. From now on, however, the PLoS journals will require authors to sign a data availability statement that guarantees that all the data used in a paper is publicly accessible to anyone at the moment the paper goes live.

That includes things like images, DNA sequence reads, raw cell counts, and so forth. The publisher suggests three ways that researchers can meet the requirements. If the underlying data (like cell counts) is numerical, it

can simply be published in a table in the paper itself. If it's a bit larger, researchers can compress it and make the archive a supplement to the paper, which PLoS will host it on its servers. If it's larger still, researchers should look to a third-party service; hosting it on an institutional server would also be an option. PLoS accepts that this won't work in some cases, as confidentiality is required for patient data, and some researchers rely on third parties for data. These exceptions, however, should be just that: exceptional. The vast majority of data should be subject to the new rules.

And the new rules are significant. Formal requests for data can sometimes get lost in spam filters or put aside for weeks, even if the person who has the data is happy to share it (which is not always the case). By shifting the default state to one where anyone with a Web browser can grab whatever data they'd like, a lot of the friction that slows down the spread of scientific data should be eliminated.

http://www.eurekalert.org/pub_releases/2014-02/uoc-dob022614.php

Decline of Bronze Age 'megacities' linked to climate change

Climate change may have contributed to the decline of a city-dwelling civilization in Pakistan and India 4,100 years ago, according to new research

Scientists from the University of Cambridge have demonstrated that an abrupt weakening of the summer monsoon affected northwest India 4,100 years ago. The resulting drought coincided with the beginning of the decline of the metropolis-building Indus Civilisation, which spanned present-day Pakistan and India, suggesting that climate change could be why many of the major cities of the civilisation were abandoned.

The research, reported online on 25 February, 2014, in the journal *Geology*, involved the collection of snail shells preserved in the sediments of an ancient lake bed. By analysing the oxygen isotopes in the shells, the scientists were able to tell how much rain fell in the lake where the snails lived thousands of years ago.

The results shed light on a mystery surrounding why the major cities of the Indus Civilisation (also known as the Harappan Civilisation, after Harappa, one of the five cities) were abandoned. Climate change had been suggested as a possible reason for this transformation before but, until now, there has been no direct evidence for climate change in the region where Indus settlements were located.

Moreover, the finding now links the decline of the Indus cities to a documented global scale climate event and its impact on the Old Kingdom in Egypt, the Early Bronze Age civilisations of Greece and Crete, and the Akkadian Empire in Mesopotamia, whose decline has previously been linked to abrupt climate change.

"We think that we now have a really strong indication that a major climate event occurred in the area where a large number of Indus settlements were situated," said Professor David Hodell, from Cambridge's Department of Earth Sciences. "Taken together with other evidence from Meghalaya in northeast India, Oman and the Arabian Sea, our results provide strong evidence for a widespread weakening of the Indian summer monsoon across large parts of India 4,100 years ago."

Hodell together with University of Cambridge archaeologist Dr Cameron Petrie and Gates scholar Dr Yama Dixit collected *Melanoides tuberculata* snail shells from the sediments of the ancient lake Kotla Dahar in Haryana, India. "As today, the major source of water into the lake throughout the Holocene is likely to have been the summer monsoon," said Dixit. "But we have observed that there was an abrupt change, when the amount of evaporation from the lake exceeded the rainfall – indicative of a drought."

At this time large parts of modern Pakistan and much of western India was home to South Asia's great Bronze Age urban society. As Petrie explained: "The major cities of the Indus civilisation flourished in the mid-late 3rd and early 2nd millennium BC. Large proportions of the population lived in villages, but many people also lived in 'megacities' that were 80 hectares or more in size – roughly the size of 100 football pitches. They engaged in elaborate crafts, extensive local trade and long-ranging trade with regions as far away as the modern-day Middle East. But, by the mid 2nd millennium BC, all of the great urban centres had dramatically reduced in size or been abandoned."

Many possible causes have been suggested, including the claim that major glacier-fed rivers changed their course, dramatically affecting the water supply and the reliant agriculture. It has also been suggested that an increasing population level caused problems, there was invasion and conflict, or that climate change caused a drought that large cities could not withstand long-term.

"We know that there was a clear shift away from large populations living in megacities," said Petrie. "But precisely what happened to the Indus Civilisation has remained a mystery. It is unlikely that there was a single cause, but a climate change event would have induced a whole host of knock-on effects. "We have lacked well-dated local climate data, as well as dates for when perennial water flowed and stopped in a number of now abandoned river channels, and an understanding of the spatial and temporal relationships between settlements and their environmental contexts. A lot of the archaeological debate has really been well-argued speculation."

The new data, collected with funding from the Natural Environment Research Council, show a decreased summer monsoon rainfall at the same time that archaeological records and radiocarbon dates suggest the beginning of the Indus de-urbanisation. From 6,500 to 5,800 years ago, a deep fresh-water lake existed at Kotla Dahar. The deep lake transformed to a shallow lake after 5,800 years ago, indicating a weakening of the Indian summer monsoon. But an abrupt monsoon weakening occurred 4,100 years ago for 200 years and the lake became ephemeral after this time.

Until now, the suggestion that climate change might have had an impact on the Indus Civilisation was based on data showing a lessening of the monsoon in Oman and the Arabian Sea, which are both located at a considerable distance from Indus Civilisation settlements and at least partly affected by different weather systems.

Hodell and Dixit used isotope geochemical analysis of shells as a proxy for tracing the climate history of the region. Oxygen exists in two forms – the lighter ^{16}O and a heavier ^{18}O variant. When water evaporates from a closed lake (one that is fed by rainfall and rivers but has no outflow), molecules containing the lighter isotope evaporate at a faster rate than those containing the heavier isotopes; at times of drought, when the evaporation exceeds rainfall, there is a net increase in the ratio of ^{18}O to ^{16}O of the water. Organisms living in the lake record this ratio when they incorporate oxygen into the calcium carbonate (CaCO_3) of their shells, and can therefore be used, in conjunction with radiocarbon dating, to reconstruct the climate of the region thousands of years ago.

Speculating on the effect lessening rainfall would have had on the Indus Civilisation, Petrie said:

"Archaeological records suggest they were masters of many trades. They used elaborate techniques to produce a range of extremely impressive craft products using materials like steatite, carnelian and gold, and this material was widely distributed within South Asia, but also internationally. Each city had substantial fortification walls, civic amenities, craft workshops and possibly also palaces. Houses were arranged on wide main streets and narrow alleyways, and many had their own wells and drainage systems. Water was clearly an integral part of urban planning, and was also essential for supporting the agricultural base.

At around the time we see the evidence for climatic change, archaeologists have found evidence of previously maintained streets start to fill with rubbish, over time there is a reduced sophistication in the crafts they used, the script that had been used for several centuries disappears and there were changes in the location of settlements, suggesting some degree of demographic shift."

"We estimate that the climate event lasted about 200 years before recovering to the previous conditions, which we still see today, and we believe that the civilisation somehow had to cope with this prolonged period of drought," said Hodell.

The new research is part of a wider joint project led by the University of Cambridge and Banaras Hindu University in India, which has been funded by the British Council UK-India Education and Research Initiative to investigate the archaeology, river systems and climate of north-west India using a combination of archaeology and geoscience. The multidisciplinary project hopes to provide new understanding of the relationships between humans and their environment, and also involves researchers at Imperial College London, the University of Oxford, the Indian Institute of Technology Kanpur and the Uttar Pradesh State Archaeology Department.

"It is essential to understand the link between human settlement, water resources and landscape in antiquity, and this research is an important step in that direction," explained Petrie. "We hope that this will hold lessons for us as we seek to find means of dealing with climate change in our own and future generations."

http://www.eurekalert.org/pub_releases/2014-02/chr-nri022514.php

New research indicates causal link between vitamin D, serotonin synthesis and autism

Dietary interventions will have relevance for prevention and possibly for treatment of autism

Oakland, CA – A new study by Rhonda Patrick, PhD and Bruce Ames, PhD of Children's Hospital Oakland Research Institute (CHORI) demonstrates the impact that Vitamin D may have on social behavior associated with Autism Spectrum Disorder (ASD). Dr. Patrick and Dr. Ames show that serotonin, oxytocin, and vasopressin, three brain hormones that affect social behavior, are all activated by vitamin D hormone. Autism, which is characterized by abnormal social behavior, has previously been linked to low levels of serotonin in the brain and to low vitamin D levels, but no mechanism has linked the two until now.

In this study, Dr. Patrick and Dr. Ames show that vitamin D hormone activates the gene that makes the enzyme tryptophan hydroxylase 2 (TPH2), that converts the essential amino acid tryptophan, to serotonin in the brain. This suggests that adequate levels of vitamin D may be required to produce serotonin in the brain where it shapes the structure and wiring of the brain, acts as a neurotransmitter, and affects social behavior. They also

found evidence that the gene that makes the enzyme tryptophan hydroxylase 1 (TPH1) is inhibited by vitamin D hormone, which subsequently halts the production of serotonin in the gut and other tissues, where when found in excess it promotes inflammation.

This mechanism explains many of the known, but previously not understood, facts about autism including: 1) the "serotonin anomaly" low levels of serotonin in the brain and high levels in the blood of autistic children; 2) the preponderance of male over female autistic children: estrogen, a similar steroid hormone, can also boost the brain levels of serotonin in girls; 3) the presence of autoimmune antibodies to the fetal brain in the mothers of autistic children: vitamin D regulates the production of regulatory T-cells via repression of TPH1. The Patrick/Ames mechanism is relevant to the prevention of autism, and likely its treatment.

The current guidelines for adequate vitamin D levels are concentrations above 30 ng/ml. Most Americans' vitamin D is made in the skin from exposure to UVB radiation; however, melanin pigment and sunscreen inhibit this action. This is an important cause of the well-known widespread vitamin D deficiency among dark-pigmented Americans, particularly those living in Northern latitudes. The most recent National Health and Examination survey reports that greater than 70% of U.S. population does not meet this requirement and that adequate vitamin D levels have plummeted over the last couple of decades. This precipitous drop in adequate levels of vitamin D in the US is concurrent with the rise in autism rates.

The study suggests dietary intervention with vitamin D, tryptophan and omega 3 fatty acids would boost brain serotonin concentrations and help prevent and possibly ameliorate some of the symptoms associated with ASD without side effects. There is little vitamin D present in food and fortification is still inadequate as is the amount in most multivitamin and prenatal supplements. Vitamin D supplements are inexpensive and offer a simple solution to raise vitamin D levels to an adequate status. In addition, vitamin D levels should be routinely measured in everyone and should become a standard procedure in prenatal care.

http://www.eurekalert.org/pub_releases/2014-02/uob-sst022614.php

Sunburns strike twice

University of Bonn: Skin inflammation following UV irradiation promotes cancer cell spread along blood vessels

Melanoma is particularly dangerous because it can form metastases in vital organs such as the lungs, liver or brain. UV radiation is considered to be the most significant triggering factor. An interdisciplinary team of researchers from the University Hospital and the LIMES Institute of the University of Bonn has now discovered that sunburns contribute to the development of this malignant disease not only through direct alteration of pigment cell genomes but also indirectly through inflammatory processes in the surrounding tissue. The results are now being published online in the renowned journal "Nature".

According to predictions from the Robert Koch Institute, approximately 20,000 people in Germany will develop malignant melanoma in 2014. More than 2500 of those affected will die from metastases to internal organs. "The inflammatory reaction of the skin after severe sun exposure promotes the early migration of melanoma cells along vessels within the body," says Prof. Dr. Thomas Tüting, professor of Experimental Dermatology at the University of Bonn Hospital and leader of the study team.

Melanoma cells migrate along blood vessels

To understand the development and early metastasis of malignant melanoma, the researchers developed experimental models in mice which allowed them to investigate the effect of inflammatory responses following UV exposure. "We repeatedly observed increased melanoma metastases in the lungs of UV-irradiated mice," reports the dermatologist Dr. Evelyn Gaffal. Analyses of melanoma tissue sections revealed the spread of tumor cells along blood vessel surfaces in inflamed skin. Using modern methods of fluorescence and electron microscopy, the researchers observed a close association between melanoma cells, inner blood vessel walls and immune cells, especially neutrophils.

Activated neutrophils pave the way for melanoma cells

Further experiments showed that neutrophils play an important role in metastasis. They are attracted by alarm signals emitted by UV-damaged keratinocytes in the epidermis. The use of special mouse strains which lack important molecules required for the activation of innate immune defense shed light on the underlying signaling pathways.

Inflammatory mediators promote melanoma cell motility

Researchers in the LIMES Institute of the University of Bonn developed new experimental methods to investigate the interaction between melanoma cells and cells of the inner blood vessel walls, known as endothelial cells. In doing so, they observed that melanoma cells can migrate particularly effectively on blood

vessel surfaces. "Melanoma cells increase their motility in an inflammatory environment," says Prof. Dr. Waldemar Kolanus.

Further investigations with human melanoma cells and modern genomic methods provided insights how inflammatory mediators stimulate melanoma cells migration. "During embryonic development pigment cell precursors travel long distances along blood vessels in the body in order to reach their final destination in the skin. These migratory programs are erroneously reactivated in melanoma cells by inflammation," says Prof. Dr. Michael Hölzel from the Institute of Clinical Chemistry and Clinical Pharmacology in Bonn.

Important insights for new treatment strategies

"Our findings may explain why patients with superficially ulcerated melanomas and neutrophil infiltration frequently develop organ metastases" says Prof. Tüting. The researchers hope to develop new forms of targeted therapy in the future which specifically interfere with inflammatory signaling cascades and inhibit the migration of melanoma cells on the surfaces of blood vessels. The interdisciplinary cooperation between different research groups in Bonn within the Collaborative Research Center 704 and the Excellence Cluster ImmunoSensation provide an excellent basis for such ambitious projects.

Publication: Ultraviolet-radiation-induced inflammation promotes angiotropism and metastasis in melanoma, Nature, DOI: 10.1038/nature13111

<http://bit.ly/1hHNv3x>

Our blender brain: How mixing ideas made us human

About 50,000 years ago we started to mash up incompatible concepts – and everything from science to fashion is the result

26 February 2014 by Mark Turner

THERE are many things that humans can't do. We can't run like cheetahs, fly like eagles or echolocate insects like bats. But the human contribution to the miracle of life is obvious: we are the origin of new ideas.

We hit upon new ideas, lots of them, on the fly, all the time. They arise constantly in our minds, and sometimes tumble out to influence other minds and change the world.

How do we do it? How does our thinking leap beyond our existing knowledge to make new ideas? The answer is that we blend multiple ideas that are already in our minds, and these blends contain new ideas that didn't exist before.

Blending is a basic mental operation, and many species may be capable of creating rudimentary blends.

Imagine, for instance, a dog that has learned the game of fetch from its master, who exploited the dog's instinct to retrieve. The dog's notion of playing fetch includes its master, but not me. Yet if I walk up to the dog with a ball, it might be able to blend its idea of playing fetch with its idea of me, so that, in the blend, there is something new. I'm now the one who throws the ball for the dog.

That is a simple blend, combining compatible notions. But human beings seem to have taken an additional step up the blending ladder. At some point, perhaps in the Upper Palaeolithic era, which began around 50,000 years ago, we developed the ability to blend ideas that are in strong conflict, or incompatible. This advanced blending capacity is the source of our creativity.

Consider the "lion man" ivory figurine, which was carved at least 32,000 years ago, and discovered, smashed to bits, in a cave in southern Germany in 1939 (its gender is actually indeterminate, but I have adopted the term "lion man" for ease of reference). Its shards lay neglected for decades, but since its reassembly in 1998 scientists have pointed to this figurine as evidence of the emergence of human creativity. What the figurine clearly shows is the mental ability to blend different concepts: lion and man are not merely held in mind at the same time, they are also used to create a new, blended, concept – a lion man, who is neither a lion nor a man. We would never confuse lions and men, yet, without being deluded, we can blend them to create a new idea. On top of this, we also blend our idea of the lion man with our idea of the carved ivory to conceive of the representation.

This may seem elementary. All over the world today, people constantly discern and create representations. Children see things in the clouds: dragons, ships, trees. People use twigs to sketch figures in the sand. But this capacity isn't elementary at all. If a person living before the Upper Palaeolithic era had possessed the flexible, creative ability for blending, he or she should have had no difficulty carving a face in stone. Yet not a single representation of a face – or anything else – has been found in the archaeological record prior to the era of the cave paintings in Europe.

One might argue that an advanced culture is needed to foster such creativity, but culture, I contend, is made possible by the capacity for advanced blending. In evolutionary terms, this capacity – and with it, the ability to create representations of our ideas – emerged fairly recently. And once it did, it changed practically everything.

Blends like the idea of the lion man can mislead us into thinking that blending is strange, rare and noticeable. On the contrary, it happens all the time, with most of it invisible to consciousness, proceeding quickly in the powerful backstage of cognition, where we can manage complex operations far beyond the capacity of consciousness.

Let's take an everyday example: the cyclic day. In our experience, there is one day and then another day and so on, in a sequence that stretches out indefinitely, forward and backward. The days in that sequence are all quite different. They don't repeat. But day after day after day, indefinitely, is too much to comprehend, too much to fit inside our working memory. It isn't mentally portable. So we blend these different days into a conception of a cyclic day.

There are analogies and disanalogies across the different days we experience. The analogies are packed into one thing in the blend: the day. The disanalogies are packed into change for that thing: the day starts over every dawn and repeats – in other words it is cyclic. Because of blending, all the days that have ever happened or will happen can be packed into a tight, tractable, manageable, human-scale idea – the cyclic day.

The cyclic day isn't just an abstraction. There is new stuff in the blend that isn't in any of the individual days in the mental web to which the blend can be applied. Indeed, almost no blend consists exclusively of a structure that is equally shared by all the ideas upon which the blend draws. The concept of the lion man, for example, is not an abstraction of what is common to the concepts of "lion" and "man".

The ideas blended in our minds often contain sharp differences. And yet, far from blocking new ideas, these impossibilities seem to create them. Consider the sentence "If I were my brother-in-law, I would be miserable". This sentence mixes up his intentionality and mine, his identity and mine, yet our talent for advanced blending allows us to understand this complex mix of causation, intentionality and participants.

Blending is a mental tool that cultures must sometimes deploy for a long time to achieve specific blends or generic blending templates. This process has resulted in art, science, religion, mathematics, language, writing, fashion, advanced social cognition and a host of other creative human activities. Thus, although advanced blending is probably a fairly recent development in human evolution, and a small step in itself, it transformed the human mind. It didn't make us human so much as give us the ability to make ourselves human, an ongoing and dynamic process, stretching over the vast scope of human meaning.

<http://bit.ly/NbqTPB>

Kepler's Alien World Count Skyrockets

The number of known planets beyond the solar system took a giant leap thanks to a new technique that verifies candidate planets found by NASA's Kepler space telescope in batches rather than one-by-one.

Feb 26, 2014 01:10 PM ET // by Irene Klotz

The new method adds 715 planets to Kepler's list of confirmed planets, which previously totaled 246, scientists said Wednesday.

Combined with other telescopes' finds, the overall exoplanet headcount now reaches nearly 1,700.

"By moving ... to statistical studies in a 'big data' fashion, Kepler has showcased the diversity and types of planets present in our galaxy," astronomer Sara Seager, with the Massachusetts Institute of Technology, wrote in an email to Discovery News.

The growing census reinforces previous findings that small planets are most common in the galaxy -- a boon for future missions aimed at finding planets in habitable zones around parent stars, Seager said. It also shows that most planets, like those in our solar system, are part of multiple-planet systems. The 715 newly confirmed planets, for example, comprise 305 planetary systems. The similarity to our own solar system ends there, however. The study confirms:

A binary star system with a total of three planets, two of which transit one star and one of which transits the second.

A star with seven planets all orbiting their parent star closer than Earth circles the sun.

A star with five confirmed planets, four of which orbit in less than 14 days and the fifth with an 87-day period. That system, newly named Kepler-169, also may have a sixth planet in a 30-day orbital period.

The planets circling Kepler-169 have plenty of elbowroom compared to Kepler-80, which has five candidate planets all circling their parent star in less than 10 days.

"We validate the four outer candidates (of Kepler-80) ... to be planets," astronomer Jack Lissauer, with NASA's Ames Research Center in Moffett Field, Calif, wrote in paper to be published in The Astrophysical Journal.

"The inner candidate has too short an orbital period for us to validate, but passes all of our other validation criteria," he wrote.

In a related paper in the same journal, astronomer Jason Rowe, also with NASA Ames, said the algorithm used to validate the 305 planetary systems has an accuracy rate of better than 99 percent.

"The vast majority of (the systems' 715 planets) have not been previously identified as planets," Rowe wrote.

The studies were based on the first two years of Kepler data. The telescope, which was launched in 2009, operated for another two years before a positioning system failure in 2013 forced NASA to suspend operations. The telescope worked by looking for slight dips in the amount of light coming from target stars caused by planets passing by, or transiting, relative to its line of sight.

NASA is reviewing proposals to use Kepler in an alternative mode for a mission known as K2.

<http://bit.ly/1fYtzgt>

Brain zap rouses people from years of vegetative state

People in a vegetative state showed signs of awareness after electric brain stimulation – and minimally conscious people were able to communicate again

26 February 2014 by Helen Thomson

TALK about an awakening. People who have been in a minimally conscious state for weeks or years have been temporarily roused using mild electrical stimulation.

Soon after it was applied to their brains, 15 people with severe brain damage showed signs of consciousness, including moving their hands or following instructions using their eyes. Two people were even able to answer questions for 2 hours before drifting back into their previous uncommunicative state.

"I don't want to give people false hope – these people weren't getting up and walking around – but it shows there is potential for the brain to recover functionality, even several years after damage," says Steven Laureys at the University of Liège in Belgium, who led the research.

People with severe brain trauma often fall into a coma. If they "awaken", by showing signs of arousal but not awareness, they are said to be in a vegetative state. This can improve to a state of minimal consciousness, where they might show fluctuating signs of awareness, which come and go, but have no ability to communicate.

External stimulation of the brain has been shown to increase arousal, awareness and aspects of cognition in healthy people. So Laureys and his colleagues wondered if it would do the same in people with severe brain damage. They used transcranial direct current stimulation (tDCS), which doesn't directly excite the brain, but uses low-level electrical stimulation to make neurons more or less likely to fire.

The team worked with 55 people who had experienced a traumatic brain injury or lack of oxygen to the brain and were in a minimally conscious or vegetative state. They placed electrodes over their left dorsolateral prefrontal cortex – an area involved in memory, decision-making and awareness. Then they delivered 20 minutes of stimulation to some of the people and a sham treatment to the others. The next day, the two groups received the opposite therapy.

During brain stimulation, 13 people with minimal consciousness and two people in a vegetative state showed signs of awareness that were observed neither before the stimulation nor after the sham treatment.

For most of these people the changes were moderate, but some recovered the ability to communicate, says Laureys. "Two patients emerged from a minimally conscious state altogether." When asked questions such as "Am I touching my nose?", they were able to answer by nodding their head or making specific eye movements.

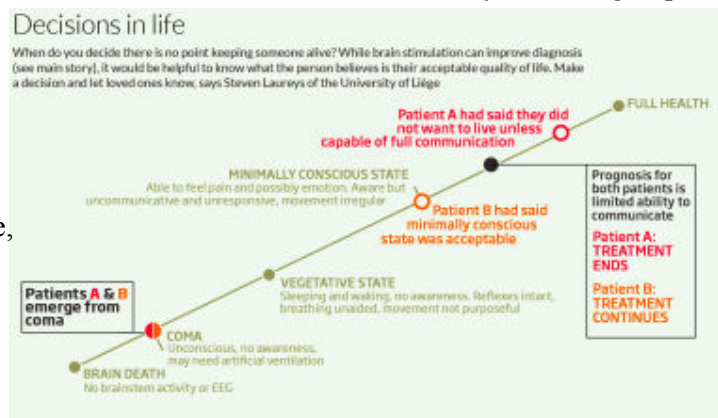
Others were able to respond to simple commands to nod, or squeeze their hand. All the effects lasted for about 2 hours. The findings will be published in the journal *Neurology*.

For some patients, it was only weeks since their trauma had happened, but others had been minimally conscious for years. This is important, says Laureys. "There's this dogma that if you don't see a change in 12 months you will never see it. This research challenges that."

"This is a very important study," says Tristan Bekinschtein, who studies consciousness at the University of Cambridge. If this treatment becomes a standard practice, he says, it will reveal a lot about how different brain networks become reactivated after severe head trauma.

It's not clear exactly how the treatment works, but it is likely that the stimulation pushes previously suppressed brain activity over a threshold. This possibly enhances processes that are involved in attention and working memory and underlie conscious tasks such as decision-making and moving.

John Whyte, director of the Moss Rehabilitation Research Institute in Philadelphia, Pennsylvania, says that tDCS might be used both as a treatment in its own right, and for screening people to diagnose their state and assess what treatment they might respond to. "This research is of considerable interest as it suggests another



potential treatment avenue," he says. "First, we need to determine whether these short-term effects can be amplified and made more durable."

Laureys's team is now doing just that – assessing the potential for more lasting arousal. The brain can be stimulated for longer periods of time as there seem to be no side effects, just a little tingling, Laureys says. Trials involving a full week of stimulation are under way. They also involve stimulating other areas of the brain. The results are not yet available.

This isn't the first time that medical interventions have aroused a silent brain. In 1999, Louis Viljoen – who had been in a persistent vegetative state for three years – began to make erratic movements at night. His doctors prescribed zolpidem, a sedative used to treat insomnia. Within minutes of being given the drug by his mother, Viljoen turned his head and said "hello mummy". The effect lasted a few hours. The drug now allows him to communicate for about 10 hours a day. Such a response is rare. Laureys's team found that zolpidem had no significant effect on any of 60 patients with brain damage (Functional Neurology, in press).

It isn't known how a sedative can rouse some patients – it may be that the damaged brain reacts differently. A drug used to treat Parkinson's called amantadine has also been found to help minimally conscious patients recover – possibly by increasing dopamine levels in brain networks vital to awareness and attention.

When people temporarily emerge from a minimally conscious state, it's hard to gauge how much they are really aware of. Laureys suggests that it might be like that moment when you wake up in a hotel and don't know where you are. But these trials raise uncomfortable questions. Is it right to rouse someone only to send them back to sleep a few hours later?

It can be challenging, admits Laureys. The patient's family is often in the room during the trials. "We explain to them that the effect will be of limited duration and that there is no room for subjectivity so we can't just ask any question. We need to keep all the trials the same." In his experience, though, the families are just happy that there are people trying new therapies.

"It's like we're opening and shutting a window for a few hours, and that could be perceived as cruel," says Joseph Fins, at Weill Cornell Medical College, New York, who was the first person to trial deep brain stimulation in a minimally conscious person. "But we didn't give these people brain damage, we are trying to make it better. These kinds of experiments show that a window exists, and now you know that you might be able to use other interventions to enhance that window."

The worst scenario, he says, is that the person has some aspects of awareness but they have been misdiagnosed as persistently vegetative. Brain stimulation could now be added to the tests used to make that diagnosis. It's an important distinction – someone in a vegetative state is thought to be unable to feel pain. Someone with minimal consciousness can feel pain and possibly emotions, too. "The key thing is getting the diagnosis right, that's the game-changer," says Fins.

It could also give doctors another tool to decide whether a person is likely to recover. About 5.3 million people in the US are living with a traumatic brain-injury-related disability, ranging from mild sensory impairment to persistent coma. "In some cases, members of your family can be left with difficult decisions about whether to remove life support," Laureys says. "And we can't make any decisions ethically if we're not sure about the diagnosis, prognosis and therapeutic options."

He says that while you are still healthy, you should discuss with friends and health professionals what you think is an acceptable quality of life and where you draw the line (see graphic).

<http://bit.ly/OJs8qg>

How can you ensure that your life is worth living?

Dramatic advances in communication with people in a minimally conscious state have provoked questions central to our ideas about what makes life worth living

TERRI SCHIAVO died after 15 years spent in a state that many fear as much or more than death itself.

In 1990, Schiavo suffered a heart attack that left her in a persistent vegetative state. With no clear record of her wishes, her fate became the subject of a bitter dispute that pitted her husband against her parents, divided US public opinion and prompted the intervention of president George W. Bush before being settled by the US Supreme Court in 2005.

Sadly, the Schiavo family's heartache is not unique. In fact, it is becoming more common. Last year, for example, a UK court ruled against resuscitating a devout Muslim who was in a minimally conscious state. His family had argued that he would have preferred to live on, believing this to be God's will.

Few people make "living wills" that specify how they would like to be treated in such situations. Once in a vegetative or minimally conscious state, they cannot express their wishes themselves, leaving physicians and family with the unenviable duty of choosing a course of action.

This scenario is about to become more fraught still. This week brings news of a remarkable discovery: stimulating the brains of people in such conditions can rouse them, for short periods, to the point where they can answer simple questions (see "Brain zap rouses people from years of vegetative state").

This discovery has clear medical benefits: it should help doctors to make better assessments of patients' conditions. The hope is that researchers will be able to extend the stimulation, resulting in more significant brain activity and even, perhaps, a return to something resembling an acceptable quality of life.

Before then, there is a host of ethical issues. No one has yet asked the obvious questions: are you suffering? Do you want to live, or die? These questions will one day be asked, even if we don't yet know how to interpret any answers. We may not know any time soon. The only way to dictate our fate is to decide and record what we consider to be a life worth living.

<http://bit.ly/1hHSOOi>

Outside Fukushima exclusion zone, residents getting minor radiation dose

Equal to the normal background, but unlikely to cause detectable health problems.

by John Timmer - Feb 27 2014, 10:10am TST

While the damaged facilities at Fukushima have dumped a lot of radioactivity into the environment, most of it has ended up either in the ocean, or in the groundwater at the site itself. Outside the 20km exclusion zone, most of the radiation came from a single plume released in the first few days of the crisis. The plume drifted to the northwest, leading to the evacuation of some communities outside of the exclusion areas.

Does any of the radiation that traveled in that plume pose a threat to the people who have since returned? To find out, a large consortium of Japanese scientists performed a monitoring project on residents in three areas near Fukushima. They found that, while radiation exposure is elevated compared to natural background, the levels are still well below safety limits, and the long-term health risks are small enough that we're unlikely to detect the impact of the added exposure.

They did find, however, that residents involved in the cleanup had the highest exposures, which suggests continued monitoring of these workers should be a priority.

The research team identified three areas to recruit residents. One was to the southwest, away from where the airborne radiation spread. A second was to the north, just east of the area where the plume extended outside the exclusion zone. And finally, there was a site to the northwest, just outside the area evacuated because of the plume. Residents in these areas were given monitoring badges, their food was sampled, and dust samples were obtained from their environment.

The Japanese government is monitoring and removing food that shows signs of significantly elevated radioactivity. Still, many residents of the areas maintain home gardens that could provide a route for radioactive contamination. The study, however, showed that most of the residents were seeing food-borne doses in the microSievert/year range, well below the limit of 1 Sv/year. Airborne exposure was also minimal.

These factors left environmental exposure as the largest potential risk. And it was larger than either of the others, with annual doses likely to be over a microSievert per year. "The mean of the dose rates in 2012 was greater than the ordinary permissible dose level of 1 mSv/y (31), particularly in the [area at the northern edge of the plume]," the authors note, "but was less than the permissible annual dose of 20 mSv/y during radiation emergencies "

All told, it was about equal to the natural background radiation in Japan (which is below that of the natural background in the US - 2 mSv/y vs. 6 mSv/y). When used to estimate the health risks of cumulative exposure, it suggests that the risk of developing a solid tumor is only increased by one percent. Since that risk starts out low, any change in cancer incidence is likely going to be below our ability to detect.

In the area near the edge of where the plume extended over land, there were some individuals who had elevated levels of environmental exposure. Follow-up interviews revealed that these people typically worked outdoors in the nearby forests, often as part of the effort to clean up the contamination. Again, this exposure is still below safety levels, but it is significantly higher than the exposure of other people in the area. And the highest dose they saw was from someone who snuck into his former home in the exclusion zone. These high exposure individuals suggest that the cleanup work may need to go on for some time, and the workers involved in it will need to be monitored carefully.

Of course, critically, this analysis excludes people from the area inside the site of the accident, or any of the people working to contain and clean up existing leaks. But it shows that, in part because of the happenstance of weather and the site's location on the Pacific, Japan itself has escaped most of the worst of Fukushima's radiation.

PNAS, 2014. DOI: 10.1073/pnas.1315684111 (About DOIs).

http://www.eurekalert.org/pub_releases/2014-02/foas-wdc022714.php

Why dark chocolate is good for your heart

New research in the FASEB Journal suggests that consumption of dark chocolate lowers the augmentation index, a key vascular health predictor, and reduces adhesion of white blood cells to the vessel wall

It might seem too good to be true, but dark chocolate is good for you and scientists now know why. Dark chocolate helps restore flexibility to arteries while also preventing white blood cells from sticking to the walls of blood vessels. Both arterial stiffness and white blood cell adhesion are known factors that play a significant role in atherosclerosis. What's more, the scientists also found that increasing the flavanol content of dark chocolate did not change this effect. This discovery was published in the March 2014 issue of The FASEB Journal.

"We provide a more complete picture of the impact of chocolate consumption in vascular health and show that increasing flavanol content has no added beneficial effect on vascular health," said Diederik Esser, Ph.D., a researcher involved in the work from the Top Institute Food and Nutrition and Wageningen University, Division of Human Nutrition in Wageningen, The Netherlands. "However, this increased flavanol content clearly affected taste and thereby the motivation to eat these chocolates. So the dark side of chocolate is a healthy one."

To make this discovery, Esser and colleagues analyzed 44 middle-aged overweight men over two periods of four weeks as they consumed 70 grams of chocolate per day. Study participants received either specially produced dark chocolate with high flavanol content or chocolate that was regularly produced. Both chocolates had a similar cocoa mass content. Before and after both intervention periods, researchers performed a variety of measurements that are important indicators of vascular health. During the study, participants were advised to refrain from certain energy dense food products to prevent weight gain. Scientists also evaluated the sensory properties of the high flavanol chocolate and the regular chocolate and collected the motivation scores of the participants to eat these chocolates during the intervention.

"The effect that dark chocolate has on our bodies is encouraging not only because it allows us to indulge with less guilt, but also because it could lead the way to therapies that do the same thing as dark chocolate but with better and more consistent results," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal.

"Until the 'dark chocolate drug' is developed, however, we'll just have to make do with what nature has given us!"

Details: Diederik Esser, Monica Mars, Els Oosterink, Angelique Stalmach, Michael Müller, and Lydia A. Afman. Dark chocolate consumption improves leukocyte adhesion factors and vascular function in overweight men. FASEB J. March 2014 28:1464-1473; doi:10.1096/fj.13-239384 ; http://www.fasebj.org/content/28/3/1464.abstract

<http://bit.ly/1fYuF5M>

Origin of organs: Thank viruses for your skin and bone

NEXT time you have a cold, rather than cursing, maybe you should thank the virus for making your skin.

27 February 2014 by Michael Slezak

Genes borrowed from viruses seem to give cells the ability to grow into tissues and organs, and even reproduce sexually. Without these genes, animals could not have evolved beyond simple blobs of cells.

Our cells often need to fuse with other cells, making big cells with multiple nuclei. They do this with the help of proteins on their outer surfaces that stick the cell's walls together and then break them open, so the insides can mix. This mixing is essential for the production of most organs – such as muscles, skin and bone – and even for reproduction, when eggs and sperm fuse. For instance, fused cells form barriers in the placenta that prevent harmful chemicals crossing into the fetus, and internal tubes like blood vessels are also made of fused cells.

But despite its importance, nobody knows how cell fusion evolved. That is partly because the proteins responsible are hard to spot. Only two types of cell fusion protein have been identified so far. The first was syncytin, found in 2000, which is essential for the formation of the human placenta. The gene for syncytin came from a virus (Nature, doi.org/c53gpz).

Then in 2002, a second protein called EFF-1 was found. It helps form the skin of the roundworm *Caenorhabditis elegans*, which biologists often study because it is so simple (Developmental Cell, doi.org/cd7mcf). By 2007 it was clear that EFF-1 was one of a family of similar proteins, called FF proteins, after a similar protein called AFF-1 was also found. Now Felix Rey of the Pasteur Institute in Paris, France, has found that the FF family of cell fusion proteins also comes from viruses.

Rey's team figured out the 3D structure of the EFF-1 protein using crystallography and X-ray diffraction – the same kinds of techniques that were used to determine the structure of DNA in the 1950s. The structure of EFF-1 resembles that of a protein made by viruses, and the active part – which does the work of linking one cell to another – is virtually identical. Viruses use the protein to rip open the membrane of a cell, which they can then

infect. In the worms, both cells must have the protein before they can fuse, but the protein still works in a similar way. He presented his results at the Lorne Conference on Protein Structure and Function in Australia last month, and they have been accepted by the journal *Cell*.

Since EFF-1 is so similar to the viral protein, the gene for it almost certainly came from a virus that infected one of the worm's ancestors, says Rey. That is not unprecedented: the human genome is littered with DNA that slipped in when viruses infected a cell of an ancestor. But few of these bits of code are known to have important functions. While EFF-1 has only been studied in *C. elegans*, Rey says many other organisms may use the same protein. Since syncytin is also viral, all the cell fusion proteins found so far are from viruses. Does that mean early animals picked up all these proteins through viral infections?

"That's the gut feeling we have," says Fasseli Coulibaly from Monash University in Melbourne, Australia. "It's the most enticing hypothesis but as scientists we need to look into it. If this is true, that's a huge advance."

It is plausible that all cell fusion stems from viral genes slipping into our genome, says Elizabeth Chen of Johns Hopkins University in Baltimore, Maryland. "But the jury is still out." Right now her team is trying to find the protein responsible for cell fusion in muscle tissue. It is too early to tell if it came from a virus.

The findings so far suggest a pattern, says Rey. If cell fusion proteins came from several sources, you wouldn't expect the first two found to be from viruses. If viruses really did gift us cell fusion, then they are responsible for complex multicellular life, says Coulibaly. Cells could have clumped together into clusters on their own, but without the ability to fuse they could not have evolved into anything advanced like sponges, let alone humans.

"Before cells can make something like skin or a digestive tract – as soon as you are thinking tissue and organs – usually you need some kind of fusion," says Coulibaly. "If it's proved, it could be a Nobel prize."

Rey goes even further. He speculates that viruses may be responsible for the very existence of multicellular organisms. Viruses come and go between different cells, exchanging genetic information between them. "This makes me think that viruses have contributed enormously to the communication between cells, and to the appearance of multicellular organisms on Earth," Rey says.

http://www.eurekalert.org/pub_releases/2014-02/uosd-mdc022714.php

More dangerous chemicals in everyday life: Now experts warn against nanosilver

Nano-silver can penetrate our cells and cause damage

Endocrine disrupters are not the only worrying chemicals that ordinary consumers are exposed to in everyday life. Also nanoparticles of silver, found in e.g. dietary supplements, cosmetics and food packaging, now worry scientists. A new study from the University of Southern Denmark shows that nano-silver can penetrate our cells and cause damage. Silver has an antibacterial effect and therefore the food and cosmetic industry often coat their products with silver nanoparticles. Nano-silver can be found in e.g. drinking bottles, cosmetics, band aids, toothbrushes, running socks, refrigerators, washing machines and food packagings.

"Silver as a metal does not pose any danger, but when you break it down to nano-sizes, the particles become small enough to penetrate a cell wall. If nano-silver enters a human cell, it can cause changes in the cell", explain Associate Professor Frank Kjeldsen and PhD Thiago Verano-Braga, Department of Biochemistry and Molecular Biology at the University of Southern Denmark. Together with their research colleagues they have just published the results of a study of such cell damages in the journal *ACS Nano*.

The researchers examined human intestinal cells, as they consider these to be most likely to come into contact with nano-silver, ingested with food. "We can confirm that nano-silver leads to the formation of harmful, so called free radicals in cells. We can also see that there are changes in the form and amount of proteins. This worries us", say Frank Kjeldsen and Thiago Verano-Braga.

A large number of serious diseases are characterized by the fact that there is an overproduction of free radicals in cells. This applies to cancer and neurological diseases such as Alzheimer's and Parkinson's.

Kjeldsen and Verano-Braga emphasizes that their research is conducted on human cells in a laboratory, not based on living people. They also point out that they do not know how large a dose of nano-silver, a person must be exposed to for the emergence of cellular changes. "We don't know how much is needed, so we cannot conclude that nano-silver can make you sick. But we can say that we must be very cautious and worried when we see an overproduction of free radicals in human cells", they say.

Nano-silver is also sold as a dietary supplement, promising to have an antibacterial, anti-flu and cancer-inhibitory effect. The nano-silver should also help against low blood counts and bad skin. In the EU, the marketing of dietary supplements and foods with claims to have medical effects is not allowed. But the nano-silver is easy to find and buy online. In the wake of the University of Southern Denmark-research, the Danish Veterinary and Food Administration now warns against taking dietary supplements with nano-silver. "The

recent research strongly suggests that it can be dangerous", says Søren Langkilde from the Danish Veterinary and Food Administration to the Danish Broadcasting Corporation (DR).

Ref: *Insights into the Cellular Response Triggered by Silver Nanoparticles using Quantitative Proteomics. ACS NANO.*
<http://dx.doi.org/10.1021/nn4050744>

http://www.eurekalert.org/pub_releases/2014-02/mgh-hfm022614.php

High-calorie feeding may slow progression of ALS

Small study provides preliminary evidence that increased calorie intake could extend survival

Increasing the number of calories consumed by patients with amyotrophic lateral sclerosis (ALS) may be a relatively simple way of extending their survival. A phase 2 clinical trial led by Massachusetts General Hospital (MGH) physicians found that ALS patients receiving a high-calorie, high-carbohydrate tube-feeding formula lived longer with fewer adverse events than participants who received a standard formula designed maintain their weight. While the small size of the trial indicates results need to be interpreted with caution, the authors are optimistic that improved nutrition could make a significant difference for patients with ALS.

"We are particularly excited because these results provide the first preliminary evidence that a dietary intervention may improve life expectancy in ALS, and they are strongly supported by epidemiological and animal data," says Anne-Marie Wills, MD, of the MGH Department of Neurology and Neurological Clinical Research Institute (NCRI), corresponding author of the paper, which has been published online in *The Lancet*. "This strategy has never been tested before in ALS, and we are optimistic that it may provide a new, effective and inexpensive therapy for this devastating illness."

Also known as Lou Gehrig's disease, ALS is a progressive neurodegenerative disease affecting motor neurons in the brain and spinal cord. Death of these nerve cells stops the transmission of neural impulses to muscle fibers, leading to weakness, paralysis and usually death from respiratory failure. ALS patients typically lose a significant amount of weight, both because their muscles atrophy from disuse and because they are physically unable to consume enough calories to maintain weight. Recent studies suggest that reduced appetite and an elevated metabolic level may also contribute to weight loss. Supplementary nutrition via a tube passing directly into the stomach is usually recommended as the disease progresses, although there is little consensus about when tube feeding should begin.

More than 15 years ago it was observed that malnutrition was associated with shorter survival in ALS patients, and many subsequent studies confirmed that patients who weigh more appear to live longer and have slower disease progression. Studies in a mouse model of ALS found that those on a high-calorie, high-fat diet gained weight and survived longer than those on a normal diet. The current study was designed primarily to test the safety and tolerability of high-calorie nutritional formulas – with or without the excess fats included in the mouse study – in patients with advanced ALS.

Carried out at 12 centers across the U.S., the study enrolled 24 ALS patients who had lost a significant percentage of their original body weight and were receiving nutrition via tube feeding. Participants were randomly divided into three groups: a control group receiving a nutritional formula designed for weight stability and two groups receiving formulas designed to provide 125 percent of the calories needed to maintain their weight. One of the high-calorie formulas was high in fats; the other was high in carbohydrates. During the four-month intervention period, participants recorded their tube feeding intake, along with anything they were able to consume by mouth and weekly measures of weight. At monthly study visits, measurements were taken of participants' fat and lean body mass; blood levels of cholesterol, insulin and other factors that could be affected by nutrition; and functions typically compromised by ALS.

At the end of the intervention period, none of the eight participants receiving the high-carbohydrate formula had withdrawn because of adverse events, while one of the six on the high-fat formula and three of the six in the control group discontinued participation because of adverse events. (Four of those who originally enrolled dropped out before the intervention began.) Those on the high-carbohydrate formula also gained a modest amount of weight, while control group participants maintained their weight. Participants receiving the high-fat formula actually lost weight, even though they had taken in more than 150 percent of the calories estimated to maintain their weight.

During the five-month follow-up period after the intervention, none of those in the high-carbohydrate group died, but one in the high-fat group and three in the control group died, all from respiratory failure. Participants in the high-carbohydrate group also had a slower drop in their functional scores than the control group, although the difference was not statistically significant. None of the adverse events that occurred in either of the high-calorie groups were cardiovascular; the high-fat formula was not associated with increases in cholesterol, and neither of the high-calorie diets caused abnormal blood glucose or insulin levels.

"While it's not possible to make clinical recommendations based on this single, small study, I think the results support the importance of avoiding weight loss in this disease," says Wills, an assistant professor of Neurology at Harvard Medical School. "We're hoping to obtain funding for a large study of whether nutrition counseling to encourage weight gain – something not currently covered by health insurers – can help slow the progression of ALS, and I'm optimistic that interventions designed to maintain or increase weight could be even more effective if started before patients have lost a significant amount of weight."

Additional co-authors of the Lancet report include Merit Cudkowicz, MD, chief of MGH Neurology and NCRI; Jane Hubbard, RD, MGH Clinical Research Center; and Eric Macklin, PhD, MGH Biostatistics Center. The study was primarily supported by a grant from the Muscular Dystrophy Association.

http://www.eurekalert.org/pub_releases/2014-02/uob-aa022614.php

An ancient 'Great Leap Forward' for life in the open ocean

University of Bristol researchers study genomic data of cyanobacteria to shed new light on how complex life evolved on Earth

It has long been believed that the appearance of complex multicellular life towards the end of the Precambrian (the geologic interval lasting up until 541 million years ago) was facilitated by an increase in oxygen, as revealed in the geological record. However, it has remained a mystery as to why oxygen increased at this particular time and what its relationship was to 'Snowball Earth' – the most extreme climatic changes the Earth has ever experienced – which were also taking place around then. This new study shows that it could in fact be what was happening to nitrogen at this time that helps solve the mystery.

The researchers, led by Dr Patricia Sanchez-Baracaldo of the University of Bristol, used genomic data to reconstruct the relationships between those cyanobacteria whose photosynthesis in the open ocean provided oxygen in quantities sufficient to be fundamental in the development of complex life on Earth.

Some of these cyanobacteria were also able to transform atmospheric nitrogen into bioavailable nitrogen in sufficient quantities to contribute to the marine nitrogen cycle, delivering 'nitrogen fertiliser' to the ecosystem. Using molecular techniques, the team were able to date when these species first appeared in the geological record to around 800 million years ago.

Dr Sanchez-Baracaldo, a Royal Society Dorothy Hodgkin Research Fellow in Bristol's Schools of Biological and Geographical Sciences said: "We have known that oxygenic photosynthesis – the process by which microbes fix carbon dioxide into carbohydrates, splitting water and releasing oxygen as a by-product – first evolved in freshwater habitats more than 2.3 billion years ago. But it wasn't until around 800 million years ago that these oxygenating cyanobacteria were able to colonise the vast oceans (two thirds of our planet) and be fertilised by enough bioavailable nitrogen to then produce oxygen – and carbohydrate food – at levels high enough to facilitate the next 'great leap forward' towards complex life.

"Our study suggests that it may have been the fixing of this nitrogen 'fertiliser' in the oceans at this time that played a pivotal role in this key moment in the evolution of life on Earth."

Co-author, Professor Andy Ridgwell said: "The timing of the spread in nitrogen fixers in the open ocean occurs just prior to global glaciations and the appearance of animals. Although further work is required, these evolutionary changes may well have been related to, and perhaps provided a trigger for, the occurrence of extreme glaciation around this time as carbon was now being buried in the sediments on a much larger scale."

Dr Sanchez-Baracaldo added: "It's very exciting to have been able to use state of the art genetic techniques to help solve an age-old mystery concerning one of the most important and pivotal moments in the evolution of life on Earth. In recent years, genomic data has been helping re-tell the story of the origins of life with increasing clarity and accuracy. It is a privilege to be contributing to our understanding of how microorganisms have contributed to make our planet habitable."

'A Neoproterozoic Transition in the Marine Nitrogen Cycle' by Patricia Sanchez-Baracaldo, Andy Ridgwell and John Raven in Current Biology

http://www.eurekalert.org/pub_releases/2014-02/uoca-css022514.php

CU-led study says Bering Land Bridge a long-term refuge for early Americans

Population of hundreds or thousands likely lived on land bridge for up to 10,000 years

A new study led by the University of Colorado Boulder bolsters the theory that the first Americans, who are believed to have come over from northeast Asia during the last ice age, may have been isolated on the Bering Land Bridge for thousands of years before spreading throughout the Americas.

The theory, now known as the "Beringia Standstill," was first proposed in 1997 by two Latin American geneticists and refined in 2007 by a team led by the University of Tartu in Estonia that sampled mitochondrial DNA from more than 600 Native Americans. The researchers found that mutations in the DNA indicated a group of their direct ancestors from Siberia was likely isolated for at least several thousand years in the region

of the Bering Land Bridge, the now-submerged plain that lies between northeast Asia and Alaska once exposed by a significantly lower sea level.

CU-Boulder researcher John Hoffecker, lead author of a short paper article appearing in the Feb. 28 issue of Science magazine, said the Beringia Standstill model gained little traction outside of the genetics community after it was proposed and has been seen by some scientists outside of the field as far-fetched. But the new paper by Hoffecker and co-authors Scott Elias of Royal Holloway, University of London, and Dennis O'Rourke of the University of Utah adds credence to the Beringia Standstill idea by further linking the genetics to the paleoecological evidence.

"A number of supporting pieces have fallen in place during the last decade, including new evidence that central Beringia supported a shrub tundra region with some trees during the last glacial maximum and was characterized by surprisingly mild temperatures, given the high latitude," said Hoffecker of CU-Boulder's Institute of Arctic and Alpine Research. The last glacial maximum peaked roughly 21,000 years ago and was marked by the growth of vast ice sheets in North America and Europe. While a debate rages on about when early humans first migrated into the New World, many archaeologists now believe it was sometime around 15,000 years ago after retreating glaciers opened access to coastal and interior routes into North America. The relatively mild summer climate in Beringia at the time was caused by North Pacific circulation patterns that brought moist and relatively warm air to the region during the last glacial maximum. Geologists believe the Beringia gateway between Siberia and Alaska was more than 600 miles wide at the time.

Hoffecker and others are now theorizing that a population of hundreds or thousands of people parked itself in central Beringia for 5,000 years or more. One key to the extended occupation may have been the presence of wood in some places to use as a fuel to supplement bone, which burns hot and fast. Experiments have shown that at least some wood is necessary to make bone practical as a fuel.

Elias, a paleoecologist and also an INSTAAR affiliate, said research using fossil pollen, plant and insect material from sediment cores from the now submerged landscape show that the Bering Land Bridge tundra environment contained enough woody plants and trees like birch, willow and alder to provide a supplement to bone. Work by Elias and others included the analysis of certain beetle species that live in very specific temperature zones, allowing them to be used as tiny thermometers. The insects indicated that temperatures there were relatively mild during last glacial maximum that ran from about 27,000 years to 20,000 years ago, only slightly cooler than temperatures in the region today.

"The climate on the land bridge and adjacent parts of Siberia and Alaska was a bit wetter than the interior regions like central Alaska and the Yukon, but not a lot warmer," said Elias. "Our data show that woody shrubs were available on the land bridge, which would have facilitated the making of fires by the people there."

Evidence from the 2007 study indicated a set of genetic mutations in mitochondrial DNA, which is passed down from mother to offspring, clearly accumulated after the divergence of people from their Asian parent groups in Siberia but before their dispersal throughout the Western Hemisphere, said O'Rourke. In addition, ancient DNA from human skeletal remains found at a 24,000-year-old archaeological site in southern Siberia also appears consistent with the divergence of Native American groups from their Asian forbearers by that time window, he said.

"The genetic record has been very clear for several years that the Native American genome must have arisen in an isolated population at least by 25,000 years ago, and the bulk of the migrants to the Americas really didn't arrive south of the ice sheets until nearly 15,000 years ago," O'Rourke said. "The paleoecological data, which I think most geneticists have not been familiar with, indicate that Beringia was not a uniform environment, and there was a shrub tundra region, or refugium, that likely provided habitats conducive to continuous human habitation."

"From my view the genetics and paleoecology data come together nicely," said Hoffecker, who co-authored a 2007 book with Elias titled "The Human Ecology of Beringia." While the weakest link to the Out of Beringia theory is the lack of archaeological evidence, Hoffecker believes future research on now submerged parts of Beringia as well as lowlands in western Alaska and eastern Siberia that still remain above water may hold clues to ancient habitation by Beringia residents, who eventually moved on to be the first group to inhabit the Americas.

Hoffecker also believes that the Beringia inhabitants during the last glacial maximum could have made successful hunting forays into the uninhabited steppe-tundra region to both the east and west, where drier conditions and more grass supported a plentiful array of large grazing animals, including steppe bison, horse and mammoth.

There is now solid evidence for humans in Beringia before the last glacial maximum, as geneticists first predicted in 1997, said Hoffecker. After the maximum, there are two sets of archaeological remains dating to

less than 15,000 years ago. "One represents a late migration from Asia into Alaska at that time," he said. "The other has no obvious source outside Beringia and may represent the people who are thought to have sheltered on the land bridge during the glacial maximum. "If we are looking for a place to put all of these people during the last glacial maximum, Beringia may be the only realistic option," said Hoffecker.

A video news story on the research is available at <http://www.colorado.edu/news>.

http://www.eurekalert.org/pub_releases/2014-02/wcmc-sut022414.php

Scientists uncover trigger for most common form of intellectual disability and autism

Finding may explain many brain disorders, lead to prevention and treatment

NEW YORK - A new study led by Weill Cornell Medical College scientists shows that the most common genetic form of mental retardation and autism occurs because of a mechanism that shuts off the gene associated with the disease. The findings, published today in *Science*, also show that a drug that blocks this silencing mechanism can prevent fragile X syndrome – suggesting similar therapy is possible for 20 other diseases that range from mental retardation to multisystem failure.

Fragile X syndrome occurs mostly in boys, causing intellectual disability as well as telltale physical, behavioral and emotional traits. While researchers have known for more than two decades that the culprit behind the disease is an unusual mutation characterized by the excess repetition of a particular segment of the genetic code, they weren't sure why the presence of a large number of these repetitions – 200 or more – sets the disease process in motion.

Using stem cells from donated human embryos that tested positive for fragile X syndrome, the scientists discovered that early on in fetal development, messenger RNA -- a template for protein production -- begins sticking itself onto the fragile X syndrome gene's DNA. This binding appears to gum up the gene, making it inactive and unable to produce a protein crucial to the transmission of signals between brain cells.

"Until 11 weeks of gestation, the fragile X syndrome gene is active – it produces its messenger RNA and protein normally. Then, all of a sudden it turns off, and stays off for the rest of the patient's lifetime, causing fragile X syndrome. But scientists have not understood why this gene gets shut off," says senior author Dr. Samie Jaffrey, a professor of pharmacology at Weill Cornell Medical College. "We discovered that the messenger RNA can jam up one strand of the gene's DNA, shutting down the gene -- which was not known before.

"This is new biology -- an interaction between the RNA and the DNA of the fragile X syndrome gene causes disease," Dr. Jaffrey says. "We are coming to understand that RNAs are powerful molecules that can regulate gene expression, but this mechanism is completely novel -- and very exciting."

The malfunction occurs suddenly -- before the end of the first trimester in humans and after 50 days in laboratory embryonic stem cells. At that point, the messenger RNA produced by the fragile X syndrome gene makes what the researchers call an RNA-DNA duplex -- a particular arrangement of molecules in which the messenger RNA is stuck onto its DNA complement. (DNA produces two complementary strands of the genetic code responsible for human development and function. The four nucleic acids in the genomic code -- A, C, G, T -- have specific complements. In the case of fragile X syndrome, the repeat sequence in question is CGG. Therefore, RNA binds to its GCC complement on one strand of DNA.)

The RNA-DNA duplex then shuts down production of the fragile X syndrome gene, causing the loss of a protein needed for communication between brain cells. The gene then remains inactive for life. A normal fragile X gene -- one with fewer than 200 CGG repeats -- stays active in a person without the disorder, and produces the necessary protein. However, the mutant fragile X gene contains more than 200 CGG repeats, resulting in fragile X syndrome. Fragile X occurs in about 1 in 4,000 males and 1 in 8,000 females.

"Because the fragile X syndrome mutation is a repeat sequence, it is very easy for just a small portion of this sequence in the messenger RNA to find a matching repeat sequence on the DNA," Dr. Jaffrey says. "This is a unique feature of repeat sequences. When there are 200 or more repeats, the RNA-DNA interaction locks into place."

Hope for treatment – and other disorders

Dr. Jaffrey and his team, which includes researchers from The Scripps Research Institute in Florida and Albert Einstein College of Medicine in the Bronx, sought to find out why the disease is switched on when the CGG repeat is present in 200 to as many as 1,000 copies. "Utilizing traditional ways to solve this puzzle has been impossible," he says. "Human fragile X syndrome genes introduced into mice and cells in the laboratory never turn off, no matter how many CGG repeats the genes have."

So the scientists turned to human embryonic stem cells. Co-authors Dr. Zev Rosenwaks, director and physician-in-chief of the Ronald O. Perleman and Claudia Cohen Center for Reproductive Medicine and director of the Stem Cell Derivation Laboratory of Weill Cornell Medical College, and Dr. Nikica Zaninovic, assistant

professor of reproductive medicine, generated stem cell lines from donated embryos that tested positive for fragile X syndrome. "These stem cells were critical to the success of this research, because they alone allowed us to mimic what happens to the fragile X gene during embryonic development," says Dr. Dilek Colak, a postdoctoral scientist in Dr. Jaffrey's laboratory and the first author of the study.

The stem cells were coaxed to become brain neurons, and at about 50 days, they differentiated in the same way that an embryo's brain is developing at 11-plus weeks when the fragile X syndrome gene is switched off. The researchers then used a drug developed by co-author Dr. Matthew Disney of the Scripps Research Institute that binds to CGG in the fragile X gene's RNA before and after the 50-day switch. Strikingly, the gene never stopped producing its beneficial protein.

That suggests a potential prevention or treatment strategy for fragile X syndrome, Dr. Jaffrey says. "If a pregnant woman is told that her fetus carries the genetic mutation causing fragile X syndrome, we could potentially intervene and give the drug during gestation. This may delay or prevent the silencing of the fragile X gene, which could potentially significantly improve the outcome of these patients," he says.

The researchers are now looking for similar RNA-DNA duplexes in other trinucleotide repeat diseases, including Huntington's disease (a degenerative brain disease), myotonic dystrophy 1 and 2 (a multisystem progressive disease), Friedrich's ataxia (a progressive nervous system disorder), Jacobsen syndrome (an intellectual disorder), and familial amyotrophic lateral sclerosis (a motor neuron disease), among others. "This completely new mechanism by which RNAs can direct gene silencing may be involved in a lot of other diseases," Dr. Jaffrey says. "Our hope is that we can find drugs that interfere with this new type of disease process."

Co-authors include Michael S. Cohen from Weill Cornell Medical College; Dr. Wang-Yong Yang from The Scripps Research Institute; and Dr. Jeannine Gerhardt from Albert Einstein College of Medicine.

This work was supported by the Tri-Institutional Stem Cell Initiative (Tri-SCI) Grant 2008-019, New York Stem Cell Foundation-Druckenmiller Fellowship, Life Sciences Research Foundation Fellowship and Tri-SCI postdoctoral fellowship, and a FRAXA postdoctoral fellowship. Portions of this project not involving non-NIH registry stem cells were supported by NIH R01 MH80420 and NIH R01 GM079235.

<http://bit.ly/1hvwZoo>

Cheese Chunks Adorn Ancient Mummies

The world's oldest cheese has been found on the necks and chests of perfectly preserved mummies buried in China's desert sand.

Feb 27, 2014 12:00 PM ET // by Rossella Lorenzi

Dating back as early as 1615 B.C., the lumps of yellowish organic material have provided direct evidence for the oldest known dairy fermentation method. The individuals were likely buried with the cheese so they could savor it in the afterlife.

Although cheese-making is known from sites in northern Europe as early as the 6th millennium B.C. and was common in Egypt and Mesopotamia in 3rd millennium B.C., until now no remains of ancient cheeses had been found.

Lumps of cheese, shown with arrowheads, were collected from the neck and chest of a female mummy known as the "Beauty of Xiaohe." Inset shows an enlarged view of a cheese lump. Yimin Yang and Yusheng Liu

The 3,600-year-old cheese was discovered during archaeological excavations carried between 2002 and 2004 at the Xiaohe cemetery, in the inhospitable Taklamakan desert in northwestern China, led by Idelisi Abuduresule from Cultural Relics and Archaeology Institute, Ürümqi.

Also known as Small River Cemetery Number 5, the burial was first discovered in 1934 by Sweden archaeologist Folke Bergman and it's part of several archaeological sites spread in the Tarim Basin.

The cemetery was built on a large natural dune and houses hundreds of mysterious mummies with Caucasian features, buried into massive wooden coffins resembling upside-down boats. "Recent DNA studies showed the population of these sites was mixed, European and Asian," Anna Shevchenko, proteomics specialist in Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany, told Discovery News.

Taklamakan literally means "go in and you won't come out." The area, with its salty, hyper-dry sands, extreme hot in summer and cold in winter, provided the perfect conditions for natural mummification.

Moreover, the boat-like coffins were covered by several layers of cowhide, which sealed them from air, water and sand as if they had been "vacuum-packed."

Skin and hair, baked onto the dehydrated corpses, remained almost intact, as well as woolen textiles, plant seeds, woven grass baskets and clumps of organic material around the neck and chest of the mummified bodies. No pottery was found that could be associated with making or consuming food.



The researchers lead by Chinese team leader Changsui Wang from the University of Chinese Academy of Sciences collected 13 samples of the yellowish organic material from 10 tombs and mummies, which included the so-called "Beauty of Xiaohe" -- a 3,800-year-old female mummy wrapped in a finely crafted shroud, bearing Caucasian features such as a long nose and light hair.

Protein analysis performed in Dresden showed the organic material wasn't butter or milk, but a cheese made by robust, easily scalable kefir fermentation. Shevchenko explained that such analysis is common in medical and biological science, but not in archaeology. "Usually, proteins are either ignored or protein bulk content is estimated to characterize the nutritional properties," Shevchenko said.

"According to common belief, they are difficult to recover from the sample matrix, totally degraded and samples heavily contaminated by environment, therefore the analyzed are hardly meaningful," she added. But according to the researchers, who have detailed their finding in an upcoming issue of the Journal of Archaeological Science, proteins do survive under extreme conditions. Furthermore, in contrast to commonly analyzed lipids, they may bear the hallmarks of technological processes used to prepare the food. Altogether, they can be highly informative molecules.

"Our work opens new perspectives in the analysis of ancient material. But most importantly, it shows the technology behind ancient cheese-making," Germany team leader Andrej Shevchenko, an analytical chemist at Germany's Max Planck Institute of Molecular Cell Biology and Genetics, told Discovery News. Indeed, the analysis revealed Xiaohe's cheese wasn't made with rennet, an chymosin containing enzyme complex from calf intestine which was widely used since ancient times for curdling ruminant milk. It was instead produced by combining milk with a mix of *Lactobacillus kefirianofaciens* and other lactic acid bacteria and yeasts.

The technique is still used today to make kefir cheese, similar to cottage cheese, and a kefir probiotic lactose-free beverage, food with a slightly sour taste first mentioned by Marco Polo in 13th century.

"It's the earliest known dairy practice that persists until present times in an almost unchanged way. The discovery moves the mysterious history of kefir as far as to the second millennium B.C., making it the oldest known dairy fermentation method," archaeologist Yimin Yang at the University of Chinese Academy of Sciences, Beijing, told Discovery News.

Edible for the lactose-intolerant inhabitants of Asia, the mummies' cheese was very simple to make. Kefir fermentation did not require slaughtering the livestock to obtain the curdling enzyme. Furthermore, milk fat might have been physically removed in kefir cheese production, as now is commonly practiced in rural areas across the Eurasia steppe and also in Tibet. "It's the first direct evidence that milking spread to Eastern Eurasia," Wang said.

Kefir production could have been scaled up or down according to the actual demand: dried kefir starter grains can be stored for years without losing their fermentation capacity. Fermented milk could be either consumed as a probiotic beverage or curdled protein mass strained into a cheese with extended shelf life and high nutrition value. "This is a technology with the potential for mass production. It could have changed the nutritional habits of ancient populations of Eastern Eurasia," Andrej Shevchenko said.

<http://bit.ly/1cft05b>

Pancreatic cancer's killer trick offers treatment hope

Pancreatic cancer's deadliest trick could be its undoing.

28 February 2014 by Michael Slezak

Despite each person's tumours having very different genetic mutations, they all cause the same metabolic changes that help it grow. What's more, drugs already exist that can block the process.

Pancreatic cancer is the most lethal of all common cancers – 95 per cent of people die within five years of diagnosis. One reason it is so deadly is that no two cases are genetically the same. That means the tumour is more likely to evolve resistance to drugs, and that genomic studies aiming to find common mutations that could be targeted by treatment have fallen flat.

So Darren Saunders and colleagues at the Garvan Institute of Medical Research in Sydney, Australia, tried a different approach. As well as looking for variations in the genome of different people's tumours, they also looked at the biological processes at work in the cells.

To do this, they switched from using dead tumour cell samples to patient-derived tumour cell lines, in which fresh samples of a person's tumour are grafted onto mice and grown to the required volumes. Growing them in animals makes for more lifelike tumours, and can produce large quantities of tissue for study. This bank of living tumour cells allowed the team to study not only the genetics of the cells, but also how genetic mutations in the mitochondria – which drive energy production in the cell – caused changes in the cell's metabolism.

To analyse the tumour cells' metabolism, they used a technique called "metabolomics". This involves crushing live tumour cells and measuring the metabolites they contain using a mass spectrometer.

"You can think of it like lines on a train map," says Saunders. "Metabolomics allows us to map those pathways and see which ones are switched on and switched off [in a cell]."

Putting together their analyses of the mitochondrial DNA in each tumour cell line and the metabolic pathways at work, the team were able to deduce how each cell line's genetics directly affected its ability to multiply. They found that pancreatic cancer cells consume not only glucose, as normal cells do, but also glutamine. This leads to the production of fatty acids – the building blocks of new cells – thereby allowing the tumours to proliferate wildly. "Instead of using fuel for energy, they switch to using fuel to build new cells," Saunders says. The team presented its results at the Lorne Cancer Conference in Australia last month.

This process has been seen before in other cancers, but this is the first time it has been shown to be involved in all pancreatic tumours, and that each tumour evolved different genetic mechanisms to do this.

The team was also able to see exactly how the cancers pulled off this trick. Each tumour they studied switched off the electron transport chain, which is involved in energy production. "The cells in each tumour are finding a different way to do that," Saunders says. Since this happened in all 12 cell lines studied so far, each originating from a different tumour, Saunders suspects it's the key change that makes pancreatic cancer so aggressive. The team now plan to genetically engineer healthy cells to produce the same metabolic behaviour. If those become cancerous, it will further prove the hypothesis.

The find offers enormous hope for treatment, says Saunders. There are drugs already known to target this chain. So it doesn't matter that each person's tumour might find different ways to switch the chain off, drugs ought to be able to reverse the process. The team is already testing the drugs in the tumour cell lines it created. If all goes well, animal testing could start within six months, says Saunders.

Finding these similarities between the tumours offers new hope for treating a cancer which seemed too varied to target effectively, says Claudio Santos at University College London. "So perhaps in this age of cancer genomics showing how diverse and heterogenous human cancer is, we should be focusing on the common effects that different mutations lead to," he says.

Personal treatment

When Andrew Biankin walked into the Garvan Institute of Medical Research in Sydney, Australia, in 1998 and said he wanted to study pancreatic cancer, the head of the department was unimpressed. "We have a problem," said Rob Sutherland. "You don't know anything about research, and I don't know anything about pancreatic cancer."

Sutherland couldn't know that he would be diagnosed with pancreatic cancer almost a decade later. By then Biankin, now at the University of Glasgow, UK, had sequenced the genomes of 100 tumours and found they were all different. So he created a way to graft tumours onto mice to test out treatments (see main story).

Biankin's team did this with Sutherland's tumour, "and hit it with about a dozen drugs to see which ones it would respond to". The drugs didn't work, and Sutherland died in 2012. But the finding that all these genetic differences trigger the same cellular pathway provides hope for others. Catherine de Lange

<http://phys.org/news/2014-02-earth.html>

How Earth was watered

Early Earth's accidental deluge via water-carrying comets has long been a stumbling block for those interested in life on other planets.

Scientists agree that life needs water to evolve. But if water only arrives through chance impacts with comets, then life elsewhere might indeed be rare. Water is common among the meteorites and other small bodies whose collisions formed the Earth, but scientists have long believed that the intense heat of the events dried out the young planet. Water must have arrived later, splashing down from comets after the planet was formed.

New research, however, is changing that view. Evidence is mounting that the planet's water arrived early, during formation, aboard meteorites and small bodies called "planetesimals." The work also suggests that though the planet-forming collisions were so energetic that they led to oceans of magma and widespread melting, even the intense heat would not have dried out the planet completely.

The emerging view of a watery birth for the Earth has raised the hopes of scientists seeking extrasolar life. If the presence of water isn't left to chance collisions but instead is a product of the planet-forming process, then oceans where life can evolve may be common after all. "It is very possible that many planets are born with liquid water oceans," said Linda Elkins-Tanton, director of the Carnegie Institution for Science's Department of Terrestrial Magnetism.

Elkins-Tanton spoke Wednesday at the Geological Lecture Hall. Her talk, "Building Earth-like Planets," was part of the Evolution Matters lecture series of the Harvard Museum of Natural History. Elkins-Tanton studies the evolution of terrestrial planets and the relationship between Earth and its life forms.

One problem with the water-from-comets theory, Elkins-Tanton said, is that evidence has emerged that water was present on Earth far earlier than previously thought. The planet's oldest rocks date back 4.03 billion years, but there's a material older than rocks, called "detrital zircons," that formed some 4.40 billion years ago, just 164 million years after the first solids began to form out of the protoplanetary disk. And some of those zircons show evidence of having been created in contact with water.

Another issue with the comet theory, Elkins-Tanton said, is that the water on most comets doesn't match that on Earth. Water is made up of oxygen and hydrogen. Hydrogen's nucleus is normally made up of one proton, but the nucleus of a different form, called deuterium, has a proton and a neutron. Scientists can fingerprint water using the ratio of regular hydrogen to deuterium. For most comets, that ratio doesn't match water on Earth, she said.

Meanwhile, the water in meteorites and planetesimals does match that of Earth. But before scientists could settle on those bodies as the source of the planet's water, they had to solve another problem. Those bodies had up to 18 percent water, much more than Earth, and scientists couldn't think of a reasonable process to explain where it all went.

The answer that has emerged, Elkins-Tanton said, is that much is lost in the development of a planet. Planetesimals that are large enough have an internal heating process, powered by the decay of an isotope of aluminum, which is unknown on Earth. This can cause water to rise to the surface, where much is lost to space. The remaining water is close to that of Earth, Elkins-Tanton said. With the right isotopes in water and roughly the right amount, scientists could point to planetesimals, not comets, as Earth's water source.

Next, they had to understand whether and how water might survive the collisions that created the planet. Evidence came from looking at other bodies, such as Mercury and the moon. Scientists examined a volatile material, potassium, on Mercury, thought to be as likely to be lost in an impact as water would be on Earth, and found a ratio similar to that on Earth, indicating that not all volatiles were lost in Mercury's planet-forming process. They also looked at the interior of the moon, which experienced a massive formative collision but no subsequent watery comet impact, and found that parts of it have as much water as Earth does. Together, these examples indicate that water could survive the planet-forming process, Elkins-Tanton said.

Computer modeling demonstrated how. The extreme heat would have boiled the water off as steam. But instead of being lost to space, it eventually would have condensed and fallen back, re-creating oceans in a cycle that repeated from collision to collision, Elkins-Tanton said.

"The evidence that we have from our solar system indicates that the chances that planets everywhere in the universe are habitable through liquid water obtained by natural accretion ... are very high."

<http://bit.ly/1htzw2V>

New debris estimates soar for Nankai Trough quake

As much as 349 million tons of debris and sediment would be generated by a major tsunami-producing earthquake in the Nankai Trough - about 11 times the amount resulting from the Great East Japan Earthquake of March 2011, the Environment Ministry said.

The disposal of the quake and tsunami waste would likely take up to 19 years and four months to complete, the ministry said Friday. The estimate did not appear to account for the possibility of radiation from a nuclear power plant accident tainting the debris, as happened in 2011.

The debris, including from buildings destroyed by the quake or subsequent fires, accounts for 322 million tons, while sediment from the tsunami accounts for 27 million tons, it said.

The ministry estimated the volumes under eight scenarios. The highest amount appeared in a situation in which tsunami originating in the Nankai Trough, a subduction zone that runs off the Pacific coast from central to southwestern Japan, hits the Tokai central region while a number of fires happen.

The new maximum estimate is far bigger than the previous forecast of 250 million tons. The ministry revised its estimates in light of the enormous amount of debris and sediment generated by the 9.0-magnitude quake and giant tsunami on March 11, 2011. In the worst-case scenario, 118 million tons of debris would be generated in the Kinki region, 98 million tons in Chubu, 86 million tons in Shikoku, 27 million tons in Kyushu, 16 million tons in Chugoku and 4 million tons in Kanto, the ministry said. The ministry also reviewed its debris estimate for a powerful quake projected to hit the Tokyo metropolitan area.

Under the new projection, the maximum amount of debris generated would be 110 million tons, up from 98 million tons, and take up to six years and six months to dispose of. Following the new estimates, the ministry will consider ways to promote debris recycling and wide-area debris disposal.

http://www.eurekalert.org/pub_releases/2014-03/mu-gwf022814.php#rssowlmlink

Global warming felt to deepest reaches of ocean

Study shows climate change has put a freshwater lid on the Antarctic ocean, trapping warm water in ocean depths

In the mid-1970s, the first available satellite images of Antarctica during the polar winter revealed a huge ice-free region within the ice pack of the Weddell Sea. This ice-free region, or polynya, stayed open for three full winters before it closed.

Subsequent research showed that the opening was maintained as relatively warm waters churned upward from kilometres below the ocean's surface and released heat from the ocean's deepest reaches. But the polynya -- which was the size of New Zealand -- has not reappeared in the nearly 40 years since it closed, and scientists have since come to view it as a naturally rare event.

Now, however, a study led by researchers from McGill University suggests a new explanation: The 1970s polynya may have been the last gasp of what was previously a more common feature of the Southern Ocean, and which is now suppressed due to the effects of climate change on ocean salinity.

The McGill researchers, working with colleagues from the University of Pennsylvania, analyzed tens of thousands of measurements made by ships and robotic floats in the ocean around Antarctica over a 60-year period. Their study, published in *Nature Climate Change*, shows that the ocean's surface has been steadily getting less salty since the 1950s. This lid of fresh water on top of the ocean prevents mixing with the warm waters underneath. As a result, the deep ocean heat has been unable to get out and melt back the wintertime Antarctic ice pack.

"Deep ocean waters only mix directly to the surface in a few small regions of the global ocean, so this has effectively shut one of the main conduits for deep ocean heat to escape," says Casimir de Lavergne, a recent graduate of McGill's Master's program in Atmospheric and Oceanic Sciences and lead author of the paper.

The scientists also surveyed the latest generation of climate models, which predict an increase of precipitation in the Southern Ocean as atmospheric carbon dioxide rises. "This agrees with the observations, and fits with a well-accepted principle that a warming planet will see dryer regions become dryer and wetter regions become wetter," says Jaime Palter, a professor in McGill's Department of Atmospheric and Oceanic Sciences and co-author of the study. "True to form, the polar Southern Ocean - as a wet place - has indeed become wetter. And in response to the surface ocean freshening, the polynyas simulated by the models also disappeared." In the real world, the melting of glaciers on Antarctica - not included in the models - has also been adding freshwater to the ocean, possibly strengthening the freshwater lid.

The new work can also help explain a scientific mystery. It has recently been discovered that Antarctic Bottom Water, which fills the deepest layer of the world ocean, has been shrinking over the last few decades. "The new work can provide an explanation for why this is happening," says study co-author Eric Galbraith, a professor in McGill's Department of Earth and Planetary Sciences and a fellow of the Canadian Institute for Advanced Research. "The waters exposed in the Weddell polynya became very cold, making them very dense, so that they sunk down to become Antarctic Bottom Water that spread throughout the global ocean. This source of dense water was equal to at least twice the flow of all the rivers of the world combined, but with the surface capped by freshwater, it has been cut off."

"Although our analysis suggests it's unlikely, it's always possible that the giant polynya will manage to reappear in the next century," Galbraith adds. "If it does, it will release decades-worth of heat and carbon from the deep ocean to the atmosphere in a pulse of warming."

The research was supported by the Stephen and Anastasia Mysak Graduate Fellowship in Atmospheric and Oceanic Sciences, by the Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery programme, by the Canadian Institute for Advanced Research (CIFAR) and by computing infrastructure provided by the Canadian Foundation for Innovation and Compute Canada.

http://www.eurekalert.org/pub_releases/2014-03/chop-aof022814.php#rssowlmlink

As one food allergy resolves, another may develop

The same food may trigger both allergies, say CHOP experts

Some children who outgrow one type of food allergy may then develop another type of allergy, more severe and more persistent, to the same food. A new study by pediatric allergy experts suggests that health care providers and caregivers carefully monitor children with food allergies to recognize early signs of eosinophilic esophagitis (EoE), a severe and often painful type of allergy that has been increasing in recent years.

"These two types of allergy have some elements in common, but patients with EoE usually don't go on to develop tolerance to the foods that trigger EoE," said pediatric allergist Jonathan M. Spergel, M.D., Ph.D., of

The Children's Hospital of Philadelphia (CHOP). Spergel directs CHOP's Center for Pediatric Eosinophilic Disorders, one of the nation's premier programs for these conditions.

Spergel is the senior author of the research, presented today by Solrun Melkorka Maggadottir, M.D., also of CHOP, at the annual meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI) today in San Diego. The organization featured the study at a press conference.

Only recently recognized as a distinct condition, EoE involves swelling and inflammation of the esophagus, along with excessive levels of immune cells called eosinophils. Often painful, EoE may cause weight loss, vomiting, heartburn and swallowing difficulties. It can affect any age group, but is often first discovered in children experiencing feeding difficulties and failure to thrive.

The study team compared EoE with IgE-mediated food allergy - the more familiar type of food allergy that occurs when antibodies mount an exaggerated immune response against proteins in particular foods. Nuts, eggs or milk, for example, may trigger hives, other skin reactions, vomiting or other symptoms.

The researchers performed a retrospective analysis of all children seen at CHOP for EoE between 2000 and 2012, a total of 1,375 patients. Of that number, 425 could be shown to have a definite food causing their condition - most commonly milk, egg, soy and wheat. Within that subgroup, 17 patients had developed EoE to a food after having outgrown IgE-mediated allergy to that specific food.

"The pattern we found in those 17 patients suggests that the two types of food allergy have distinct pathophysiologies - they operate by different mechanisms and cause different functional changes," said Spergel. "However, this pattern also raises the possibility that prior IgE-mediated food allergy may predispose a patient to developing EoE to the same food."

Spergel added that approximately 10 percent of patients who undergo desensitization therapy for IgE-mediated foods allergies subsequently develop EoE to the same food - a fact that health care providers should consider in managing care for patients with food allergies. In desensitization therapy, a clinician exposes a patient to miniscule amount of an allergy-producing food, then gradually increases the amount, aiming for the patient to become tolerant to that food.

Funds from the Joint Center for Gastroenterology and Nutrition of CHOP-HUP and the CHOP Food Allergy Family Research Fund supported this study. Spergel is on both the CHOP staff and the faculty of the Perelman School of Medicine at the University of Pennsylvania. His co-authors are all from either or both institutions.

Maggadottir et al, "Development of Eosinophilic Esophagitis to Food after Development of IgE Tolerance to the Same Food, abstract 990, presented March 2, 2014 at the AAAAI Annual Meeting.

http://www.eurekalert.org/pub_releases/2014-03/su-ndc022814.php#rssowlmlink

Newly discovered catalyst could lead to the low-cost production of clean methanol

An international research team has discovered a potentially clean, low-cost way to convert carbon dioxide into methanol, a key ingredient in the production of plastics, adhesives and solvents, and a promising fuel for transportation.

Mark Schwartz, Precourt Institute for Energy at Stanford University.

Scientists from Stanford University, SLAC National Accelerator Laboratory and the Technical University of Denmark combined theory and experimentation to identify a new nickel-gallium catalyst that converts hydrogen and carbon dioxide into methanol with fewer side-products than the conventional catalyst. The results are published in the March 2 online edition of the journal Nature Chemistry.

"Methanol is processed in huge factories at very high pressures using hydrogen, carbon dioxide and carbon monoxide from natural gas," said study lead author Felix Studt, a staff scientist at SLAC. "We are looking for materials that can make methanol from clean sources under low-pressure conditions, while generating low amounts of carbon monoxide." The ultimate goal is to develop a large-scale manufacturing process that is nonpolluting and carbon neutral using clean hydrogen, the authors said.

"Imagine if you could synthesize methanol using hydrogen from renewable sources, such as water split by sunlight, and carbon dioxide captured from power plants and other industrial smokestacks," said co-author Jens Nørskov, a professor of chemical engineering at Stanford. "Eventually we would also like to make higher alcohols, such as ethanol and propanol, which, unlike methanol, can be directly added to gasoline today."

Industrial methanol

Worldwide, about 65 million metric tons of methanol are produced each year for use in the manufacture of paints, polymers, glues and other products. In a typical methanol plant, natural gas and water are converted to synthesis gas ("syngas"), which consists of carbon monoxide, carbon dioxide and hydrogen. The syngas is then converted into methanol in a high-pressure process using a catalyst made of copper, zinc and aluminum.

"We spent a lot of time studying methanol synthesis and the industrial process," Studt said. "It took us about three years to figure out how the process works and to identify the active sites on the copper-zinc-aluminum catalyst that synthesize methanol."

Once he and his colleagues understood methanol synthesis at the molecular level, they began the hunt for a new catalyst capable of synthesizing methanol at low pressures using only hydrogen and carbon dioxide. Instead of testing a variety of compounds in the lab, Studt searched for promising catalysts in a massive computerized database that he and co-author Frank Abild-Pedersen developed at SLAC.

"The technique is known as computational materials design," explained Nørskov, the director of the SUNCAT Center for Interface Science and Catalysis at Stanford and SLAC. "You get ideas for new functional materials based entirely on computer calculations. There is no trial-and-error in the lab first. You use your insight and enormous computer power to identify new and interesting materials, which can then be tested experimentally." Studt compared the copper-zinc-aluminum catalyst with thousands of other materials in the database. The most promising candidate turned out to be a little-known compound called nickel-gallium.

"Once we got the name of the compound out of the computer, someone still had to test it," Nørskov said. "We don't do lab experiments here, so we have to have a good experimental partner."

Nørskov turned to a research group at the Technical University of Denmark led by co-author Ib Chorkendorff. First, the Danish team carried out the task of synthesizing nickel and gallium into a solid catalyst. Then the scientists conducted a series of experiments to see if the new catalyst could actually produce methanol at ordinary room pressure.

The lab tests confirmed that the computer had made the right choice. At high temperatures, nickel-gallium produced more methanol than the conventional copper-zinc-aluminum catalyst, and considerably less of the carbon monoxide byproduct.

"You want to make methanol, not carbon monoxide," Chorkendorff said. "You also want a catalyst that's stable and doesn't decompose. The lab tests showed that nickel-gallium is, in fact, a very stable solid."

While these results show promise, a great deal of work lies ahead. "We'd like to make the catalyst a little more clean," Chorkendorff added. "If it contains just a few nanoparticles of pure nickel, the output drops quite a bit, because pure nickel is lousy at synthesizing methanol. In fact, it makes all sorts of chemical byproducts that you don't want."

Nickel is relatively abundant, and gallium, although more expensive, is widely used in the electronics industry. This suggests that the new catalyst could eventually be scaled up for industrial use, according to the authors. But to make methanol synthesis a truly carbon-neutral process will require overcoming many additional hurdles, they noted.

Other co-authors of the study are Jens Hummelshøj of SLAC; and Irek Sharafutdinov, Christian Elkjaer and Søren Dahl of the Technical University of Denmark.

The research was supported by the U.S. Department of Energy, The Danish National Research Foundation and the Danish Ministry of Science, Technology and Innovation.

<http://nyti.ms/1bZqjPV>

Rare Mutation Kills Off Gene Responsible For Diabetes

A new study based on genetic testing of 150,000 people has found a rare mutation that protects even fat people from getting Type 2 diabetes.

By Gina Kolata March 2, 2014

The effect is so pronounced - the mutation reduces risk by two-thirds - that it provides a promising new target for developing a drug to mimic the mutation's effect.

The mutation destroys a gene used by pancreas cells where insulin is made. Those with the mutation seem to make slightly more insulin and have slightly lower blood glucose levels for their entire lives.

Already Pfizer, which helped finance the study, and Amgen, which owns a company whose data played a key role in the research, are starting programs aimed at developing drugs that act like the mutation, the companies said. But Timothy Rolph, a Pfizer vice president, cautioned it can take 10 to 20 years to get a drug to market after discovering something new about human genetics and disease.

The study, published Sunday in *Nature Genetics*, involved a mutation so rare that finding it was only recently possible, with vast data from large numbers of people, researchers said.

"The study is a tour de force, and the authors are the top people in the field," said Dr. Samuel Klein, director of the center for human nutrition at Washington University School of Medicine, who was not involved in the study. This is the first time in diabetes research that a mutation that destroys a gene has proved beneficial, noted Louis Philipson, director of the Kovler Diabetes Center at the University of Chicago. For drug development, he said, "that is very powerful."

For scientists, the result was a surprise because the same mutation that protects people from diabetes, by destroying one copy of the gene, known as ZnT8, has the opposite effect in some strains of mice. Destroying that gene actually causes diabetes in the animals.

The work began four years ago when a group of geneticists from academic institutions and Pfizer decided to search for gene mutations that protect against diabetes. Usually researchers look for mutations that increase - rather than decrease - the risk of diseases, with the aim of determining who gets a disease, and why.

The group started with populations in Finland and Sweden, where 28,000 people had been studied for years. The data included their ages, weights and diseases, including diabetes.

They compared people at either end of the spectrum of diabetes risk. One group of 352 people had Type 2 diabetes even though their risk seemed low. Their average age was about 50, they were lean and they did not smoke. The other group of 406 people was just the opposite. Their average age was about 80, and, Dr. Rolph said, "they had all the bad habits - they were overweight, they drank, they smoked." And yet these people did not have diabetes.

Two of the fat older people who were free of diabetes turned out to have a mutation that destroyed one copy of the ZnT8 gene. It was intriguing, but hard to know if the association was meaningful with only two people.

So the researchers expanded their work, studying the genes of 18,000 people in Sweden, fat and thin, old and young, with diabetes and without. They found another 31 people who seemed protected from diabetes and had mutations that destroyed the ZnT8 gene.

Then Dr. David Altshuler, deputy director of the Broad Institute of Harvard and M.I.T. and the study's lead author, met with Dr. Kari Stefanson, chief executive of deCODE Genetics, a company with data on genes and diseases for the entire population of Iceland. The American drug company, Amgen, bought deCODE and its valuable genetic database.

Dr. Stefanson searched deCODE's database and quickly found 39 people out of 5,440 who had a mutation that destroyed the gene and who did not have diabetes. In contrast, just nine out of 3,727 diabetes patients had the mutation.

"It took us five minutes," Dr. Stefanson said. "It was a lovely little afternoon in our conference room."

At that point, Dr. Altshuler said, the group wrote a paper and submitted it to a medical journal. It was rejected, he said, after one of the reviewers said it must be wrong because it contradicted what was known from studies with mice.

The group went back for more data. They mapped the genes of 13,000 more people and once again found mutations destroying the same gene and associated with a markedly reduced risk of Type 2 diabetes.

This time their paper was accepted for publication by Nature Genetics, Dr. Altshuler said.

Now the researchers are asking whether the mutation has any bad health effects. So far, Dr. Stefanson said, none has been found. With his data he has established that people with the mutation are no more likely to get 750 diseases he searched for.

http://www.eurekalert.org/pub_releases/2014-03/uoth-acm022814.php#rssowlmlink

Ancient Chinese medicine put through its paces for pancreatic cancer

The bark of the Amur cork tree (Phellodendron amurense) has traveled a centuries-long road with the healing arts.

SAN ANTONIO - Now it is being put through its paces by science in the fight against pancreatic cancer, with the potential to make inroads against several more. UT Health Science Center researcher A. Pratap Kumar was already exploring the cork tree extract's promise in treating prostate cancer when his team found that deadly pancreatic cancers share some similar development pathways with prostate tumors.

In a paper published today in the journal Clinical Cancer Research, the researchers show that the extract blocks those pathways and inhibits the scarring that thwarts anti-cancer drugs. Dr. Jingjing Gong, currently pursuing post-doctoral studies at Yale University, conducted the study as a graduate student in Dr. Kumar's laboratory in the Department of Pharmacology.

"Fibrosis is a process of uncontrolled scarring around the tumor gland," said Dr. Kumar, a professor of urology in the School of Medicine at the Health Science Center and the study's principal investigator. "Once you have fibrotic tissue, the drugs cannot get into the cancer." Liver and kidney tumors also develop fibrosis and the resulting resistance to drugs, he said, and there are no drugs currently targeting that pathway in those cancers. The two pathways, or proteins, that contribute to fibrosis in those tumors also encourage Cox-2, an enzyme that causes inflammation, and the cork tree extract appears to suppress that as well, Dr. Kumar said. The complex interrelationship of these substances is "the million-dollar question," he said, and solving that question is one of the next steps in his research.

The potential of natural substances to treat and cure disease has great appeal, but the advantage of cork tree extract, available as a dietary supplement in capsule form, is that it already has been established as safe for use in patients. In a promising prostate cancer clinical study of 24 patients that Dr. Kumar helped spearhead, all the patients tolerated the treatment well, he said. Now researchers are analyzing the results, he said, and with more funding they plan to expand the study to a much larger group of patients.

The dietary supplement is marketed as *Nexrutine* by Next Pharmaceuticals of Salinas, Calif., which provided a supply of the compound for the studies.

<http://nyti.ms/1g3Yu4S>

Infant Sleep Machines at Maximum Volume Reported as Hearing Risk
Devices that produce soothing sounds in order to lull infants to sleep can be loud enough at maximum volume to damage their hearing, researchers reported Monday.

By CATHERINE SAINT LOUIS MARCH 3, 2014

Infant sleep machines emit white noise or nature sounds to drown out everyday disturbances to a baby's sleep. The machines, sometimes embedded in cuddly stuffed animals, are popular gifts at baby showers and routinely recommended by parenting books and websites. Some sleep experts advise parents to use these noisemakers all night, every night, to ensure the best rest for a newborn. Many parents say their babies become so used to the sounds of rainfall or birds that they will not nap without them.

Researchers at the University of Toronto evaluated 14 popular sleep machines at maximum volume and found they produced between 68.8 to 92.9 decibels at 30 centimeters, about the distance one might be placed from an infant's head. Three exceeded 85 decibels, the workplace safety limit for adults on an eight-hour shift for accumulated exposure as determined by National Institute for Occupational Safety and Health. One machine was so loud that two hours of use would exceed workplace noise limits. At 100 centimeters, all the machines tested were louder than the 50-decibel limit averaged over an hour set for hospital nurseries in 1999 by an expert panel concerned with improving newborn sleep and their speech intelligibility.

"These machines are capable of delivering noise that we think is unsafe for full-grown adults in mines," said Dr. Blake Papsin, the senior author of the paper and the chief otolaryngologist at the Hospital for Sick Children in Toronto. The study was published in the journal *Pediatrics*. Dr. Papsin got the idea for this study after a parent brought a portable white noise machine to the hospital that sounded as roaring as a carwash.

"Unless parents are adequately warned of the danger, or the design of the machines by manufacturers is changed to be safer, then the potential for harm exists, and parents need to know about it," said Dr. Gordon B. Hughes, the program director of clinical trials for the National Institute on Deafness and Other Communication Disorders, who was not involved in the study.

Safe use is possible, the study's authors suggest. "Farther away is less dangerous, a lower volume is better and shorter durations of time, all things that deliver less sound pressure to the baby," Dr. Papsin said.

Yet some models are designed to be affixed to the crib, like Homedics' SoundSpa Glow Giraffe and Baby Einstein's Sea Dreams Soother. The findings are bound to surprise many parents.

After finding a recommendation for white noise in "Happiest Baby on the Block," Naomi Tucker, 39, bought a machine so that her daughter, Chiara, 15 months, could fall asleep nightly to ocean waves. The device masks sirens and household noise in the family's two-bedroom apartment in Los Angeles.

A fan outside her door is "an extra barrier of sound, so we don't have to tiptoe," said Ms. Tucker, a family therapist. For naps in the stroller or the car, she and her husband use a white noise app on an old cellphone.

"It's surprising because I hadn't thought of it, but I can see why that would be the case," Ms. Tucker said of the study finding. Her daughter's Graco device is set to maximum volume, but it is still not all that loud, she said. It is also five feet from the crib.

Dr. Marc Weissbluth, a pediatrician and author of "Healthy Sleep Habits, Happy Child," said parents could still use the machines, with new precautions. "If it's too close or it's too loud, this might not be healthy for your baby," he said. But "a quiet machine that's far away may cause no harm whatsoever."

The study authors recommended that manufacturers limit the maximum noise level of infant sleep machines. Michelle Landesman, the customer care director at Marpac, said that the company's Dohmie sound conditioner for babies has a decibel range of 50 to 75. "Our measurements are only taken six inches away from the machine, and that's obviously much closer than we'd recommend," she said.

Ashley Mowrey, a spokeswoman for Graco, declined to specify the loudest output for its Sweet Slumber Sound Machine.

Brian J. Fligor, an audiologist and a spokesman for the American Academy of Audiology, said that the new study may have overestimated the sound exposure to infants by roughly seven decibels. Dr. Fligor questioned the authors' way of accounting for the differences between the ear canals of adults and newborns.

"I don't see these results as a call for drastic reduction in use," he said.

A concern, briefly raised in the Pediatrics study, is whether listening to white noise can be detrimental to auditory development. A 2003 study published in the journal *Science* found continuous white noise delayed development of the brain's hearing center in newborn rats.

In humans, the brain of a newborn is learning to differentiate sounds at different pitches even during sleep, said Lisa L. Hunter, scientific director of research in the division of audiology at Cincinnati Children's Hospital. "If you've conditioned them to white noise, there's every indication that they might not be as responsive as they otherwise should be to soft speech," she said.

The new study did not ask parents how these machines were used in households. Six parents interviewed for this article said they used them nightly, and all through the night, for their children.

Lauren Toner Perry, 32, a senior kindergarten teacher at Hutchison School in Memphis was given an infant sleep machine at her baby shower. She has used it to mask the clattering of dishes in the kitchen while her 4-month-old daughter sleeps. Now she is reconsidering, even though it is pretty quiet. Still, Mrs. Perry said, "It's kind of next to her crib."

<http://phys.org/news/2014-03-restaurants-tablets-dining.html>

Restaurants in US turn to tablets to speed dining

At the Bolt Burgers restaurant in downtown Washington, diners can order a meal through a live person, but many prefer to use the touchscreen tablets.

"I absolutely loved it, and was thinking I wished we had this kind of thing back in Wisconsin," said John Morrissey of Kenosha, Wisconsin, where he is police chief. Many customers at the fast casual eatery use a tablet installed at a kiosk or one of the electronic menu tablets handed to diners when they enter.

"The number of people who prefer to use technology is much greater than we expected," says co-owner Mike Davidson.

Joe Spinelli, another co-owner, said younger customers who are at ease with technology are big tablet users. "People like the speed, and in our business, speed is everything," he said.

Bolt Burgers is among the early adopters of tablets and technology to view, order and pay for meals.

Some of the largest US restaurant chains have announced they are installing tablets to boost efficiency and respond to customer interests. Some 800 restaurants in the Chili's restaurant chain have been installing the tablet supplied by Ziosk, a Texas-based firm which makes the tabletop devices for ordering and paying as well as for news and entertainment while dining.

"Guests love the Ziosk," company marketing chief John Regal told AFP. "They can control the pace of their meal. They can order either with the server or the device."

Getting out the door

Customers who want to leave quickly without waiting for their server to bring a check can pay with a tablet.

"We can get you out the door right away instead of having to wait 10 minutes or more," Regal says.

Regal says the tablets are being used to complement waiters, not to replace them. Initial orders go through the server and the tablets are used for reorders, desserts and to pay. "It's technically possible" to order everything on the tablet, but customers still want to interact with people at a restaurant, Regal said. "The Ziosk is really a second or third person on the service team," he said.

Having a tablet on the table "is a way for restaurants to differentiate themselves, and it gives the servers a little extra time to interact with the customers." Ziosk installs the tablets without any initial cost to the restaurants, and charges a monthly fee. But restaurants can recover that and in some cases boost income because they get a share of revenues from tablet ads and fee-based games, the company says.

A Ziosk rival is the Intel-backed group E la Carte, which recently announced a deal to install its Presto tablets in 1,800 Applebee's restaurants by the end of 2014. The Presto tablets similarly allows diners to pay at their table, add drinks or desserts and play games. The company is working on new functions such as video streaming, social media interaction.

"Let's face it, everyone who has ever been to a restaurant has been frustrated by waiting for their check," said Applebee's president Mike Archer in a statement. "Starting out, our goal was to create a way for guests to control when and how they pay their check. What we learned after nearly two years of testing is we can provide much more. The Presto tablet will deliver our guests a robust slate of offerings for not only transactions, but entertainment, social interaction and more, moving forward."

At the Consumer Electronics Show, Intel chief Brian Krzanich said that tablets were helping restaurants and consumers. "What's really interesting is they've found that waiters have received 15 percent higher tips—better dining experience, better tips for the waiter," Krzanich said.

A National Restaurant Association study found use of tablets and kiosks is growing. Just seven percent in an October survey said they had used a restaurant touchscreen terminal. But more than 40 percent said they would use one if offered. The number increases among people with children. "The restaurant industry is labor-intensive so it makes sense that operators are using technology to boost efficiency and productivity," says Hudson Riehle, a senior vice president for research at the restaurant association. Riehle says the technology is positive for consumers as well: "Using the tablet can allow people to find not only the sourcing of a product but also how it is prepared, the nutritional value and a host of other information that previously wasn't available." The tablet on a table "allows people a chance to read a newspaper online or play a game to occupy their kids," says Mary Chapman at the research firm Technomic. "But the downside is that restaurants lose the ability of the server to control the experience."