http://www.scientificamerican.com/article.cfm?id=truck-driver-has-gps-jammer-accident-2013-08

Truck Driver with GPS Jammer Accidentally Jams Newark Airport

Jamming company-issued GPS in vehicles not just a bad career move

CNET

No reasonable employee wants their boss to know where they are all the time.

Just as no reasonable boss wants his employees to know where she is all the time.

In the former case, those who have to drive around know that one way to get around the problem is to purloin an (entirely illegal) GPS jammer.

I understand from my underworld contacts that such a jammer can be obtained for less than $100.

Gary Bojczak may have thought this a sound investment. For, as CBS New York reports, he admitted to investigators that he put one in the truck he drove on behalf of an engineering company called Tilcon.

Even then, you might think this was just an ill-judged infraction.

However, Bojczak tended to drive by Newark airport in New Jersey. The enterprising souls there were trying out a new system called Smartpath. This, according to its maker Honeywell, lets airports "increase airport capacity, decrease air traffic noise, and reduce weather-related delays."

Sadly, though, it can be jammed by passing trucks that happen to enjoy a GPS jammer.

As the New Jersey Star-Ledger reported, the FCC explained: "The signals emanating from the vehicle were blocking the reception of GPS signals used by the air traffic control system."

So Bojczak was fined $31,875 on Friday. And, yes, he was also fired for his misdirection.

Though the Smartpath system was only being tested at the time Bojczak was intercepted, it has now been installed at Newark.

So please try not to jam it.

http://bit.ly/1cGWqTq

If it isn't life-threatening, don't call it cancer

Cancer screening too often leads to scare diagnoses and unnecessary treatments. It's time to rethink our approach, says cancer specialist Laura Esserman

- 12 August 2013 by **Tiffany O'Callaghan**

You have written new recommendations for cancer screening. Why?

Our view used to be simple, and it made sense: we observed that people who had early stage disease had much better outcomes than those diagnosed at later stages. So the thought was, if we could make earlier diagnoses, we could dramatically decrease mortality from different cancers.

But for many cancers, that hasn't happened...

It turns out it was too simple a view of cancer. Cancer encompasses a whole range of diseases – including some which are pretty slow growing and would never come to clinical attention except through screening. The problem is that screening finds more of those indolent cancers. What we need is a 21st-century definition of cancer.

The term cancer is now used to cover a broad range of diseases. Should this change?

In our culture, cancer means, "Oh my goodness, if I don't do something right away, I'm going to die". But if you have a condition that means you are at risk of developing cancer in the next 10 to 20 years, most people would say that's a high risk, not cancer. We have to stop calling things cancer that don't meet the definition people use. If we rename some of these, we would be better off – people and their physicians wouldn't panic, and we would be able to give more appropriate treatments.

You recommend more research into what happens to so-called precancerous diseases when they are left alone. What might we find?

Take Barrett's oesophagus as an example. It affects the lining of the oesophagus and has been called oesophageal precancer. Brian Reid at the Fred Hutchinson Cancer Research Center in Seattle followed people with Barrett's over a long period without intervening. That's how we discovered it is not in fact a precancerous condition; it's a normal response to acid reflux. But because it was called a precancer people were scoped, biopsied and treated. We would never have known to change this approach if someone didn't have the courage to do something different.

How can we better determine which precancers are likely to be dangerous?

We need to make it clear to diagnostic companies that it is important to develop markers for very low risk conditions, so we can be confident in telling patients they do not need aggressive treatment. Perhaps in some cases they can be followed and we only intervene if there is a change.

How big a problem is cancer overdiagnosis?

It depends on the condition, but it can range from 25 to 60 per cent of cancers found. Instead of thinking of the

problem as overdiagnosis, I think we are better off saying that cancers come in many flavours: some are very fast growing, some grow slowly but are aggressive, and some grow slowly and aren't aggressive. We have to get our minds around what we have learned in the last 20 years. Are there things that we can do instead of surgery? Can we tailor treatment to tumour size? Can we prevent some of these cancers from growing? These are opportunities. We can do things better for patients – one size does not fit all.

http://bit.ly/165loqd

DNA reveals details of the peopling of the Americas

Migrants came in three distinct waves that interbred once in the New World

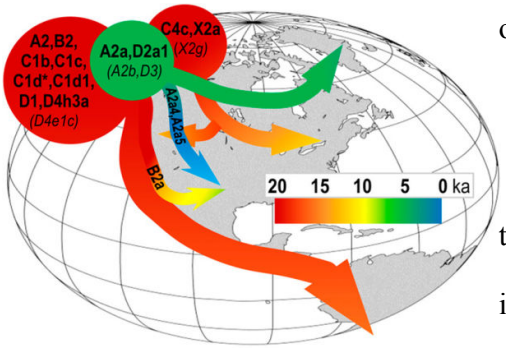
By Tina Hesman Saey

The first people to settle the Americas had a distinctive genetic style, and additional waves of migrants added regional flair, a new analysis of mitochondrial DNA from Native Americans from Canada and the United States suggests.

About 15,000 to 18,000 years ago, the first migrant wave spilled from Asia down the Pacific coast and then pushed inland, eventually peopling the land from "the tip of South America all the way to Hudson Bay," says Andrew Kitchen, a genetic anthropologist at the University of Iowa who was not involved in the new research. That first migrant wave contained the ancestors of all South and Central American tribes, and North Americans, too. But something different was going on in North America, an international team of researchers has discovered.

The scientists examined the DNA of mitochondria, tiny power plants within cells that get passed down from mother to child. Scientists use mitochondrial DNA from living populations to decipher ancient movements of their ancestors. Most studies have examined only a small part of the mitochondria's circular piece of DNA. But Antonio Torroni, a geneticist at the University of Pavia in Italy, and his coauthors compiled complete mitochondrial genomes from 41 native North Americans and combined that data with information from previous studies.

The result is the clearest picture yet of the complicated movements of people into the Americas, says Theodore Schurr, a molecular anthropologist at the University of Pennsylvania.



The analysis, published August 12 in the Proceedings of the National Academy of Sciences, supports the widely accepted notion of an initial coastal migration wave. A second wave of migration probably left Siberia only a couple thousand years after the first wave. Instead of trickling down the coast, the second group slipped through an ice-free corridor running from Alaska into what is now southern Canada, the team found. The second wave never made it south of the present-day United States.

In this schematic overview, the 16 mtDNA founder lineages are associated with three major migratory events. Note that the location of the three spheres is approximate. In parentheses (and in italics) are indicated those founder lineages that are not yet sufficiently analyzed. Two additional events are indicated by stealth arrows. The first arrow corresponds to the recent southward spread of the Athapaskans (marked by A2a4 and A2a5). The second arrow marks the major in situ expansion of B2a.

The mixture of first-wave and second-wave genetic signatures in some Native Americans today indicates that the newcomers and existing populations interbred.

A third wave of migration started around 4,000 years ago in Alaska and swept mostly eastward across Canada. Previous studies of human migration into the Americas have sometimes focused on two types of languages that emerged among the tribes: the Na-Dene language family, including Navajo, Apache and Tlingit, and non-Na-Dene languages, including Algonquin, Ojibwe and Chippewa. Scientists had thought the language groups reflected genetic separation, with the second wave being restricted to the Na-Dene language family. But Torroni and his colleagues discovered that second-wave genetic marks occurred in people who spoke languages from both groups. The finding suggests that the languages developed after the people arrived, and gives a more dynamic picture of what was happening in eastern North America, says Kitchen.

And the cultural change could even have happened within a generation, Torroni says. "Language mutates much faster than the DNA."

A. Achilli et al. Reconciling migration models to the Americas with the variation of North American native mitogenomes. Proceedings of the National Academy of Sciences published online August 12, 2013 [Go to]

http://www.bbc.co.uk/news/science-environment-23672150

Near-death experiences are 'electrical surge in dying brain'

A surge of electrical activity in the brain could be responsible for the vivid experiences described by near-death survivors, scientists report.

By Rebecca Morelle Science reporter, BBC World Service

A study carried out on dying rats found high levels of brainwaves at the point of the animals' demise. US researchers said that in humans this could give rise to a heightened state of consciousness. The research is published in the Proceedings of the National Academy of Sciences.

The lead author of the study, Dr Jimo Borjigin, of the University of Michigan, said: "A lot of people thought that the brain after clinical death was inactive or hypoactive, with less activity than the waking state, and we show that is definitely not the case. "If anything, it is much more active during the dying process than even the waking state."

Consciousness

From bright white lights to out-of-body sensations and feelings of life flashing before their eyes, the experiences reported by people who have come close to death but survived are common the world over. However, studying this in humans is a challenge, and these visions are little understood.

To find out more, scientists at the University of Michigan monitored nine rats as they were dying.

In the 30-second period after the animal's hearts stopped beating, they measured a sharp increase in high-frequency brainwaves called gamma oscillations. These pulses are one of the neuronal features that are thought to underpin consciousness in humans, especially when they help to "link" information from different parts of the brain. In the rats, these electrical pulses were found at even higher levels just after the cardiac arrest than when animals were awake and well.

Dr Borjigin said it was feasible that the same thing would happen in the human brain, and that an elevated level of brain activity and consciousness could give rise to near-death visions. "This can give us a framework to begin to explain these. The fact they see light perhaps indicates the visual cortex in the brain is highly activated - and we have evidence to suggest this might be the case, because we have seen increased gamma in area of the brain that is right on top of the visual cortex," she said.

"We have seen increased coupling between the lower-frequency waves and the gamma that has been shown to be a feature of visual awareness and visual sensation." However, she said that to confirm the findings a study would have to be carried out on humans who have experienced clinical death and have been revived.

Commenting on the research, Dr Jason Braithwaite, of the University of Birmingham, said the phenomenon appeared to be the brain's "last hurrah". "This is a very neat demonstration of an idea that's been around for a long time: that under certain unfamiliar and confusing circumstances - like near-death - the brain becomes overstimulated and hyperexcited," he said.

Striking

"Like 'fire raging through the brain', activity can surge through brain areas involved in conscious experience, furnishing all resultant perceptions with realer-than-real feelings and emotions." But he added: "One limitation is that we do not know when, in time, the near-death experience really occurs. Perhaps it was before patients had anaesthesia, or at some safe point during an operation long before cardiac arrest.

"However, for those instances where experiences may occur around the time of cardiac arrest - or beyond it - these new findings provide further meat to the bones of the idea that the brain drives these fascinating and striking experiences"

Dr Chris Chambers, of Cardiff University, said: "This is an interesting and well-conducted piece of research. We know precious little about brain activity during death, let alone conscious brain activity. These findings open the door to further studies in humans. "[But] we should be extremely cautious before drawing any conclusions about human near-death experiences: it is one thing to measure brain activity in rats during cardiac arrest, and quite another to relate that to human experience."

http://www.eurekalert.org/pub_releases/2013-08/uoma-tsn081313.php

Toxicologist says NAS panel 'misled the world' when adopting radiation exposure guidelines

Toxicologist Edward Calabrese reviews how a linear dose-response approach to ionizing radiation exposure was adopted and offers evidence supporting his view that 2 geneticists suppressed evidence to keep the NAS from considering a non-linear model

AMHERST, Mass. – In two recently published peer-reviewed articles, toxicologist Edward Calabrese of the University of Massachusetts Amherst describes how regulators came to adopt the linear no threshold (LNT)

dose-response approach to ionizing radiation exposure in the 1950s, which was later generalized to chemical carcinogen risk assessment.
He also offers further evidence to support his earlier assertions that two geneticists deliberately suppressed evidence to prevent the U.S. National Academy of Sciences (NAS) from considering an alternative, threshold model, for which there was experimental support. Calabrese's articles appear in the July 26 and August 4 issues of Archives of Toxicology.
Calabrese says, "The regulatory research community needs to hear about this. This isn't an academic debate; it's practical, because all of our rules about chemical and low-level radiation are based on unvalidated assumptions and scientific panel decisions made without sound evidence. Now, after all these years, it's very hard when people have been frightened to death of any exposure whatsoever, to persuade them that we don't need to be scared by certain low-dose exposures."
The first of Calabrese's recent articles is a straightforward history of the LNT model for ionizing radiation mutation, a concept accepted by radiation geneticists in the 1950s and recommended by national and international advisory committees for risk assessment and human exposure guidelines and later generalized to chemical carcinogens ever since. It is now used by public health and regulatory agencies worldwide, he notes.
In the second of the two articles, Calabrese repeats his earlier accusations that the distinguished radiation geneticist Hermann Muller, in his acceptance speech for the 1946 Nobel Prize, "made deceptive statements" intended to "promote the acceptance of the linear dose-response model for risk assessment for ionizing radiation" and that Muller's advocacy agenda was "masked" by long-time colleague Curt Stern. Their actions affected "key publications in the mutation literature," enhancing acceptance of the linear dose-response and hiding "Muller's deceptions," Calabrese adds.
His own career-long research on hormesis, which is a non-linear, threshold-based or biphasic approach to dose-response and risk assessment for ionizing radiation and toxic chemicals, provides evidence that low-dose exposure of some chemicals and ionizing radiation are benign or even helpful. In three "substantial validation tests" of the threshold, hormesis and linear no-threshold models, Calabrese and colleagues say, "only the hermetic (biphasic) dose-response made consistently accurate predictions."
The UMass Amherst toxicologist has argued for many years that a reappraisal of cancer risk assessment methods is urgently needed because the LNT model was incorporated into U.S. regulatory policy based on faulty assumptions and by Muller and Stern's manipulation of the scientific literature.
Calabrese's interpretation of this history is supported by letters and other materials he has compiled, many from formerly classified files. Muller and Stern had done many of the key experiments contributing to health risk assessment of ionizing radiation and Muller served on NAS's Biological Effects of Atomic Radiation (BEAR) committee through which the linear dose-response approach to risk assessment became firmly entrenched, Calabrese related. He offers further evidence that the two successfully suppressed evidence from a key experiment with fruit fly sperm that challenged their views on dose-response.

http://www.sciencedaily.com/releases/2013/08/130813112301.htm

Decellularized Mouse Heart Beats Again After Regenerating With Human Heart Precursor Cells

For the first time, a mouse heart was able to contract and beat again after its own cells were stripped and replaced with human heart precursor cells

For the first time, a mouse heart was able to contract and beat again after its own cells were stripped and replaced with human heart precursor cells, said scientists from the University of Pittsburgh School of Medicine. The findings, reported online today in Nature Communications, show the promise that regenerating a functional organ by placing human induced pluripotent stem (iPS) cells -- which could be personalized for the recipient -- in a three-dimensional scaffold could have for transplantation, drug testing models and understanding heart development.
In the United States, one person dies of heart disease every 34 seconds, and more than 5 million people suffer from heart failure, meaning a reduced ability to pump blood, said senior investigator Lei Yang, Ph.D., assistant professor of developmental biology, Pitt School of Medicine. More than half of heart disease patients do not respond to current therapies and there is a scarcity of donor organs for transplant.
"Scientists have been looking to regenerative medicine and tissue engineering approaches to find new solutions for this important problem," Dr. Yang said. "The ability to replace a piece of tissue damaged by a heart attack, or perhaps an entire organ, could be very helpful for these patients."
For the project, the research team first "decellularized," or removed all the cells, from a mouse heart, a process that takes about 10 hours using a variety of agents. Then, they repopulated the remaining heart framework, or

scaffold, with multipotential cardiovascular progenitor (MCP) cells. These replacement cells were produced by reverse engineering fibroblast cells from a small skin biopsy to make induced pluripotent stem cells and then treating the iPS cells with special growth factors to further induce differentiation.

"This process makes MCPs, which are precursor cells that can further differentiate into three kinds of cells the heart uses, including cardiomyocytes, endothelial cells and smooth muscle cells," Dr. Yang explained. "Nobody has tried using these MCPs for heart regeneration before. It turns out that the heart's extracellular matrix -- the material that is the substrate of heart scaffold -- can send signals to guide the MCPs into becoming the specialized cells that are needed for proper heart function."

After a few weeks, the mouse heart had not only been rebuilt with human cells, it also began contracting again, at the rate of 40 to 50 beats per minute, the researchers found. More work must be done to make the heart contract strongly enough to be able to pump blood effectively, and to rebuild the heart's electrical conduction system correctly so that the heart rate speeds up and slows down appropriately.

In the future, it might be possible to take a simple skin biopsy from a patient to derive personalized MCPs that can be used to seed a biologic scaffold and regenerate a replacement organ suitable for transplantation, Dr. Yang noted. The model also could be used as a lab-based method to preclinically test the effect of new drugs on the heart or to study how the fetal heart might develop.

"One of our next goals is to see if it's feasible to make a patch of human heart muscle," he added. "We could use patches to replace a region damaged by a heart attack. That might be easier to achieve because it won't require as many cells as a whole human-sized organ would."

Tung-Ying Lu, Bo Lin, Jong Kim, Mara Sullivan, Kimimasa Tobita, Guy Salama, Lei Yang. Repopulation of decellularized mouse heart with human induced pluripotent stem cell-derived cardiovascular progenitor cells. Nature Communications, 2013; 4 DOI: 10.1038/ncomms3307

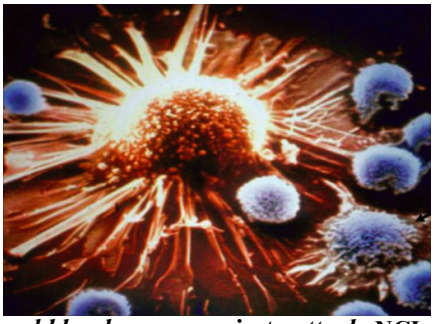
http://arstechnica.com/science/2013/08/stem-cells-turned-into-cancer-killing-immune-cells/

Stem cells turned into cancer-killing immune cells

In cases where immune therapy works, it could allow mass production of treatment.

by John Timmer - Aug 14 2013, 12:25am TST

In addition to fighting off invaders that arrive from outside the body, the immune system is also able to identify cells that have gone bad inside the body. Even though cancer cells look a lot like normal ones, immune cells can often tell the difference—enough that people who receive long-term treatments of immunosuppressive drugs have a higher incidence of cancer. But the immune system clearly has its limits, or cancer wouldn't be a problem. Cancer cells evolve ways to avoid detection or use the immune system's own signals to tamp down its activity. A number of researchers have been looking for ways to reestablish the immune system's superiority, boosting it in a way that it once again clears out cancer cells. One option for doing so has been to simply boost the cells that already recognize a tumor by isolating them and growing them in large numbers in culture.



T cells, colored blue here, move in to attack. **NCI**

This doesn't consistently work, however, as it can be hard to identify and isolate tumor-specific immune cells. A team of researchers has figured out a way of taking stem cells, converting them into immune cells, and directing them to attack one type of cancer.

When most people think of immune function, they tend to think of the cells that make antibodies, called B cells. The antibodies they make stick to invading cells and viruses, keeping the invaders from infecting cells and helping to attract immune cells to destroy them. But there's a second branch of the immune system that targets human cells after they become infected. The T cells recognize strange or unfamiliar proteins on the surface of human cells. When they spot them, the T cells attack and kill the infected cell while boosting the rest of the immune response.

Cancer cells can also have odd-looking proteins on their surface. These proteins can be recognized by T cells, which will then attempt to kill the cancer cell. In many cases, these anti-cancer T cells are present in the bodies of cancer patients; they're just not active in large enough numbers to keep the cancer in check. Some researchers have reasoned that getting more of these cells into the body could give the immune system an edge, so they set about isolating them, growing large numbers outside the body and then putting them back into the bloodstream.

For some cancers, initial trials of this technique suggested it could have promise. But it's not always easy to identify and isolate the immune cells that are targeting a cancer, nor is it necessarily easy to grow large numbers of them in culture.

The alternative is to use stem cells, which do grow extremely well in culture and can be available in large numbers. The problem is that stem cells don't start out recognizing anything in particular. In the body, both T and B cells mature through an elaborate process that gets rid of any cells that recognize normal, healthy human proteins and selects for those that actually have a reasonable chance of recognizing an invader. It's simply not possible to put stem cells through a similar process in a culture dish.

The new paper involves a clever solution to most of these problems. The authors started with existing T cells, which would have already gone through the selection process that prevents them from attacking normal cells. They then used the techniques that have been developed to induce them to adopt a stem cell fate to grow them up into large numbers.

Most of the results, however, would recognize something other than the cancer involved. So the authors engineered a hybrid receptor, with one part that recognizes a common leukemia protein and another part that plugs in to the normal T cell receptor system. They inserted these into their stem cells, converting all of them into cells that could recognize leukemia. They then converted the stem cells into T cells.

There were a couple of oddities about the resulting T cells. To begin with, they could recognize both the leukemia protein and whatever was recognized by their normal receptor. Because they expressed the receptors during their normal maturation process, they didn't mature normally. That said, they did recognize leukemia, and they generated a robust response to cancerous cells, clearing them from mice they were tested in.

Essentially, the technique mass-produces cells that are trained to kill any cell that has a specific protein. If only cancer cells have the protein, only cancer cells get killed.

That makes the technique very flexible, because you can essentially direct it to any protein provided you find another protein that sticks to it—an antibody, its normal partner, etc. The challenge is that it's very difficult to find a protein that's exclusively expressed on cancer cells, meaning there's a real risk that these cells could accidentally end up targeting healthy tissue. Some extensive safety testing would seem to be in order.

Nevertheless, the work is a nice demonstration of the potential of induced stem cells as well as the degree to which we can manipulate the immune system. Not every type of cancer seems likely to be vulnerable to immune attack, but techniques like these may ultimately help control the ones that the immune system does attack.

Disclosure: About 15 years ago, I think I went to a party at the last author's apartment. I didn't realize this when choosing the cover the paper, and it did not influence my coverage.

Nature Biotechnology, 2013. DOI: 10.1038/nbt.2678 (About DOIs).

http://www.sciencedaily.com/releases/2013/08/130813134517.htm

New Compound Prevents First Steps of Fungal Infection

A team of researchers has discovered a chemical compound that prevents fungal cells from adhering to surfaces

Targeting serious and sometimes deadly fungal infections, a team of researchers at Worcester Polytechnic Institute (WPI) and the University of Massachusetts Medical School (UMMS) has discovered a chemical compound that prevents fungal cells from adhering to surfaces, which, typically, is the first step of the infection process used by the human pathogen Candida albicans (C. albicans).

After screening 30,000 chemical compounds in a series of tests with live C. albicans, the team found one molecule that prevented the yeast from adhering to human cells or to polystyrene, a common plastic used in many medical devices. Named "filastatin" by the researchers, this molecule now emerges as a candidate for new anti-fungal drug development and as a potential protective material to embed on the surfaces of medical devices to prevent fungal infections.

The team, led by co-principal investigators Paul Kaufman, PhD, professor of molecular medicine at UMMS, and Reeta Rao, PhD, associate professor of biology and biotechnology at WPI, reports its findings in the paper "Chemical screening identifies filastatin, a small molecule inhibitor of Candida albicans adhesion, morphogenesis, and pathogenesis," published online in advance of print by the journal Proceedings of the National Academy of Sciences (PNAS).

"In humans, the most widespread fungal pathogen is Candida albicans, which is also one of the most frequent causes of hospital-acquired infections," the authors write. "We conclude that filastatin is not toxic to the human cell line under our assay conditions, but is unique in that it can impair fungal adhesion both to inert surfaces and to cultured human epithelial cells."

Infection by C. albicans causes common chronic illnesses like thrush and vaginitis, which affect millions of people globally each year and are not easily cleared by the handful of anti-fungal drugs now available. While most fungal infections do not cause serious harm, if one spreads to the bloodstream it can be deadly.

Hospitalized patients with catheters or central intravenous lines are at risk as the fungi can grow on those devices and enter the body. Similarly, patients with implanted medical devices like pacemakers or prosthetic hips or knees are also at risk if the implant carries a fungus into the body. Also, people with compromised immune systems are at greater risk for serious fungal infections. Because of the lack of effective drugs against C. albicans and other pathogenic fungi, the mortality rate for systemic fungal infections is between 30 and 50 percent.

Typically, a blood stream infection of C. albicans or a similar pathogen begins with fungal cells attaching to a surface -- a catheter, for example, or epithelial cells lining the mouth -- to form what is known as a biofilm. Next, the ovoid shaped yeast cells morph into an invasive filamentous form, extending pointed filaments that penetrate and damage surrounding tissues. In the current study, the team found that filastatin curtailed both steps: it largely prevented C. albicans from adhering to various surfaces, and it significantly reduced filamentation (inspiring the name filastatin).

As a next step, the team tested filastatin's impact on C. albicans cells that had grown unfettered in test wells and had already adhered to the polystyrene walls. When the compound was added to the culture mix, it knocked off many of the fungal cells already stuck to the polystyrene. The inhibitory effects of filastatin were further tested on human lung cells, mouse vaginal cells, and live worms (C. elgans) exposed to the fungus to see if it would reduce adhesion and infection. In all cases, the novel small molecule had significant protective effects without showing toxicity to the host tissues.

Research is now focused on teasing out the precise molecular mechanisms filastatin uses to prevent adhesion and filamentation. "We need to find the target of this molecule," Rao said. "We have some good leads, and the fact that we aren't seeing toxicity with host cells is very encouraging, but there is more work to be done."

Additional studies on filastatin are underway at both WPI and UMMS. "The molecule affects multiple clinically relevant species, so we're pursuing the idea that it provides a powerful probe into what makes these organisms efficient pathogens," Dr. Kaufman said. "In this era of budget gridlock in Washington, our ability to get funding from the Center for Clinical and Translational Research at UMMS to support this work was essential for allowing us to pursue our ideas for novel ways to approach this important class of hospital-acquired infections."

The project was also funded by a grant from a WPI/UMMS pilot program established to promote collaborations between researchers at the universities to advance early stage translational research. "Joint research programs, such as the pilot program between our institutions, are central to WPI's work in the life sciences," said Michael Manning, PhD, associate provost for research ad interim, at WPI. "As this collaboration between Professors Rao and Kaufman demonstrates so well, both institutions can leverage their complementary expertise for the ultimate advancement of scientific discovery and public health."

Terence R. Flotte, MD, UMMS executive deputy chancellor, provost, and dean of the School of Medicine, agreed. "The faculty of UMass Medical School and WPI possess scientific knowledge and expertise in disciplines that complement each other," he said. "The creation of this type of multidisciplinary team collaboration between the two universities allows us to work synergistically to solve problems important for improving human health."

A. Fazly, C. Jain, A. C. Dehner, L. Issi, E. A. Lilly, A. Ali, H. Cao, P. L. Fidel, R. P. Rao, P. D. Kaufman. Chemical screening identifies filastatin, a small molecule inhibitor of Candida albicans adhesion, morphogenesis, and pathogenesis. Proceedings of the National Academy of Sciences, 2013; 110 (33): 13594 DOI: 10.1073/pnas.1305982110

http://www.scientificamerican.com/article.cfm?id=radioactive-water-leaks-from-fukushima

Radioactive Water Leaks from Fukushima: What We Know

The lingering questions include how the radioactivity might contaminate ocean life that humans eat

By Jeremy Hsu and LiveScience | Tuesday, August 13, 2013 | 9

Here is what you need to know about the radioactive water leaking from Japan's Fukushima nuclear plant into the Pacific Ocean.

Scientists on both sides of the Pacific have measured changing levels of radioactivity in fish and other ocean life since the March 2011 earthquake and tsunami triggered a nuclear meltdown at Japan's Fukushima Daiichi nuclear plant. On Aug. 2, 2013, when Japan's Tokyo Electric Power Co. (TEPCO) gave its first estimate of how much radioactive water from the nuclear plant has flowed into the ocean since the disaster, the company was finally facing up to what scientists have recognized for years.

"As an oceanographer looking at the reactor, we've known this since 2011," said Ken Buesseler, a marine chemist at the Woods Hole Oceanographic Institute in Woods Hole, Mass. "The news is TEPCO is finally admitting this."

TEPCO estimated that between 20 trillion and 40 trillion becquerels (units of radioactivity representing decay per second) of radioactive tritium have leaked into the ocean since the disaster, according to the Japanese newspaper Asahi Shimbun. The Fukushima plant is still leaking about 300 tons of radioactive water into the ocean every day, according to Japanese government officials. [Infographic: Inside Japan's Nuclear Reactors]
Japan is haunted by two lingering questions from this aftermath of the disaster: First, how the radioactivity might seriously contaminate ocean life that represents a source of seafood for humans; second, whether it can stop the leaks of radioactive water from the Fukushima plant.

Radioactivity is not created equal

The Fukushima plant is leaking much less contaminated water today compared with the immediate aftermath of the nuclear meltdown in June 2011 — a period when scientists measured 5,000 to 15,000 trillion becquerels of radioactive substances reaching the ocean. Even if radioactivity levels in the groundwater have spiked recently, as reported by Japanese news sources, Buesseler expects the overall amount to remain lower than during the June 2011 period.
"The amount of increase is still much smaller today than it was in 2011," Buesseler told LiveScience. "I'm not as concerned about the immediate health threat of human exposure, but I am worried about contamination of marine life in the long run."
The biggest threat in the contaminated water that flowed directly from Fukushima's reactors into the sea in June 2011 was huge quantities of the radionuclide called cesium. But the danger has changed over time as groundwater became the main source for leaks into the ocean. Soil can naturally absorb the cesium in groundwater, but other radionuclides, such as strontium and tritium, flow more freely through the soil into the ocean. (TEPCO is still coming up with estimates for how much strontium has reached the ocean.)
Tritium represents the lowest radioactive threat to ocean life and humans compared with cesium and strontium. Cesium's radioactive energy is greater than tritium, but both it and tritium flow in and out of human and fish bodies relatively quickly. By comparison, strontium poses a greater danger because it replaces the calcium in bones and stays for much longer in the body.

Not fishing for trouble

A number of fish species caught off the coast of the Fukushima Prefecture in 2011 and 2012 had levels of cesium contamination greater than Japan's regulatory limit for seafood (100 becquerels per kilogram), but both U.S. and Japanese scientists have also reported a significant drop in overall cesium contamination of ocean life since the fall of 2011. The biggest contamination risks came from bottom-dwelling fish near the Fukushima site. [In Photos: Fukushima Butterflies Plagued With Defects]
The radioactive groundwater leaks could still become worse in the future if TEPCO does not contain the problem, U.S. scientists say. But they cautioned against drawing firm conclusions about the latest impacts on ocean life until new peer-reviewed studies come out.
"For fish that are harvested 100 miles [160 kilometers] out to sea, I doubt it'd be a problem," said Nicholas Fisher, a marine biologist at Stony Brook University in Stony Brook, N.Y. "But in the region, yes, it's possible there could be sufficient contamination of local seafood so it'd be unwise to eat that seafood."
The overall contamination of ocean life by the Fukushima meltdown still remains very low compared with the effects of naturally occurring radioactivity and leftover contamination from U.S. and Soviet nuclear weapons testing in the 1960s. Fisher said he'd be "shocked" if the ongoing leaks of contaminated water had a significant impact on the ocean ecosystems.

Source of radioactive water

TEPCO is facing two huge issues in stopping the radioactive water leaks. First, groundwater from nearby mountains is becoming contaminated as it flows through the flooded basements of the Fukushima plant's reactor buildings. The water empties into the nuclear plant's man-made harbor at a rate of about 400 tons per day — and TEPCO has struggled to keep the water from leaking beyond existing barriers into the ocean.
"This water issue is going to be their biggest challenge for a long time," said Dale Klein, former head of the U.S. Nuclear Regulatory Commission. "It was a challenge for the U.S. during Three Mile Island [a partial nuclear meltdown in Pennsylvania on March 28, 1979], and this one is much more challenging."
Second, TEPCO must also deal with contaminated water from underground tunnels and pits that hold cables and pipes for the Fukushima nuclear plant's emergency systems. The underground areas became flooded with highly radioactive water during the initial meltdown of the Fukushima plant's reactors, and have since leaked water into the ocean despite TEPCO's efforts to seal off the tunnels and pits.
TEPCO has also been racing to deal with the problem of storing hundreds of thousands of tons of radioactive water from the Fukushima plant, said Hiroaki Koide, a nuclear engineer at Kyoto University in Japan. The

Japanese utility is testing a water decontamination system called ALPS that can remove almost all radioactive substances except for tritium, but has put much of the contaminated water in storage tanks in the meantime.
"The tanks are an emergency solution that is not suitable for long-time storage," Koide said. "Water will leak from any tank, and if that happens, it will merge with the groundwater."

What must be done

So what solutions exist beyond building more storage tanks? Klein reviewed a number of possible solutions with TEPCO when he was picked to head an independent advisory committee investigating the Fukushima nuclear accident.

One possible solution involves using refrigerants to freeze the ground around the Fukushima plant and create a barrier that stops the inflow of groundwater from the mountains. TEPCO is also considering a plan to inject a gel-like material into the ground that hardens into an artificial barrier similar to concrete, so that it can stop the contaminated groundwater from flowing into the ocean.

Such barriers could help hold the line while TEPCO pumped out the water, treated it with purification systems such as ALPS, and then figured out how to finally dispose of the decontaminated water.

"My priority would be stop the leak from the tunnel immediately," Klein said. "Number two would be to come up with a plan to stop the inflow and infiltration of groundwater. Number three is to come up with an integrated systematic water treatment plan."

Meanwhile, both Japanese and U.S. scientists continue to gather fresh scientific data on how the radioactivity impacts ocean life. Despite low contamination levels overall, studies have shown great differences in certain species depending on where they live and feed in the ocean.

"The most straightforward thing the Japanese can do now is measure the radionuclides in fish tissue, both at the bottom of the ocean and up in the water column at different distances from the release of contaminated groundwater," Fisher said.

http://www.bbc.co.uk/news/health-23679363

Dyslexia 'seen in brain scans' of pre-school children

Brain scans may allow detection of dyslexia in pre-school children even before they start to read, say researchers.

By Michelle Roberts Health editor, BBC News online

A US team found tell-tale signs on scans that have already been seen in adults with the condition. And these brain differences could be a cause rather than a consequence of dyslexia - something unknown until now - the Journal of Neuroscience reports. Scans could allow early diagnosis and intervention, experts hope. The part of the brain affected is called the arcuate fasciculus.

Shrinkage

Among the 40 school-entry children they studied they found some had shrinkage of this brain region, which processes word sounds and language. They asked the same children to do several different types of pre-reading tests, such as trying out different sounds in words. Those children with a smaller arcuate fasciculus had lower scores. It is too early to say if the structural brain differences found in the study are a marker of dyslexia. The researchers plan to follow up groups of children as they progress through school to determine this.

Lead researcher Prof John Gabrieli said: "We don't know yet how it plays out over time, and that's the big question. "We do not know how many of these children will go on to develop problems. But anyway, we want to intervene before that, and the younger you do that the better. We already know that reading programmes and interventions can really help."

Early intervention

In the study, the volume of the left arcuate had a particularly strong link with poorer pre-reading test results. The left arcuate fasciculus connects an area of the brain involved in speech production with another used to understand written and spoken language. A larger and more organised arcuate fasciculus could aid in communication between those two regions, the researchers say.

Prof Gabrieli said: "This brain area fits with a lot of what we already know. So it's a good candidate."

A few years ago, US doctors described the case of a child who developed dyslexia after radiation treatment for a brain tumour. The same brain region - the arcuate fasciculus - was involved.

A spokeswoman for the British Dyslexia Association said brain imaging was providing "increasing evidence" of notable differences between the brains of people with and without dyslexia.

"It is particularly exciting to envisage a future where this technology could be part of a cluster of indicators that would identify a risk of dyslexic difficulties," she said.

But she said there needed to be far more research to determine if in the future it might be possible to diagnose dyslexia with a brain scan.

http://www.sciencedaily.com/releases/2013/08/130813200911.htm

Early Surgery Better Than Watchful Waiting for Patients With Severe Mitral Valve Regurgitation

Patients with severe mitral valve regurgitation who are otherwise healthy should have mitral valve repair surgery sooner rather than later, even if they feel no symptoms, a Mayo Clinic-led study by U.S. and European researchers found.

The results challenge the long-held belief that it is safer to "watch and wait" until a patient has symptoms, such as shortness of breath. This is the largest study to show that patients who undergo surgery early after diagnosis have improved long-term survival and lower risk of heart failure.

The findings will be published Tuesday in the Journal of the American Medical Association.

Mitral valve regurgitation is common and increasing in frequency; it is estimated that by 2030, close to 5 million Americans will have moderate to severe mitral valve regurgitation.

It occurs when the mitral valve does not close properly, causing blood to be pumped backward instead of forward. Oxygen-rich blood is thus unable to move through the heart to the rest of the body as efficiently.

A heart murmur is often the first sign of mitral valve prolapse. As mitral valve disease progresses, symptoms may be absent due to the body's ability to compensate. This initial lack of symptoms preserves quality of life, but prevents patients from being alerted to the seriousness of their condition.

One of the most severe complications is heart failure, in which the heart is unable to pump enough blood to the rest of the body, causing shortness of breath, fluid buildup, fatigue and death.

"The results of the current study showed that early surgery provided significant benefits over watchful waiting -- and interestingly, were of a magnitude greater than we anticipated," says lead author Rakesh Suri, M.D., D.Phil., a cardiovascular surgeon at Mayo Clinic in Rochester.

"This is perhaps counterintuitive. Patients assume they are more severely affected if they need surgery. Actually the opposite is true. Once a patient develops severe mitral valve leakage -- even without symptoms -- we now know that it is preferable to promptly repair the leakage rather than letting the heart deteriorate.

"Our study shows that the quicker we can stop the leak the better the outcome. In essence early surgery, ideally mitral repair, performed at low risk, is the best way for patients with severe mitral regurgitation to live the longest and to enjoy those years without developing disabling heart failure symptoms."

In the study of 1,021 patients with severe mitral valve regurgitation without symptoms or other classical triggers of surgery, 446 underwent mitral valve repair surgery within three months of diagnosis, while 575 had an initial period of medical monitoring and surgery remained a possible option for the future.

The study used the Mitral Regurgitation International Database consisting of participants from six centers in France, Italy, Belgium and the United States. Mayo Clinic was the only U.S. clinical center.

Participants were followed for an average of 10 years, the longest of any study examining when to operate.

Long-term survival rates were significantly higher for patients who had surgery within three months of diagnosis than for those who avoided surgery for the initial three months following diagnosis (86 percent versus 69 percent at 10-year follow-up).

In addition, long-term heart failure risk was lower for patients who had surgery early (7 percent versus 23 percent at 10-year follow-up). There was no difference between the two groups in late-onset atrial fibrillation, another concern for patients with severe mitral valve regurgitation.

Years ago, the risk of surgery and complications was greater, and watchful waiting made more sense, says senior author Maurice Enriquez-Sarano, M.D., a cardiologist at Mayo Clinic in Rochester. But today, specialized high volume valve repair centers centers have a greater than 95 percent success rate for mitral valve repair.

In addition, the operative risk of death today is less than 1percent, while it was more than 10 times higher in the 1980s, he says.

"The potential benefit of performing surgery to correct the mitral regurgitation before symptoms occur has been hotly debated, and the comparative effectiveness of the surgical and medical approach was previously unknown," Dr. Enriquez-Sarano says. "If surgery is appropriate, depending on age, other conditions and goals in life, we have the opportunity today to eliminate the disease before it gets worse. We can restore life expectancy."

http://www.eurekalert.org/pub_releases/2013-08/cwru-cdr080813.php

CWRU dental researchers discover how an oral bacterium can trigger colorectal cancer

Researchers from Case Western Reserve University School of Dental Medicine have discovered how a common oral bacterium can contribute to colorectal cancer, a finding that opens promising new research avenues for the development of approaches to prevent and treat the disease.

"We found this cancer is linked to an infection from [the bacterium]," said Yiping Han, professor of periodontics at the dental school and the study's lead investigator. "This discovery creates the potential for new diagnostic tools and therapies to treat and prevent the cancer."

The results of the research appear in the current issue of Cell Host & Microbe, in conjunction with a second study from a different research group that highlights how the bacteria can speed the accumulation of cancerous cells.

The researchers also learned how to prevent the microorganism, called Fusobacterium nucleatum (Fn), from attaching to colon cells and potentially triggering a cascade of changes that can lead to cancer.

The latest findings advance research from 2011, in which Han and her team identified an adhesive molecule on Fn's surface, called FadA, which can attach to VE-cadherin, a cell receptor from the cadherin group on blood vessels.

As Han completed the work on FadA and VE-cadherin, researchers from Harvard University and the University of British Columbia discovered the presence of Fn was higher in malignant tumors compared to the surrounding tissue.

Han said she immediately suspected Fn interacted with cells in the colon similarly to those in blood vessels and shifted her lab's work to focus on colorectal cancer.

"This was one of those serendipitous scientific moments in making this discovery," Han said.

Because her lab was able to track Fn's ability to attach to the VE-cadherin receptor on blood vessels, Han said it didn't take long before her team found how FadA attached to the E-cadherin receptor on cells in the colon.

Subsequently, FadA's attachment to E-cadherin set in motion a protein called ß-catenin, which, among its many functions, produces two important actions in the cancer process: an inflammatory response that alters the immune system, and another that spurs cancer cell growth.

Han's lab designed a novel synthetic peptide that prevents FadA from attaching to E-cadherin and inciting actions that lead to cancer development.

They also found that the FadA gene levels are 10 to 100 times higher than normal in precancerous and malignant colon polyps.

Thus, Han said, "FadA can be used as a diagnostic marker for early detection of colon cancer. It can also be used to determine if treatment works effectively at reducing Fn load in the colon and the mouth."

A patent application has been filed on work associated with this research.

At the same time, Han emphasized that the results highlight the importance of oral health. Fn is an opportunistic bacterium that increases dramatically in gum disease.

Contributing to the article, "Fusobacterium nucleatum promotes colorectal carcinogenesis by modulating E-cadherin/ß-catenin signaling via its unique FadA adhesin" were: Mara Roxana Rubinstein,Xiaowei Wang and Guifang Cai (Case Western Reserve School of Dental Medicine);, and Wendy Liu andYujun Hao (University Hospitals Case Medical Center).

The National Institute of Dental and Craniofacial Research of the National Institutes of Health funded the research

http://www.eurekalert.org/pub_releases/2013-08/yu-guo081213.php

Growing use of MRIs leading to more invasive breast cancer surgery

Heavy use of magnetic resonance imaging (MRI) may be leading to unnecessary breast removal in older women with breast cancer, according to a study by Yale School of Medicine researchers in the current issue of Breast Cancer Research and Treatment.

"These data are concerning because the long-term benefits associated with bilateral mastectomy for older women with breast cancer are unclear," said the study's lead author Cary Gross. M.D., associate professor of internal medicine at Yale School of Medicine and director of the Cancer Outcomes, Public Policy, and Effectiveness Research (COPPER) Center at Yale Cancer Center.

"Patient concern about recurrence and survival must be balanced with the increased risk for complications associated with more aggressive cancer surgery, particularly when there is no proven benefit of the more aggressive option," Gross added.

The research team tracked the use of breast MRI and surgical care of 72,461 female Medicare beneficiaries age 67-94 who were diagnosed with breast cancer during 2000 to 2009.

The team found a considerable increase in the use of preoperative breast MRI over the study period from 1% in 2000-2001 to 25% in 2008-2009. The researchers also found that women who received an MRI were more

likely to subsequently undergo more aggressive surgical treatment. In women who received mastectomy, 12.5% of those who had MRI received bilateral mastectomy, while only 4.1% of those who did not have MRI had bilateral mastectomy.

The study also revealed that women undergoing MRI were more likely to have a contralateral prophylactic mastectomy (surgery to remove both breasts when cancer was only found in one breast). Among women who underwent mastectomy, 6.9% of women who had an MRI underwent contralateral prophylactic mastectomy, compared to 1.8% in women who did not have an MRI.

"There has been no randomized controlled clinical trial demonstrating improved outcomes for women who undergo preoperative breast MRI at any age," said Brigid Killelea, M.D., assistant professor of surgery at Yale School of Medicine, and first author on the study. "Breast conserving therapy, when feasible, remains the preferred approach for women with early stage breast cancer."

Other authors on the study include Jessica Long, Anees Chagpar, Xiaomei Ma, Pamela Soulos, and Joseph Ross.

This study was supported by the National Cancer Institute (5R01CA149045) and the P30 Cancer Center Support Grant (CCSG) at the Yale Comprehensive Cancer Center.

Citation: Breast Cancer Research and Treatment, Published Online August 14, 2013 Doi: 10.1007/s10549-013-2656-1

http://www.eurekalert.org/pub_releases/2013-08/uoc--smo081313.php

6 months of fish oil reverses liver disease in children with intestinal failure, study shows

Children who suffer from intestinal failure, most often caused by a shortened or dysfunctional bowel, are unable to consume food orally. Instead, a nutritional cocktail of sugar, protein and fat made from soybean oil is injected through a small tube in their vein.

For these children, the intravenous nutrition serves as a bridge to bowel adaptation, a process by which the intestine recovers and improves its capacity to absorb nutrition. But the soybean oil, which provides essential fatty acids and calories, has been associated with a potentially lethal complication known as intestinal failure–associated liver disease, which may require a liver and/or intestinal transplant. Such a transplant can prevent death, but the five-year post-transplant survival rate is only 50 percent.

Previous studies have shown that replacing soybean oil with fish oil in intravenous nutrition can reverse intestinal failure–associated liver disease. However, the necessary duration of fish oil treatment had not been established in medical studies.

Now, a clinical trial conducted at the Children's Discovery and Innovation Institute at Mattel Children's Hospital UCLA has found that, compared with soybean oil, a limited duration (24 weeks) of fish oil is safe and effective in reversing liver disease in children with intestinal failure who require intravenous nutrition. The researchers believe that fish oil may also decrease the need for liver and/or intestinal transplants — and mortality — associated with this disease.

The researchers' study, "Six Months of Intravenous Fish Oil Reverses Pediatric Intestinal Failure Associated Liver Disease," is published online in the Journal of Parenteral and Enteral Nutrition.

"With this particular study, we set out to determine if a finite period of six months of intravenous fish oil could safely reverse liver damage in these children, and we have had some promising results," said lead author Dr. Kara Calkins, an assistant professor in the department of pediatrics in the division of neonatology and developmental biology at UCLA. "But because intravenous fish oil is not yet approved by the Food and Drug Administration and is much more costly than soybean oil, it is typically not covered by insurance. As a result, this oil is considered experimental and is currently available only under special protocols. If it proves safe and effective for patients, we hope it would eventually be available for wider use."

For the study, intravenous soybean oil was replaced with intravenous fish oil in 10 patients between the ages of 2 weeks and 18 years who had advanced intestinal failure–associated liver disease and who were at high risk for death and/or transplant. The researchers compared these subjects with 20 historical controls who had received soybean oil.

Results showed that the children receiving fish oil had a much higher rate of reversal of liver disease than those who received the standard soybean oil. In fact, after 17 weeks of fish oil, nearly 80 percent of patients experienced a reversal of their liver disease, while only 5 percent of the soybean patients saw a reversal.

The next phase of research will involve following children for up to five years after they stop fish oil to determine if their liver disease returns and if transplant rates are truly decreased, the study authors said.

"We are also trying to better understand how fish oil reverses this disease by investigating changes in proteins and genes in the blood and liver," Calkins said. "These studies will provide the scientific and medical community with a better understanding of this disease and how intravenous fish oil works."

For Isabella Piscione, who was one of the first patients at UCLA to receive the fish oil treatment under compassionate use, her outcome with the treatment paved the way for researchers to establish the six-month

protocol. Because of multiple surgeries due to an obstruction in her intestines, Isabella was left with only 10 centimeters of intestine. She depended on intravenous nutrition for survival, which unfortunately resulted in liver damage.
When Isabella started the fish oil treatment, she was just over 6 months old and was listed for a liver and bowel transplant. Within a month of starting the treatment, her condition started to improve. By six months, her liver had healed, and she no longer needed a transplant.
"We cried tears of joy each week that we saw her getting better and better," said her father, Laureano Piscione. "She is a success story."
Study co-authors from UCLA included Dr. James Dunn; Dr. Stephen Shew; Laurie Reyen, R.N.; Dr. Douglas Farmer; Dr. Sherin Devaskar; and Dr. Robert Venick.
The study was funded by a grant from a National Institutes of Health (NIH/NCRR M01-RR00865). Calkins has received funding from NIH K12HD00140 and T32G075776. Calkins and Venick have received funding from the Today's and Tomorrow's Children Fund.
Intravenous fish oil was purchased with funds from the UCLA Department of Pediatric Surgery, the Women's Auxiliary Club at UCLA and Dr. James Yoo of the UCLA Department of Surgery.

http://www.eurekalert.org/pub_releases/2013-08/wkh-mhd081413.ph

Most herniated discs result from avulsion, not rupture, suggests study in spine

ISSLS award-winning paper questions assumptions about how herniated discs happen

Philadelphia, Pa. - Herniated discs in the lower (lumbar) spine most often result from avulsion (separation) of the tissue connection between the disc and spinal bone, rather than rupture of the disc itself, according to a study in Spine. The journal is published by Lippincott Williams & Wilkins, a part of Wolters Kluwer Health.
The results suggest that surgeons may need to pay more attention to failure of the vertebral end plate junction (EPJ)—the attachment between the spinal bone and discs—as the main cause of herniated lumbar discs. The study by Dr S. Rajasekaran and colleagues of Hanga Hospital, Tamil Nadu, India, was named winner of the International Society for the Study of the Lumbar Spine (ISSLS) 2013 Prize for Lumbar Spine Research.
How Do Herniated Discs Occur? Study Questions Conventional Wisdom
The study included 181 patients undergoing surgery for herniated lumbar discs. Sometimes called ruptured or "slipped" discs, herniated discs are a major cause of low back pain. They occur when the soft material inside the disc (nucleus pulposus) leaks through the tough outer covering of the disc (annulus fibrosis).
Dr S. Rajasekaran and coauthors performed an in-depth analysis of available data for each patient, including x-rays, CT and MRI scans, surgical observations, and microscopic studies. To avoid the effects of disc degeneration, the study excluded patients older than 60 and patients with disease affecting multiple discs.
The results suggested that the EPJ had become avulsed, or torn off, in 65 percent of cases, making EPH avulsion the most common mechanism of lumbar disc herniation. In these cases of EPJ avulsion, a piece of the bone and/or cartilage connecting the disc to the vertebra had actually broken off.
In contrast, true rupture of the outer disc surface, or annulus fibrosis, was seen in only eleven percent of cases overall. Sometimes an EPJ avulsion was not visible on x-rays, but was apparent at surgery. Most EPJ avulsions were visible on CT scans.
In some cases, avulsed EPJ healed in the time between initial injury and surgery to repair the herniated disc. This was sometimes accompanied by narrowing of the spinal canal—a common problem called spinal stenosis.
Implications for Prevention and Treatment of Herniated Discs?
The results may lead spinal surgeons to rethink conventional wisdom regarding how herniated lumbar discs occur. Rupture (breaking open) of the annulus fibrosus has traditionally been regarded as the main mechanism of disk herniation.
"Our study shows that the incidence of EPJ failure has been grossly underrated, probably because of the difficulty of documentation," the researchers write. They present a suggested classification system for herniated lumbar discs, based on the "anatomy of failure."
In most cases, there was no clear traumatic event before symptoms related to herniated disc appeared. This suggested that after fracture, the process of disc herniation could take several months.
"The evidence of EPJ failure opens up opportunities for prevention, repair and biological strategies that may prevent progression of lumbar disc herniation after the initial event of EPJ avulsion," the researchers write. In particular, the time after initial fracture or avulsion may provide a "window of opportunity" for some type of treatment to prevent the injury from progressing to a herniated disc.
The study by Dr Rajasekaran and colleagues was named best clinical paper in the 2013 ISSLS Prize for Lumbar Spine Research. The ISSLS Prizes are sponsored by DePuy Synthes Spine in order to encourage new basic science, biomechanical, and clinical lumbar spine research.

http://www.sciencedaily.com/releases/2013/08/130814095644.htm

Low-Grade Prostate Cancers May Not Become Aggressive With Time -- Adds Support for 'Watch and Wait' Approach

Prostate cancer aggressiveness may be established when the tumor is formed and not alter with time, according to a study published in Cancer Research, a journal of the American Association for Cancer Research.

Researchers found that after the introduction of widespread prostate-specific antigen (PSA) screening, the proportion of patients diagnosed with advanced-stage cancers dropped by more than six-fold in 22 years, but the proportion diagnosed with high Gleason grade cancers did not change substantially. This suggests that low-grade prostate cancers do not progress to higher grade over time.

Cancer stage refers to the extent or spread of the disease, and cancer grade, called Gleason grade for prostate cancer, refers to the aggressiveness of the disease.

"We were able to look at finely stratified time periods to capture pre-PSA, early-PSA, and late-PSA eras within one study. Over time, because of PSA screening, men have been more likely to be diagnosed with prostate cancer at an earlier stage, before the disease has had an opportunity to grow and spread. If Gleason grade also progressed over time, we would expect a similar decrease in high Gleason grade disease over time," said Kathryn Penney, Sc.D., instructor in medicine at the Harvard Medical School and associate epidemiologist at the Channing Division of Network Medicine at Brigham and Women's Hospital in Boston, Mass. "We were surprised by just how constant the incidence of high-grade disease has been over time."

This study adds more evidence to the argument that patients who are diagnosed with low-grade prostate cancers can opt for an active surveillance, or "watch and wait" approach instead of getting treated right away.

Penney and colleagues used data from 420 participants recruited to the Physicians' Health Study and 787 participants recruited to the ongoing Health Professionals Follow-up Study. All participants were diagnosed with prostate cancer between 1982 and 2004, and treated with surgery. The researchers reanalyzed prostate tissue collected from these patients to assess Gleason grade.

The researchers divided the data into four time periods based on when the participants received a diagnosis and treatment: 1982-1993, 1993-1996, 1996-2000, and 2000-2004, to represent the pre-PSA and PSA eras. They found that the number of participants who had undergone PSA screening increased from 42 percent in 1994 to 81 percent in 2000.

They also found that the number of late-stage cancers decreased from 19.9 percent in the 1982-1993 group to just 3 percent in the 2000-2004 group, reflecting an 85 percent drop in stage at diagnosis. However, there was only a moderate decrease in high Gleason grade cancers, from 25.3 percent in the 1982-1993 group to 17.6 percent in the 2000-2004 group, reflecting a 30 percent drop.

With further analyses, the researchers found that the moderate drop in high Gleason grade cancers was not because progression to more aggressive disease was prevented through screening, but because of an increased diagnosis of low-grade disease that would not have been detected without PSA screening.

"Radical prostatectomy or radiation therapy, the usual treatments for prostate cancer, can have negative side effects such as impotence and incontinence; choosing active surveillance could prevent this decline in quality of life," said Penney. "Men with low-grade disease at diagnosis should seriously consider talking with their doctors about active surveillance."

K. L. Penney, M. J. Stampfer, J. L. Jahn, J. A. Sinnott, R. Flavin, J. R. Rider, S. Finn, E. Giovannucci, H. D. Sesso, M. Loda, L. A. Mucci, M. Fiorentino. Gleason Grade Progression Is Uncommon. Cancer Research, 2013; 73 (16): 5163 DOI: 10.1158/0008-5472.CAN-13-0427

http://www.eurekalert.org/pub_releases/2013-08/jhub-psf081413.php

Pilot study finds ER patients drinking high-octane beer

Study shows feasibility of collecting alcohol brand consumption data in ER departments

Five beer brands – Budweiser, Steel Reserve, Colt 45, Bud Ice and Bud Light – were consumed in the highest quantities by emergency room patients, according to a new pilot study from researchers at The Center on Alcohol Marketing and Youth (CAMY) at the Johns Hopkins Bloomberg School of Public Health. Three of these are "malt liquors" with higher alcohol content than regular beer.

The pilot study, published by Substance Use and Misuse, is the first study of its kind to assess alcohol consumption by brand and type from patients reporting to the emergency department with injury.

"Recent studies reveal that nearly a third of injury visits to Level I trauma centers were alcohol-related and frequently a result of heavy drinking," said lead study author David Jernigan, PhD, CAMY director. "Understanding the relationship between alcohol brands and their connection to injury may help guide policy

makers in considering taxation and physical availability of different types of alcohol given the harms associated with them."
The study was conducted in an urban medical center at the Johns Hopkins Hospital Emergency Department in East Baltimore on Friday and Saturday nights between April 2010 and June 2011. Of the 105 respondents who admitted to drinking alcohol before their injury, 73 (69%) were male, and 72 (69%) were African American, reflecting the demographic profile of the neighborhood in which the emergency department is located.
The research team also tracked the ER patients' consumption of alcohol by type and compared it to national market share data from Impact Databank, a market research firm that tracks the U.S. market for alcoholic beverages by type and brand. The study found that the proportion of distilled spirits consumed by the ER sample was higher than the market share for distilled spirits in the U.S. More specifically, vodka, gin and brandy/cognac were over-represented compared to their market share in the national distilled spirits market. The same was true for 'ready-to-drink' beverages (RTDs). Women in the ER sample were more likely to report consuming higher quantities of RTDs.
Although beer was consumed at a lower proportion in the ER sample compared to the proportion of its consumption in the national market share for beer, men in the ER sample were more likely to report consuming higher quantities of beer or malt liquors, which has higher alcohol content than regular beer.
Four malt liquors - Steel Reserve, Colt 45, Bud Ice and King Cobra - accounted for almost 50 percent (46%) of the beer consumed by the sample. Yet these four beverages accounted for only 2.4 percent of beer consumption in the general population.
The next step, according to study authors, would be to pursue this type of research be further explored in a larger sample of emergency department admissions for injury, across multiple cities and hospitals. Policy implications of this kind of research could include requirements for clear labeling of alcohol content on malt beverage containers, including serving size labeling; limits on malt liquor availability and marketing; and graduated taxation of beer based on alcohol content to discourage consumption of higher-alcohol products.
This research was supported with funding from the Centers for Disease Control and Prevention.
This research was supported with funding from the Johns Hopkins Center for Injury Research and Policy, with funding from the National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Cooperative Agreement number 5R49CE001507, and conducted by the Center on Alcohol Marketing and Youth monitors the marketing practices of the alcohol industry to focus attention and action on industry practices that jeopardize the health and safety of America's youth. The Center was founded in 2002 at Georgetown University with funding from The Pew Charitable Trusts and the Robert Wood Johnson Foundation. The Center moved to the Johns Hopkins Bloomberg School of Public Health in 2008 and is currently funded by the federal Centers for Disease Control and Prevention. For more information, visit http://www.camy.org.

http://bit.ly/17pCezj

Legalize It: Marijuana Gaining Acceptance in U.S.

Attorney General Eric Holder's recent comments calling for reform of long mandatory sentences for low-level drug offenders have opened a floodgate of mixed reactions.

Aug 14, 2013 12:30 PM ET // by Paul Greenberg

His comments have also fast-tracked arguments about legalization of marijuana. Holder's comments, coupled with CNN chief medical correspondent Sanjay Gupta's recent reversal of his objections to medical marijuana have reignited the national conversation about the controversial drug. In some quarters it appears the cultural attitude toward marijuana is shifting in favor of legalization, particularly for medical use.
A cadre of experts from the scientific community are adding credibility to the uphill battle to legalize the drug for medicinal use. Chief among them is Sunil Aggarwal, M.D., Ph.D., a resident in physical medicine and rehab. Aggarwal's support of cannabis was bolstered by his own study of 176 patients who suffered chronic pain and were treated with cannabis.
"For 139 of them, I did a retrospective, and the bottom line is a wide variety of chronic pain syndromes were being well-managed using cannabis," Aggarwal said. "In several cases there was a reduction of other drugs to manage chronic pain, or a reduction in dosages of these drugs. Nobody showed any adverse effects from this drug."
Aggarwal, who has become a high profile voice in the fight to legalize cannabis for the treatment of pain, says other countries are way ahead of the United States on this issue.
"If you look across Western Europe, South America and even India, there is widespread use," said Aggarwal. "It has been legal in parts of this world for a long time. We are catching up to the recognition of its uses that has long been known elsewhere. Ultimately we need a sound public health policy for both medicinal usage and as a relaxant for social usage of cannabis."
One problem is the historical stigma the drug carries that is hard to overcome via state and federal laws. Even today, when some states have legalized marijuana, individuals who operate cannabis-related businesses meet up

with roadblocks, said Betty Aldworth, deputy director of the National Cannabis Industry Association, a trade group that represents nearly 300 cannabis-related businesses at the federal level.
"I think it's safe to say that things like Gupta's change of heart and Holder's statements are reflective of a broader shift in the public's view of marijuana," Aldworth said. "Through polling we know that the vast majority of Americans believe patients should have access to medical marijuana, and that a slim majority of Americans support adults being able to choose whether or not they would like to use it. Once we realize that, it is not too far a step to say that marijuana should be provided by licensed, responsible businesses."
The glitch in that step has to do with taxation, Aldworth said. "In section 280E of a 1980s tax code, it states that you cannot take small business deductions from your taxes for activities involved in trafficking illegal products. While other businesses are taxed between 15 and 30 percent, marijuana providers are punished with federal tax rates that reach up to 80 percent."
That means that even if a state legalizes marijuana, businesses are still subject to stringent federal tax guidelines.
"It's important for the public to understand that as we shift from a culture that keeps marijuana underground and forces it in the hands of cartels and criminals, to a culture that allows patients to access their medicine safely in a secure facility, that these business owners are really participating in important ways in their state economies," Aldworth said.
Still, there are detractors in high places who base their objections to legalization on scientific evidence.
"Studies show that 9 percent of those exposed to marijuana will become addicted," said Nora Valkow, M.D., Director of the National Institute on Drug Abuse at the National Institutes of Health. "If you are less than 17 or 18 years old, that goes up to 16 percent."
Even for the majority of teens who do not become addicted, Valkow says there are additional known health risks.
"My main concern with marijuana is the potential detrimental effects it can have on the developing human brain," she said. "Exposure in adolescence can ultimately affect cognitive performance, mood and motivation and drive. Marijuana can also have adverse effects on adults. If you are taking it with a high content of THC it can make you psychotic."
As for legalizing marijuana for the treatment of pain, Valkow says the idea is premature.
"We have to learn from history," she said. "There's a lot of excitement that the drug is benign and can be a panacea for a wide variety of diseases. But research much be done. The concept of legalizing marijuana for pain is one that would need randomized clinical trials that evaluate what concentrations of the active ingredients of marijuana are necessary for the optimal control of pain. What are the doses? None of that work has been done."

http://www.sciencedaily.com/releases/2013/08/130814144705.htm

Computer Chip Based On Human Brain Developed

Today's computing chips are incredibly complex and contain billions of nano-scale transistors, allowing for fast, high-performance computers, pocket-sized smartphones that far outpace early desktop computers, and an explosion in handheld tablets.

Despite their ability to perform thousands of tasks in the blink of an eye, none of these devices even come close to rivaling the computing capabilities of the human brain. At least not yet. But a Boise State University research team could soon change that.
Electrical and computer engineering faculty Elisa Barney Smith, Kris Campbell and Vishal Saxena are joining forces on a project titled "CIF: Small: Realizing Chip-scale Bio-inspired Spiking Neural Networks with Monolithically Integrated Nano-scale Memristors."
Team members are experts in machine learning (artificial intelligence), integrated circuit design and memristor devices. Funded by a three-year, $500,000 National Science Foundation grant, they have taken on the challenge of developing a new kind of computing architecture that works more like a brain than a traditional digital computer.
"By mimicking the brain's billions of interconnections and pattern recognition capabilities, we may ultimately introduce a new paradigm in speed and power, and potentially enable systems that include the ability to learn, adapt and respond to their environment," said Barney Smith, who is the principal investigator on the grant.
The project's success rests on a memristor -- a resistor that can be programmed to a new resistance by application of electrical pulses and remembers its new resistance value once the power is removed. Memristors were first hypothesized to exist in 1972 (in conjunction with resistors, capacitors and inductors) but were fully realized as nano-scale devices only in the last decade.
One of the first memristors was built in Campbell's Boise State lab, which has the distinction of being one of only five or six labs worldwide that are up to the task.

The team's research builds on recent work from scientists who have derived mathematical algorithms to explain the electrical interaction between brain synapses and neurons. "By employing these models in combination with a new device technology that exhibits similar electrical response to the neural synapses, we will design entirely new computing chips that mimic how the brain processes information," said Barney Smith.
Even better, these new chips will consume power at an order of magnitude lower than current computing processors, despite the fact that they match existing chips in physical dimensions. This will open the door for ultra low-power electronics intended for applications with scarce energy resources, such as in space, environmental sensors or biomedical implants.
Once the team has successfully built an artificial neural network, they will look to engage neurobiologists in parallel to what they are doing now. A proposal for that could be written in the coming year.
Barney Smith said they hope to send the first of the new neuron chips out for fabrication within weeks.
This material is based upon work supported by the National Science Foundation under Grant No. CCF-1320987 to Boise State University. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation.

http://bit.ly/13xfNLB

New Measure of Consciousness Tracks Our Waking States

This fairly simple metric for neural activity could guide treatment for people with brain injuries

By Helen Shen and Nature magazine | Wednesday, August 14, 2013

In most people, the line between consciousness and unconsciousness is as clear as day. But in many people with brain injuries who can neither talk nor move, the differences can be harder to spot.
Neuroscientists have now devised a single metric of brain activity that could help to distinguish between different states of consciousness and guide medical treatment for people with brain injuries. The work is reported today in Science Translational Medicine.
“Nothing else we have can do that reliably,” says Joseph Giacino, director of rehabilitation neuropsychology at Harvard Medical School’s Spaulding Rehabilitation Hospital in Boston, Massachusetts. “This is a very significant study.”
The metric relies on the idea that consciousness involves widespread communication between different areas of the brain, with each region performing specialized functions. Loss of consciousness during sleep or anaesthesia, or from brain injury, may be caused by the disengagement of brain regions from one another.
Neurophysiologist Marcello Massimini of the University of Milan in Italy and his colleagues, who carried out the latest research, have found that electromagnetic stimulation of conscious people’s brains sets off a cascade of activity and generates unique responses in different brain regions. In unconscious people, however, the activity either fails to spread, or there is little variation in the responses from different brain areas.
In the latest study, the researchers present a mathematical measure to quantify the extent and richness of response to the stimulus — a mild electromagnetic pulse applied through the scalp. They applied the technique to 52 people in Italy, Belgium and the United States between 2005 and 2009.
Hidden signs
In healthy participants, the metric was high during wakefulness, but was cut by about half during anaesthesia-induced unconsciousness and in some stages of sleep. The metric was similarly low for people clinically diagnosed as vegetative — wakeful, but unaware and unresponsive. For the two study participants diagnosed with locked-in syndrome, who were fully aware but able to respond only minimally, the metric was high. And people with brain injuries who were diagnosed with intermediate states of consciousness fell between the two extremes.
These distinctions could help physicians to determine when and how aggressively to pursue different treatment options. The metric could also be used to monitor how well treatments are working, explains Massimini. “That one number tells you how the brain’s doing,” he says.
None of the people with brain injuries recovered during the course of the study, so researchers could not determine long-term changes in the measure. But in some of the healthy participants, the measure was used to track changes between wakefulness and varying degrees of sedation induced by anaesthetic. Massimini says that the next step will be to try the technique with more injured people over a longer time period, to see whether the metric can chart the recovery of consciousness.
Adrian Owen, a neuroscientist at the University of Western Ontario in London, Canada, has pioneered the use of functional brain imaging to diagnose levels of consciousness in people with brain injuries, but his technique requires the use of magnetic resonance imaging and the active concentration of the patient. He says that Massimini’s method is easier to apply, and does not require anything of the patient. “This looks very exciting,” says Owen.

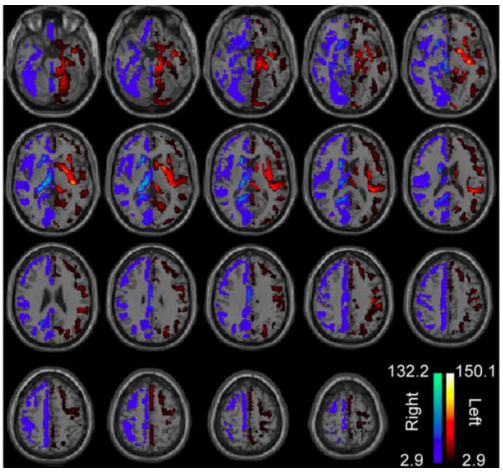
http://www.sciencedaily.com/releases/2013/08/130814190513.htm

Researchers Debunk Myth of 'Right-Brained' and 'Left-Brained' Personality Traits

Chances are, you've heard the label of being a "right-brained" or "left-brained" thinker. Logical, detail-oriented and analytical? That's left-brained behavior. Creative, thoughtful and subjective? Your brain's right side functions stronger -- or so long-held assumptions suggest.

But newly released research findings from University of Utah neuroscientists assert that there is no evidence within brain imaging that indicates some people are right-brained or left-brained.

For years in popular culture, the terms left-brained and right-brained have come to refer to personality types, with an assumption that some people use the right side of their brain more, while some use the left side more.



Following a two-year study, University of Utah researchers have debunked that myth through identifying specific networks in the left and right brain that process lateralized functions.

Lateralization of brain function means that there are certain mental processes that are mainly specialized to one of the brain's left or right hemispheres.

During the course of the study, researchers analyzed resting brain scans of 1,011 people between the ages of seven and 29.

In each person, they studied functional lateralization of the brain measured for thousands of brain regions -- finding no relationship that individuals preferentially use their left -brain network or right- brain network more often.

"It's absolutely true that some brain functions occur in one or the other side of the brain. Language tends to be on the left, attention more on the right. But people don't tend to have a stronger left- or right-sided brain network. It seems to be determined more connection by connection, " said Jeff Anderson, M.D., Ph.D., lead author of the study, which is formally titled "An Evaluation of the Left-Brain vs. Right-Brain Hypothesis with Resting State Functional Connectivity Magnetic Resonance Imaging."

It is published in the journal PLOS ONE this month.

Significant lateralization of gray matter density. show more Colored regions included ROIs that showed significantly greater left- or right-lateralization of gray matter density across 1011 subjects, correcting for multiple comparisons using a false discovery rate correction of $q<0.05$ across 7266 ROIs. Color bars show t-statistics for the left and right hemispheres, respectively. Images are in radiologic format with subject left on image right. **Nielsen JA, Zielinski, Ferguson, Lainhart, Anderson**

Researchers obtained brain scans for the population they studied from a database called INDI, the International Neuroimaging Data-Sharing Initiative.

The participants' scans were taken during a functional connectivity MRI analysis, meaning a participant laid in a scanner for 5 to 10 minutes while their resting brain activity was analyzed.

By viewing brain activity, scientists can correlate brain activity in one region of the brain compared to another. In the study, researchers broke up the brain into 7,000 regions and examined which regions of the brain were more lateralized.

They looked for connections -- or all of the possible combinations of brain regions -- and added up the number of connections for each brain region that was left- lateralized or right-lateralized. They discovered patterns in brain imaging for why a brain connection might be strongly left- or right-lateralized, said Jared Nielsen, a graduate student in neuroscience who carried out the study as part of his coursework.

"If you have a connection that is strongly left- lateralized, it relates to other strongly lateralized connection only if both sets of connections have a brain region in common," said Nielsen. Results of the study are groundbreaking, as they may change the way people think about the old right-brain versus left-brain theory, he said.

"Everyone should understand the personality types associated with the terminology 'left-brained' and 'right-brained' and how they relate to him or her personally; however, we just don't see patterns where the whole left-brain network is more connected or the whole right-brain network is more connected in some people. It may be that personality types have nothing to do with one hemisphere being more active, stronger, or more connected," said Nielsen.

Nielsen JA, Zielinski, Ferguson, Lainhart, Anderson. An Evaluation of the Left-Brain vs. Right-Brain Hypothesis with Resting State Functional Connectivity Magnetic Resonance Imaging. PLoS ONE, 2013 DOI: 10.1371/journal.pone.0071275

http://www.bbc.co.uk/news/science-environment-23686913

Criminologists identify family killer characteristics

Men who kill their families can be separated into four distinct types.

By Melissa Hogenboom Science reporter, BBC News

British criminologists have made the assessment after studying newspaper records of "family annihilator" events over the period from 1980 to 2012. A family break-up was the most common trigger, followed by financial difficulties and honour killings. Writing in the Howard Journal of Criminal Justice, the team lists the four types as self-righteous, anomic, disappointed, and paranoid.

Each category has slightly different motivations and many cases also have a hidden history of domestic abuse.

In four out of five cases the murderers went on to kill themselves or attempted to do so.

The research revealed the most frequent month for the crime was in August, when fathers were likely to be with their children more often because of school holidays.

The four types

- ***Self-righteous: Killer seeks to locate blame for his crimes upon the mother who he holds responsible for the breakdown of the family. For these men, their breadwinner status is central to their idea of the ideal family. (case study: Brian Philcox)***
- ***Anomic: The family has become firmly linked to the economy in the mind of the killer. The father sees his family as the result of his economic success, allowing him to display his achievements. However, if the father becomes an economic failure, he sees the family as no longer serving this function. (case study: Chris Foster)***
- ***Disappointed: This killer believes his family has let him down or has acted in ways to undermine or destroy his vision of ideal family life. An example may be disappointment that children are not following the traditional religious or cultural customs of the father. (case study: Mohammed Riaz)***
- ***Paranoid: Those who perceive an external threat to the family. This is often social services or the legal system, which the father fears will side against him and take away the children. Here, the murder is motivated by a twisted desire to protect the family. (case study: Graham Anderson)***

The cases have also become more common with more than half occurring since the year 2000. Only six cases were found in the 1980s.

One of the study's authors, David Wilson of Birmingham City University, UK, said a reason for this increase could be "men feeling they need to exercise power and control" over their family.

It was often men who had invested "too heavily in a very stereotypical conception of what it means to be a husband and a father within an institution called a family", Prof Wilson told BBC News. "Their view of the family is very black and white, and doesn't reflect the increasingly dynamic role that women can play in the economy and in the institution of the family itself." He added: "The thing that struck me was the kind of extraordinary ways that men thought up to kill their children. "They jumped from bridges with children in their arms; they drove into canals with children in the backseats. These were extraordinary histrionic, controlling ways of committing murder. "This was a group of men who were not in any way previously known to the criminal justice system. This is a very different profile of male murderers than we normally find in criminological research."

Private lives

The new study differs from previous explanations for the family killer. These have pointed to revenge or altruism as causes or that an incident leads a man to snap. But Prof Wilson's group said these explanations were not reflected in many cases they reviewed. He explained that the private nature of some families could be a reason why fathers had seemed loving fathers and dutiful husbands. For this reason, he added, it was important to take domestic violence seriously and encourage "more people to become aware of other people's lives".

Keith Hayward, a professor of criminology at Kent University, was not involved with the new study.

He said that it was valuable work that other researchers could further develop, but constructing "typologies" from second-hand media reports was problematic, and "not always helpful for policy development".

"There are a number of ungrounded assumptions going on about 'motivations'. This is reflected in the four categories, which overlap and thus don't seem that rigorous to me." Prof Hayward recognised that getting access to the killers was in many cases impossible, but without detailed insight into their life histories, "it's all inference", he said.

The researchers did state that there were disadvantages of using only newspaper reports, but argued that interviews with family members "lifted a lid on the reality of life behind closed doors" which helped determine possible motives.

The study found 71 cases of the family annihilator, with a small minority of 12 women which the team will follow up with future research.

http://phys.org/news/2013-08-frequent-severe.html

Heat waves to become more frequent and severe, research says

Climate change is set to trigger more frequent and severe heat waves in the next 30 years regardless of the amount of carbon dioxide (CO2) we emit into the atmosphere, a new study has shown.

Extreme heat waves such as those that hit the US in 2012 and Australia in 2009—dubbed three-sigma events by the researchers—are projected to cover double the amount of global land by 2020 and quadruple by 2040. Meanwhile, more-severe summer heat waves—classified as five-sigma events—will go from being essentially absent in the present day to covering around three per cent of the global land surface by 2040.

The new study, which has been published today, Thursday 15 August, in IOP Publishing's journal Environmental Research Letters, finds that in the first half of the 21st century, these projections will occur regardless of the amount of CO2 emitted into the atmosphere.

After then, the rise in frequency of extreme heat waves becomes dependent on the emission scenario adopted. Under a low emission scenario, the number of extremes will stabilise by 2040, whereas under a high emission scenario, the land area affected by extremes will increase by one per cent a year after 2040.

Lead author of the study, Dim Coumou, from the Potsdam Institute for Climate Impact Research, said: "We find that up until 2040, the frequency of monthly heat extremes will increase several fold, independent of the emission scenario we choose to take. Mitigation can, however, strongly reduce the number of extremes in the second half of the 21st century."

Under a high emission scenario, the projections show that by 2100, 3-sigma heat waves will cover 85 per cent of the global land area and five-sigma heat waves will cover around 60 per cent of global land.

"A good example of a recent three-sigma event is the 2010 heat wave in Russia, which expanded over a large area stretching from the Baltic to the Caspian Sea. In the Moscow region the average temperature for the whole of July was around 7°C warmer than normal—it was around 25°C. In some parts, temperatures above 40°C were measured," continued Coumou.

In their study, Dim Coumou, from the Potsdam Institute for Climate Impact Research, and Alexander Robinson, from Universidad Complutense de Madrid, used state-of-the-art climate models to project changes in the trend of heat extremes under two future warming scenarios—RCP2.6 and RCP8.5—throughout the 21st century. The historic period was also analysed, and the results showed that the models can accurately reproduce the observed rise in monthly heat extremes over the past 50 years.

Co-author of the study, Alexander Robinson, said: "Our three- and five-sigma thresholds are defined by the variability a region has experienced in the past, so the absolute temperatures associated with these types of event will differ in different parts of the world. Nonetheless these events represent a significant departure from the normal range of temperatures experienced in a given region."

According to the research, tropical regions will see the strongest increase in heat extremes, exceeding the threshold that is defined by the historic variability in the specific region. The results show that these changes can already be seen when analysing observations between 2000 and 2012.

"Heat extremes can be very damaging to society and ecosystems, often causing heat-related deaths, forest fires or losses to agricultural production. So an increase in frequency is likely to pose serious challenges to society and some regions will have to adapt to more frequent and more severe heat waves already in the near-term," continued Coumou.

Historic and future increase in the global land area affected by monthly heat extremes, Dim Coumou and Alexander Robinson 2013 Environ. Res. Lett. 8 034018, iopscience.iop.org/1748-9326/8/3/034018/article

http://www.eurekalert.org/pub_releases/2013-08/cp-sr080813.php

Study reveals much-needed strategy to protect against deadly liver fibrosis

Central role of the immune molecule interleukin 33 (IL-33) in the formation of liver fibrosis

Chronic liver disease is a leading cause of death in the United States, in part because it often causes the formation of harmful scar tissue - a process known as fibrosis. A study published by Cell Press August 15 in the journal Immunity reveals the central role the immune molecule interleukin 33 (IL-33) plays in the formation of liver fibrosis. The findings suggest that drugs targeting this molecule could serve as a new treatment strategy to protect against liver fibrosis.

"Currently, the therapeutic options for liver fibrosis are limited and not curative," says senior study author Stefan Wirtz of Friedrich-Alexander University Erlangen-Nuremberg. "We identified novel immunological factors that contribute to the development of liver fibrosis, opening up new avenues for the treatment of this serious condition."

Liver fibrosis refers to the accumulation of harmful deposits of extracellular matrix (ECM) proteins, and it can eventually lead to organ failure. Past studies have suggested that this kind of damage is associated with

abnormal immune responses in the liver, but very little was known about the molecules and cells that contribute to fibrosis.
In the new study, Wirtz and his team found that the amount of IL-33 in the blood was higher than normal in patients with liver disease. Following up on this observation, they discovered that injection of IL-33 into mice caused ECM proteins to build up in the liver, whereas mice that were genetically modified to lack IL-33 were largely protected from fibrosis. The researchers went on to identify the immune networks underlying IL-33's harmful effects and discovered that this molecule activates immune cells called type 2 innate lymphoid cells (ILC2), which had never before been linked to liver disease.
"Our findings reveal IL-33 as a novel biomarker that could potentially lead to early detection of fibrosis in patients, which may be extremely valuable for preventing further damage to the liver," Wirtz says. "Moreover, the study shows that drugs targeting IL-33 or ILC2 responses could be a promising strategy to protect against fibrosis and chronic liver disease."
Immunity, Mchedlidze et al.: "Interleukin-33-dependent innate lymphoid cells mediate hepatic fibrosis."

http://www.medscape.com/viewarticle/809519?src=rss

Heavy Coffee Consumption Linked With Increased Risk of All-Cause Death

***Drinking more than four cups of coffee per day does more than increase the risk of the jitters, a new study suggests*[1].**

Michael O'Riordan

COLUMBIA, South Carolina - Researchers report that heavy coffee consumption, defined as more than 28 cups of coffee per week, is associated with an increased risk of all-cause mortality among men. For men and women 55 years of age and younger, the association between heavy coffee consumption and all-cause mortality is more pronounced. "Typically, people have been concerned that coffee could be unhealthy, particularly caffeine," **Dr Chip Lavie** (Ochsner Medical Center, New Orleans, LA), one of the study authors, told **heart*wire*** . "If you give a massive acute dose of caffeine, you raise your pulse and blood pressure, and that can be toxic. So years ago, people had the thought that maybe coffee could be a bad or unhealthy thing to be drinking."
Previous studies had suggested an association between heavy coffee consumption and all-cause mortality and coronary heart disease, but many of these older studies are compromised, because heavy coffee drinkers were also smokers, two habits that went hand in hand. When adjusted for smoking, the coffee didn't appear to be very toxic, said Lavie, and most of the later studies suggested that coffee consumption wasn't harmful.
In fact, said Lavie, there are some potential benefits of coffee, although these data are not particularly strong. As reported previously by **heart*wire*** , there are studies suggesting coffee might protect against heart failure, **diabetes**, stroke, and other conditions.

A Cup Is 8 oz, Not 20!

In this latest study, which is published online August 15, 2013 in the *Mayo Clinic Proceedings*, lead investigator **Dr Junxiu Liu** (University of South Carolina, Columbia) and colleagues assessed the data from the **Aerobics Center Longitudinal Study**. The retrospective analysis included 43 727 participants followed for a median of 17 years, during which time 2512 deaths occurred. Of these deaths, 32% were the result of cardiovascular disease.

It certainly looks like people who report intakes of low amounts of coffee are not getting significant harm.

Despite the limitations of the study, Lavie told **heart*wire*** , "it certainly looks like people who report intakes of low amounts of coffee are not getting significant harm, and that's up to about 28 cups a week, which is a decent amount of coffee." He pointed out that a cup of coffee as measured is an 8-oz cup, and not the supersized 20-ounce cups typical of Starbucks and other coffee chains.
In a multivariate analysis, men who drank more than 28 cups of coffee had a statistically significant 21% increased risk of all-cause mortality. In women, the risk was not statistically significant. In men younger than 55 years of age, drinking more than 28 cups per week was associated with a 56% increased risk of death compared with nondrinkers. In younger women, such heavy consumption increased the risk of death 113% compared with those who did not drink coffee.
Overall, there was no association between coffee consumption and cardiovascular mortality.
"Explaining why, we can try to tease stuff out, but I don't really have a good reason to explain why noncardiovascular mortality is increased," said Lavie. "And noncardiovascular mortality includes a lot of different things--it includes cancer and mortality from suicides and accidents and infections. Why would a high amount of coffee increase noncardiovascular mortality, particularly in young people? The mechanism is not clear. It might be only an association. It may not be that coffee caused the death. This is the case with studies that aren't randomized, and we're never going to get a randomized study of something like coffee."
Honestly, for myself, I could easily go some days having a sixth cup of coffee.

Still, Lavie said, there are strengths to the analysis, including the long-term follow-up, the number of participants, and the fact they were able to adjust for cardiorespiratory fitness. For people who like coffee, including himself, Lavie said the study suggests coffee is relatively safe if people limit themselves to less than four cups of coffee per day. For those who consume more, Lavie said the research is not intended to scare anyone, but it can't hurt for people to think about the association.
"Honestly, for myself, I could easily go some days having a sixth cup of coffee, but this is leading me now to try to limit myself to the third, and maybe occasionally have the fourth," said Lavie. "Most days now I'm sticking with two or three cups. And honestly, for most people, it's a habit. There's something to the first or second cup, but if you're drinking it all day long it's really just a habit. And if you have a signal for increased mortality, and you know about that, it might make people think or stop after the third cup."
Liu J, Sui X, Lavie CJ, et al. Association of coffee consumption with all-cause and cardiovascular disease mortality. Mayo Clin Proc *2013; DOI:10.1016/j.mayocp.2013.06.020. Available at: http://www.mayoclinicproceedings.org/home.*

http://www.eurekalert.org/pub_releases/2013-08/tuhs-ssf081513.php

Study shows feral cat control could benefit from different approach

Vasectomies could be more effective than neuters in population management

NORTH GRAFTON, Mass. - New research from Tufts University scientists shows that feral cats that undergo a vasectomy or hysterectomy could reduce a feral colony's numbers more effectively than the traditional approach of neutering. This may be because vasectomized cats retain reproductive hormones, in addition to not being able to reproduce, and therefore protect their turf from sexually intact competitors.
The findings, derived from a computer-based model and published in the August 15 issue of the Journal of the American Veterinary Medical Association, support trap-vasectomy-hysterectomy-release (TVHR) as a better alternative to trap-neuter-release (TNR). While used with success in small colonies and controlled environments, the data is lacking to support TNR's efficacy over large areas, noted Robert J. McCarthy, D.V.M., lead author and clinical associate professor of small animal surgery at the Cummings School of Veterinary Medicine at Tufts University.
"This opens up new conversations," McCarthy said. "The computer model indicates that vasectomy and hysterectomy should be much more effective at reducing or eliminating feral cat populations than the traditional approach of neutering. The next step is to gather evidence on how it actually works in the field."
Even small populations of feral cats can have a negative impact on public health and other wildlife. Neutering, a surgical procedure which involves castration or removal of the uterus and ovaries, is used as an alternative to lethal means in feral cat population control. Dominant males that are castrated in a TNR program become sexually inactive and are replaced in the breeding hierarchy by the next most dominant male. It is also difficult or impossible to capture all resident cats so sexually intact cats that haven't been captured repopulate an area quickly. Spayed and neutered cats live longer so the population does not decrease as fast as it would otherwise. With vasectomies (leaving the testicles intact) and hysterectomies (leaving the ovaries intact), however, the production of reproductive hormones continues.
"With TVHR, a male cat's life span, sexual drive and social status aren't altered with a vasectomy, so he'll fend off competing males who try to intrude into his area even though he can't actually produce offspring," said J. Michael Reed, one of the authors and professor of biology in the Tufts' School of Arts and Sciences. Interestingly, an intact female cat that mates with a vasectomized male enters into a prolonged 45-day pseudo-pregnancy period, which further reduces the chance of fertile mating in the colony, said Reed.
Stephen H. Levine, a professor of civil and environmental engineering at Tufts University School of Engineering, developed the computer model to rapidly compare the predicted efficacy of vasectomy (vs. castration) and hysterectomy (vs. ovariohysterectomy). Each computer run simulated the cat population over 6,000 days (a number greater than the typical lifetime of a feral cat), tracking individual cats on a daily basis. New cats were added to the population as they were born and deceased ones removed.
The simulation showed that to reduce the population by a quarter, 57 percent of the cats in a colony had to be removed by lethal means or captured, neutered and released. TVHR, however, could reduce the population by half with an annual capture rate of 35 percent and at that rate could completely eliminate the colony within 11 years. (TNR required capturing 82 percent of the cats in order to eliminate the colony in 11 years.)
The researchers point out that the popularity of TNR in the U.S. has been in part due to a goal of maximizing feral cats' quality of life (e.g. extended life span, vaccinations, assessment for infectious disease) and reducing undesirable behaviors such as aggression and vocalization while still eliminating colonies over time.
Robert J. McCarthy, DVM, MS, DACVS; Stephen H. Levine, PhD; J. Michael Reed, PhD. "Estimation of effectiveness of three methods of feral cat population control by use of a simulation model." J Am Vet Med Assoc. Published August 15, 2013. http://avmajournals.avma.org/doi/pdf/10.2460/javma.243.4.502

http://www.eurekalert.org/pub_releases/2013-08/uoic-cac081513.php

Celery, artichokes contain flavonoids that kill human pancreatic cancer cells

Celery, artichokes, and herbs, especially Mexican oregano, all contain apigenin and luteolin, flavonoids that kill human pancreatic cancer cells in the lab by inhibiting an important enzyme, according to two new University of Illinois studies.

URBANA, Ill. – "Apigenin alone induced cell death in two aggressive human pancreatic cancer cell lines. But we received the best results when we pre-treated cancer cells with apigenin for 24 hours, then applied the chemotherapeutic drug gemcitabine for 36 hours," said Elvira de Mejia, a U of I professor of food chemistry and food toxicology. The trick seemed to be using the flavonoids as a pre-treatment instead of applying them and the chemotherapeutic drug simultaneously, said Jodee Johnson, a doctoral student in de Mejia's lab who has since graduated. "Even though the topic is still controversial, our study indicated that taking antioxidant supplements on the same day as chemotherapeutic drugs may negate the effect of those drugs," she said. "That happens because flavonoids can act as antioxidants. One of the ways that chemotherapeutic drugs kill cells is based on their pro-oxidant activity, meaning that flavonoids and chemotherapeutic drugs may compete with each other when they're introduced at the same time," she explained.

Pancreatic cancer is a very aggressive cancer, and there are few early symptoms, meaning that the disease is often not found before it has spread. Ultimately the goal is to develop a cure, but prolonging the lives of patients would be a significant development, Johnson added.

It is the fourth leading cause of cancer-related deaths, with a five-year survival rate of only 6 percent, she said.

The scientists found that apigenin inhibited an enzyme called glycogen synthase kinase-3β (GSK-3β), which led to a decrease in the production of anti-apoptotic genes in the pancreatic cancer cells. Apoptosis means that the cancer cell self-destructs because its DNA has been damaged.

In one of the cancer cell lines, the percentage of cells undergoing apoptosis went from 8.4 percent in cells that had not been treated with the flavonoid to 43.8 percent in cells that had been treated with a 50-micromolar dose. In this case, no chemotherapy drug had been added. Treatment with the flavonoid also modified gene expression. "Certain genes associated with pro-inflammatory cytokines were highly upregulated," de Mejia said.

According to Johnson, the scientists' in vitro study in Molecular Nutrition and Food Research is the first to show that apigenin treatment can lead to an increase in interleukin 17s in pancreatic cells, showing its potential relevance in anti-pancreatic cancer activity.

Pancreatic cancer patients would probably not be able to eat enough flavonoid-rich foods to raise blood plasma levels of the flavonoid to an effective level. But scientists could design drugs that would achieve those concentrations, de Mejia said.

And prevention of this frightening disease is another story. "If you eat a lot of fruits and vegetables throughout your life, you'll have chronic exposure to these bioactive flavonoids, which would certainly help to reduce the risk of cancer," she noted.

Flavonoid apigenin modified gene expression associated with inflammation and cancer and induced apoptosis in human pancreatic cancer cells through inhibition of GSK-3β/NF-κB signaling cascade is available pre-publication online in Molecular Nutrition and Food Research at http://onlinelibrary.wiley.com/doi/10.1002/mnfr.201300307/pdf.

Interactions between dietary flavonoids apigenin or luteolin and chemotherapeutic drugs to potentiate anti-proliferative effect on human pancreatic cancer cells in vitro is available pre-publication online in Food and Chemical Toxicology at http://ac.els-cdn.com/S0278691513004912/1-s2.0-S0278691513004912-main.pdf?_tid=c3b88f9a-05ce-11e3-9281-00000aab0f01&acdnat=1376587315_bee4241362cd03044f56c15dc7011e67.

The U of I's J.L. Johnson and E. Gonzalez de Mejia co-authored both studies, which were funded by USDA.

http://bit.ly/1271o5N

Ancient climate change picked the crops we eat today

Thank climate change for our daily bread. High levels of carbon dioxide in the atmosphere after the last ice age drove us to cultivate wheat.

10:41 15 August 2013 by Sara Reardon

Farming arose in the Fertile Crescent in the Middle East 10,000 years ago. Over the next two millennia, people all over the world took up the practice. This suggests that some global event triggered this simultaneous development. A spike in atmospheric CO2 seen after the last ice age has been put forward as the culprit – the gas was released from the ocean in abundance when ocean circulation patterns changed as the ice sheets started to melt. But if that's the case, why did we domesticate some grain species and not others?

To find out, Georg Frenck at the University of Sheffield, UK, and colleagues went back to the roots of our modern food crops. They tracked down ancient species of wild barley and wheat that are known to be precursors to today's modern crops.

The seeds of these species have been found alongside human remains in a 23,000-year-old archaeological site in Israel, suggesting that hunter-gatherers were collecting and eating these species in the Fertile Crescent during the last ice age.

Sensitive seeds

The team grew the wheat and barley precursors under varying conditions. One set was exposed to levels of CO2 seen during the last ice age and one to the elevated levels seen when farming first arose. Four wild grass species that aren't eaten today, but were also known to grow in the region at that time, were also grown under the same conditions.

All the plants grew larger under high levels of CO2, but the relatives of wheat and barley grew twice as large and produced double the seeds. This suggests the species are especially sensitive to high levels of CO2, Frenck says, making them the best choice for cultivation after the last ice age.

Frenck says the group intends to look at whether other food staples around the world are similarly affected by elevated CO2 levels. For instance, people in Asia began cultivating millet around this time, and people in North America started domesticating maize into the corn we grow today. They also plan to compare the effects of CO2 on legumes such as peas.

Jessica Blois, a palaeoecologist at the University of California, Merced, says that the work ties in nicely with previous findings that suggest the rise in CO2 after the last ice age affected more than just the climate. However, she points out that because the experiment only ran for the duration of the plants' lives rather than over successive generations, the findings might not accurately reflect what happened thousands of years ago as different plant species probably evolved different ways of adapting to the new CO2 system.

http://www.scientificamerican.com/article.cfm?id=rethinking-rabies

Experts Urge Mass Dog Vaccination to Eradicate Rabies

Some rabies infections may not be lethal, but be especially wary of dog bites

By Maryn McKenna | Thursday, August 15, 2013 | 6

Last year a team of researchers from Peru and the U.S. made a discovery that challenged one of the most widely held assumptions about rabies—that the virus is nearly always fatal unless doctors administer a vaccine before it reaches the brain. Based on the results of blood tests, the scientists learned that half a dozen villagers in a remote part of the Peruvian Amazon had previously been infected—probably through bites from vampire bats, which are common in the area. But instead of suffering the agonizing deaths for which rabies is infamous, the villagers had recovered and apparently developed immunity to further infection.

Image: EVAN KAFKA Getty Images

The discovery put the Peruvians on a short list of people who have survived rabies without a vaccine. The best-known member of that select group is Jeanna Giese, a Wisconsin teenager who lived through the disease in 2004, also after contact with a bat. Out of desperation, Giese's physician improvised a risky treatment that included putting the girl into a controlled coma, which apparently allowed her body enough time to destroy the microscopic intruder. Doctors have since refined the treatment, now known as the Milwaukee protocol, and tried it on at least 39 other never vaccinated patients. Five more people have survived.

The mixed success rates, and the 2012 Peruvian study, underscore how little scientists know about rabies, despite its long history as a menace to humanity. Based on accumulating evidence, though, researchers now recognize that not all rabies infections are equal or universally fatal. Many different animals, including dogs, bats, foxes and raccoons, carry various strains of the rabies virus. The varieties hosted by bats and foxes appear to be weaker, and some people's immune systems may be able to defeat them without a vaccine. Dogs, however, carry a more virulent strain that has rarely been vanquished without medical intervention. To this day, canines remain the largest and most dangerous group of rabies carriers worldwide.

Even if doctors one day perfect a treatment for the later stages of rabies, the procedure would likely be complicated and expensive. Most public health experts think that the best way to control rabies is to vaccinate the most dangerous hosts: all domestic and stray dogs, particularly in the developing world. One such veterinary program in the Philippines has dramatically reduced deaths among humans, and others are under way in India and Tanzania.

Dreaded Disease

Rabies kills about 55,000 people every year worldwide—an admittedly smaller toll than, say, AIDS or influenza. The virus's horrific reputation is nonetheless richly deserved. Symptoms emerge slowly in anywhere

from a few weeks to—in rare cases—more than a year after contact with a rabid animal. The rabies virus crawls from nerve cell to nerve cell, eventually making its way from the site of the bite or wound to the brain. Fatigue, fever and chills gradually give way to hallucinations, anxiety, violent convulsions and the telltale foaming at the mouth once the virus reaches the salivary glands. Death is painful and terrifying, which is why standard medical practice calls for keeping patients sedated in the last phases of the disease.

Louis Pasteur's development of a rabies vaccine in 1885 prevented such gruesome outcomes if doctors acted quickly. (More than a century later most rabies deaths in the industrial world—including one or two each year in the U.S.—occur because a bite was not recognized or not taken seriously.) But his success had an unintended consequence: as explained in the 2012 book Rabid: A Cultural History of the World's Most Diabolical Virus (Viking Adult), rabies became a low priority for the budding field of biomedical research.

So when 15-year-old Giese entered Children's Hospital of Wisconsin in Milwaukee in 2004 with full-blown rabies, one month after a bite from a bat flitting around her church, there was still no successful treatment. She was feverish, semiconscious and jerking involuntarily.

Her physician, Rodney E. Willoughby, Jr., a pediatric infectious disease specialist, had never seen a case of rabies. He scoured the scant medical literature and found a gleam of hope: an experiment in which keeping rats anesthetized somehow allowed them to recover from a rabies infection. The rabies virus disrupts the usual electrical and chemical communication between neurons in the brain stem, which in turn loses its ability to regulate the heart and lungs. Perhaps, Willoughby reasoned, effectively silencing the brain with general anesthetics—while keeping the patient alive with a heart-bypass machine and mechanical ventilator—would buy the immune system enough time to destroy the virus. He decided to try it.

Against all odds, the therapy succeeded. Giese survived the viral storm, although she suffered some brain damage and spent two years relearning how to speak, stand and walk. She graduated from college in 2011 and now works as an animal caretaker and motivational speaker. Meanwhile Willoughby has continued to tinker with his intervention. But even he admits that the procedure is not a viable option for most clinics, because it demands so many resources.

In fact, some researchers wonder whether the Milwaukee protocol is truly effective at all. These naysayers have proposed that the real secret to at least some patients' survival is the fact that they were bitten by animals other than dogs that transmit either very tiny doses of rabies virus or strains that the human immune system can clear on its own.

Canine Carriers

While doctors debate whether the Milwaukee protocol works, public health experts agree that the most effective way to deal with rabies is to stop the disease at its source. Globally, domesticated and stray dogs are responsible for nearly all the 55,000 rabies deaths every year, according to the World Health Organization. The burden tends to fall most heavily on people (especially children) in rural areas, which have limited access to the rabies vaccine given annually to more than 15 million people to try to prevent the illness after someone has been exposed.

That leaves preventing rabies in dogs as the best option for reducing the number of deaths in humans. On a purely economic basis, mass dog vaccination certainly makes sense. Canine vaccines are not only less expensive than injections for people, they are far less expensive than critical care treatment of a human rabies case. But it can be difficult, politically speaking, to get anyone to pay attention to the health and welfare of dogs when people's needs remain so much more obvious in so many parts of the world, says Charles Rupprecht, formerly rabies chief at the U.S. Centers for Disease Control and Prevention and now director of research at the nonprofit Global Alliance for Rabies Control (GARC). “Medicine addresses human health issues, and agriculture addresses livestock—dogs are neither,” he says. “It takes vision to see that this is a public health problem: you vaccinate dogs, human rabies cases come down, and you can put your public health dollars toward other goals.”

Despite the daunting numbers—by one estimate the world count of stray dogs is 375 million—GARC researchers believe that dog vaccination programs are logistically feasible, and they have established pilot projects in Africa and Asia (some with support from the Bill & Melinda Gates Foundation). On the Philippine island of Bohol (human population: 1.3 million), researchers vaccinated an estimated 70 percent of the dog population. Before 2007 about 10 people died from rabies each year; since 2008 only one person has died of the disease.

Persuading people to vaccinate their pets is not always easy. Dealing with stray dogs is even more challenging. Because of a relentless rise in the number of rabies deaths in rural China, mostly in the south, that country has organized several mass killings of dogs, which disease-control experts and animal-rights activists have harshly criticized. Even if the cullings are effective in the short term, the stray populations inevitably rebound, as will

the virus. Meanwhile the popularity of keeping dogs as pets—around half of which may be unvaccinated—continues to increase as Chinese workers become more prosperous.
Perhaps vaccinating dogs will seem like a more workable plan once researchers figure out how to do away with injections, which require rounding up animals, as well as proper refrigeration and storage of the inoculations. A few especially promising projects spread food pellets laced with vaccines, similar to the blocks of treated fishmeal that have been used to control raccoon rabies in the U.S. Some of the food pellets also include sterilizing contraceptives to reduce numbers of unvaccinated newborns and shrink the size of stray populations. Rupprecht points out that if such vaccines, still in development for dogs, can be commercialized, they would find a ready market in China and India, the countries with the largest populations of strays and the most deaths from rabies. The necessary business know-how and technical acumen are already in place: China and India happen to be the biggest vaccine-manufacturing countries in the developing world.

http://phys.org/news/2013-08-scientists-sequence-genome-human-closest.html

Scientists sequence genome of human's closest invertebrate relative

Botryllus schlosseri, a small sea creature, can regenerate its entire body from its blood vessels alone. Stanford researchers hope that sequencing its genome will lead to advances in regenerative and transplant medicine for humans.

Phys.org - At first glance, Botryllus schlosseri has very little in common with humans. The small sea creature fuses together with others to form colonies that look like psychedelic blobs, encrusting rocks and seaweeds. It can reproduce asexually, and an entire individual can be regenerated from its blood vessels alone.
And yet, Botryllus is humans' closest living invertebrate relative. (Invertebrates lack a spinal column.) Now, a group led by Stanford scientists has sequenced its genome, making it possible to find the genetic basis for some of the animal's amazing regenerative abilities and immunity features, which potentially could be applied to human medicine.

Botryllus schlosseri is humans' closest living invertebrate relative. Credit: Chris Patton

In total, the group sequenced the animal's 580 million base pairs of DNA. (The human genome, by comparison, consists of more than 3 billion base pairs.) Though the researchers haven't studied the entire genome, they found evidence that Botryllus makes a useful invertebrate model for studying human genetics, in particular for highlighting the evolution of immunity and stem cell-mediated regeneration.
The researchers compared the Botryllus genome with several vertebrate and invertebrate genomes. Focusing on genes involved in various human diseases – affecting things such as heart and eye development, pregnancy and cancer – they found homologous genes for each in Botryllus, far more matches than in any of a dozen other invertebrates commonly used in research. An additional investigation of blood-related genes revealed that Botryllus was probably the first invertebrate to have vasculature in the same context of the human circulatory system, with blood cells traveling through blood vessels.
For example, in looking at a set of 20 genes that encode for humans' hematopoietic stem cells – cells that can self-renew and differentiate into other types of blood cells – they found 14 that are also expressed in cells isolated from the Botryllus stem cell niche. The scientists are now investigating how these genes function in Botryllus.
"The whole body can regenerate from the vasculature alone: the heart, digestive system, sophisticated tissues," said Ayelet Voskoboynik, a scientist at Stanford's Stem Cell Institute and Hopkins Marine Station, and the lead author on the study. "And it can do this relatively fast, probably using stem cells. Now that we have the genome, we can try to understand the mechanism behind it."
The study of Botryllus' genome could also lead to advances in transplant medicine. When two genetically distinct Botryllus colonies come into contact with each other, they either fuse their blood vessels to create a single organism, or reject one another and maintain individuality. When the blood vessels between the two colonies fuse into one interconnected network, the stem cells from each partner colony begin to circulate throughout the other.
The stem cells compete and in many cases one partner's stem cells "win" – and any new or replacement tissue grown through the fused colony does so based on the "winner's" genetic code.
A similar process occurs in humans who undergo an allogeneic transplant – when a patient receives tissue or cells from a non-identical donor. For instance, if a patient receives bone marrow or a ligament graft from a donor, over time, the recipient's cells replace the donor tissue.

In some instances, particularly concerning transplants of bone marrow or hematopoietic stem cells, the recipient's body rejects the donor cells. Voskoboynik suspects that studying the genetic basis for this interaction in Botryllus could lead to improvements in human therapies.
"If we can learn what makes a highly competitive stem cell a winner, and why others are rejected, we could hope to apply that knowledge to improve the success rate of allogeneic transplantations in humans," Voskoboynik said.
An important byproduct of the research, Voskoboynik said, was that Botryllus' complicated genome required the team to develop a new sequencing technique. The method, which has been patented, yielded exceptionally long, accurate sequences of DNA.
Additionally, rather than creating an average of the genetic information encoded on each paired chromosome, as standard techniques do, the new method yielded individual results from each chromosome. That advance, Voskoboynik said, could play a critical role in studying human diseases that occur as the result of different versions of genes existing on paired chromosomes.
The study was recently published in the peer-reviewed journal eLIFE.
More information: elife.elifesciences.org/content/2/e00569

http://www.sciencedaily.com/releases/2013/08/130815133058.htm?

Dad's Genes Build Placentas, Explaining Grandsire Effect

Placentas support the fetus and mother, but those organs grow according to blueprints from dad, according to new research at Cornell University.

The study, published in the Proceedings of the National Academy of Sciences in June, shows that the genes in a fetus that come from the father dominate in building the fetal side of the placenta.
Genes work in pairs: one from each parent. But about 1 percent of mammalian genes choose sides, a phenomenon called genomic imprinting. Imprinted genes use molecules that bind to DNA (epigenetic tags) to quiet one half and let the other lead. In the study, the researchers discovered 78 new imprinted genes using horse-donkey hybrids.
"This is the first study to offer an unbiased profile of novel imprinted genes in a mammal other than mice," said lead author Xu Wang, a postdoctoral associate in the laboratory of Andrew Clark, professor of molecular biology and genetics and the study's senior author. Strikingly, a majority of the imprinted candidates were paternally expressed, and this expression bias was lost when the transcriptomes of fetal tissues were examined. At the same time, as in mice, paternally imprinted genes heavily regulate placental development in these animals.
"Mouse experiments showed that if all DNA comes from the mother, the embryo grows quite well, but not the placenta, suggesting some degree of sex-based division of labor between programming the placenta and the embryo," said Wang. "Our results confirm what these past findings suggested."
The methods used in the study may also help breeders.
"This discovery explains what breeders call the maternal grandsire effect," said co-senior author Doug Antczak, equine geneticist at Cornell's College of Veterinary Medicine. "Some genes, like so-called speed genes in great racehorses, skip a generation and only express in grandchildren if their carrier was a certain sex. For example, most foals of history's best racehorse, Secretariat, raced poorly. So did his sons' offspring. But many of his daughters' foals were outstanding racehorses. We've developed a new approach that can identify imprinted genes that may be linked to racehorse traits and which could help breeders' decision-making."
Better understanding of genomic imprinting may offer insights into several human diseases. Mistakes in imprinting genes can impair development, spurring genetic problems that can cause gigantism, dwarfism, neurological failures, incomplete sexual development and others. Funding was provided by the Cornell Center for Vertebrate Genomics, Zweig Memorial Fund and Morris Animal Foundation.
X. Wang, D. C. Miller, R. Harman, D. F. Antczak, A. G. Clark. Paternally expressed genes predominate in the placenta. Proceedings of the National Academy of Sciences, 2013; 110 (26): 10705 DOI: 10.1073/pnas.1308998110

http://www.eurekalert.org/pub_releases/2013-08/uoc--eop081613.php

Effects of Parkinson's-disease mutation reversed in cells

UCSF study shows potential for new treatment strategy

UC San Francisco scientists working in the lab used a chemical found in an anti-wrinkle cream to prevent the death of nerve cells damaged by mutations that cause an inherited form of Parkinson’s disease. A similar approach might ward off cell death in the brains of people afflicted with Parkinson’s disease, the team suggested in a study reported online in the journal Cell on August 15.

The achievement marks a pharmacologic milestone as the first highly specific targeting of a member of an important class of enzymes called kinases to increase rather than to inhibit their activity, according to UCSF chemist Kevan Shokat, PhD, the senior scientist on the study.

The research raises hope that similar pharmaceutical strategies might be used for combatting other diseases, including diabetes and cancer, he said.

Mutations that cause malfunction of the targeted enzyme, PINK1, are directly responsible for some cases of early-onset Parkinson's disease. Loss of PINK1 activity is harmful to the cell's power plants, called mitochondria, best known for converting food energy into another form of chemical energy used by cells, the molecule ATP.

In Parkinson's disease, poorly performing mitochondria have been associated with the death of dopamine-producing nerve cells in a region of the brain called the substantia nigra, which plays a major role in control of movement. Loss of these cells is a hallmark of Parkinson's disease and the cause of prominent symptoms including rigidity and tremor.

A UCSF team led by Shokat, a Howard Hughes Medical Institute Investigator, used the chemical, called kinetin, to increase mutant PINK1 enzyme activity in nerve cells to near normal levels. "In light of the fact that mutations in PINK1 produce Parkinson's disease in humans, the finding that kinetin can speed mutated PINK1 activity to near normal levels raises the possibility that kinetin may be used to treat these patients," Shokat said.

The researchers also found that, in nerve cells with normal PINK1, kinetin boosted enzyme activity beyond typical levels.

This finding may be relevant for the most common forms of Parkinson's disease, in which PINK1 is not mutated, because a previous study showed that similar overactivity of PINK1 can slow the development of abnormal movement in a fruit-fly model of Parkinson's disease caused by another defect.

This defect is elevated production of the protein alpha-synuclein, also a cause of some inherited cases of Parkinson's disease.

The demonstration in the new study that PINK1 can be boosted in human nerve cells that lack PINK1 mutations therefore suggests that kinetin might also have therapeutic potential in common cases of Parkinson's disease in which PINK1 is not mutated, Shokat said.

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease, and the 14th leading cause of death in the United States, according to the U.S Centers for Disease Control and Prevention. Current treatments primarily aim to boost availability of dopamine to brain regions where dopamine-producing nerve cells have been lost.

Although many drugs that inhibit the activity of kinases have been developed over the past decade, including 15 currently approved to treat cancer, Shokat said none has yet been marketed to directly boost activity of a kinase.

The breakthrough in revving up PINK1 activity pharmacologically stemmed from Shokat's unconventional approach.

He targeted the enzyme's "substrate," a molecule that binds to an enzyme and undergoes a quick chemical transformation as a result. PINK1 uses ATP as a substrate, and the chemical reaction helps PINK1 in turn drive the activation of another enzyme, called Parkin.

Both of these enzymes are among a small number that previously have been strongly linked to Parkinson's disease. PINK1 and Parkin act together to monitor the health of mitochondria, and help trigger repair or disposal of damaged mitochondria within the cells, thereby promoting cell survival.

"Therapeutic approaches for enhancing the activity of PINK1 had not been considered, because scientists had not conceived of the idea of developing a new substrate for the enzyme," Shokat said.

"We found that a small molecule, called KTP, speeds chemical reactions catalyzed by PINK1 better than ATP, the natural substrate. That kind of better-than-natural response is essentially unheard of."

KTP is too big to fit into other kinases, Shokat said, but PINK1 has a larger ATP "pocket" to hold KTP.

After discovering the potential of KTP, the researchers then determined that kinetin is converted to KTP within cells. Experimentally, kinetin, which can cross blood vessels to get into the brain, has been given by mouth to treat a rare, genetic, neurological disease called familial dysautonomia.

Other researchers on the UCSF study include graduate student Nicholas Hertz, PhD; post-doctoral fellows Martin Sos, PhD and Amandine Berthet, PhD; UCSF faculty members Ken Nakamura, MD, PhD from the Gladstone Institute, and Kurt Thorn, PhD, and Al Burlingame, PhD.

The research was funded by the National Institutes for Health and by the Michael J. Fox Foundation.

Hertz and Shokat are inventors on a patent application related to kinetin and PINK1. UCSF has licensed the patent application to Mitokinin LLC, and Hertz and Shokat are cofounders and members of the company.

http://bit.ly/1cJvfbo

World's oldest temple built to worship the dog star

THE world's oldest temple, Göbekli Tepe in southern Turkey, may have been built to worship the dog star, Sirius.

16 August 2013 by Anil Ananthaswamy

The 11,000-year-old site consists of a series of at least 20 circular enclosures, although only a few have been uncovered since excavations began in the mid-1990s.

Each one is surrounded by a ring of huge, T-shaped stone pillars, some of which are decorated with carvings of fierce animals.

Two more megaliths stand parallel to each other at the centre of each ring (see illustration).

Göbekli Tepe put a dent in the idea of the Neolithic revolution, which said that the invention of agriculture spurred humans to build settlements and develop civilisation, art and religion.

There is no evidence of agriculture near the temple, hinting that religion came first in this instance.

"We have a lot of contemporaneous sites which are settlements of hunter-gatherers.

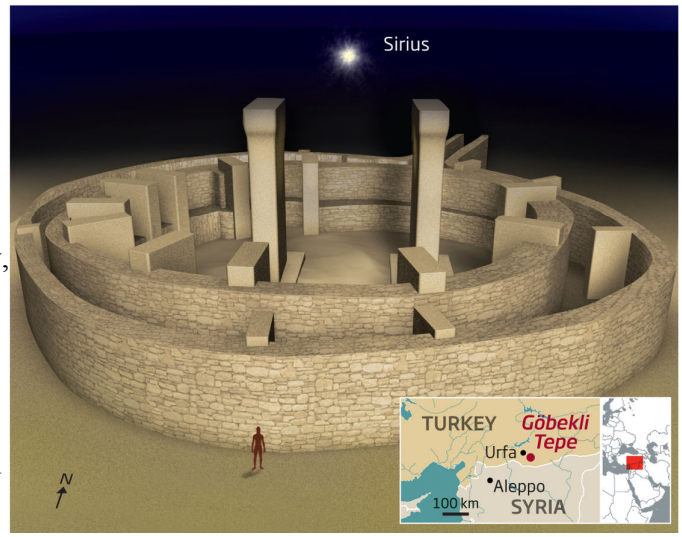
Göbekli Tepe was a sanctuary site for people living in these settlements," says Klaus Schmidt, chief archaeologist for the project at the German Archaeological Institute (DAI) in Berlin.

But it is still anybody's guess what type of religion the temple served.

Giulio Magli, an archaeoastronomer at the Polytechnic University of Milan in Italy, looked to the night sky for an answer.

Sirius worship

The Göbekli Tepe temple's central pillars, set within circular enclosures, would have framed the rising of the dog star, Sirius, at different points in time



After all, the arrangement of the pillars at Stonehenge in the UK suggests it could have been built as an astronomical observatory, maybe even to worship the moon.

Magli simulated what the sky would have looked like from Turkey when Göbekli Tepe was built.

Over millennia, the positions of the stars change due to Earth wobbling as it spins on its axis.

Stars that are near the horizon will rise and set at different points, and they can even disappear completely, only to reappear thousands of years later.

Today, Sirius can be seen almost worldwide as the brightest star in the sky – excluding the sun – and the fourth brightest night-sky object after the moon, Venus and Jupiter.

Sirius is so noticeable that its rising and setting was used as the basis for the ancient Egyptian calendar, says Magli.

At the latitude of Göbekli Tepe, Sirius would have been below the horizon until around 9300 BC, when it would have suddenly popped into view.

"I propose that the temple was built to follow the 'birth' of this star," says Magli.

"You can imagine that the appearance of a new object in the sky could even have triggered a new religion."

Using existing maps of Göbekli Tepe and satellite images of the region, Magli drew an imaginary line running between and parallel to the two megaliths inside each enclosure.

Three of the excavated rings seem to be aligned with the points on the horizon where Sirius would have risen in 9100 BC, 8750 BC and 8300 BC, respectively (arxiv.org/abs/1307.8397).

The results are preliminary, Magli stresses.

More accurate calculations will need a full survey using instruments such as a theodolite, a device for measuring horizontal and vertical angles.

Also, the sequence in which the structures were built is unclear, so it is hard to say if rings were built to follow Sirius as it rose at different points along the horizon.

Ongoing excavations might rule out any astronomical significance, says Jens Notroff, also at DAI.

"We are still discussing whether the monumental enclosures at Göbekli Tepe were open or roofed," he says.

"In the latter case, any activity regarding monitoring the sky would, of course, have been rather difficult."

http://bit.ly/1abNJQ1

Head hurts? Zap the wonder nerve in your neck

"IT WAS like red-hot pokers needling one side of my face," says Catherine, recalling the cluster headaches she experienced for six years. "I just wanted it to stop."

16 August 2013 by Linda Geddes

But it wouldn't – none of the drugs she tried had any effect.

Thinking she had nothing to lose, last year she enrolled in a pilot study to test a handheld device that applies a bolt of electricity to the neck, stimulating the vagus nerve – the superhighway that connects the brain to many of the body's organs, including the heart.

The results of the trial were presented last month at the International Headache Congress in Boston, and while the trial is small, the findings are positive. Of the 21 volunteers, 18 reported a reduction in the severity and frequency of their headaches, rating them, on average, 50 per cent less painful after using the device daily and whenever they felt a headache coming on.

This isn't the first time vagal nerve stimulation has been used as a treatment – but it is one of the first that hasn't required surgery. Some people with epilepsy have had a small generator that sends regular electrical signals to the vagus nerve implanted into their chest. Implanted devices have also been approved to treat depression. What's more, there is increasing evidence that such stimulation could treat many more disorders from headaches to stroke and possibly Alzheimer's disease (see "The many uses of the wonder nerve").

The latest study suggests it is possible to stimulate the nerve through the skin, rather than resorting to surgery. "What we've done is figured out a way to stimulate the vagus nerve with a very similar signal, but non-invasively through the neck," says Bruce Simon, vice-president of research at New Jersey-based ElectroCore, makers of the handheld device. "It's a simpler, less invasive way to stimulate the nerve."

Cluster headaches are thought to be triggered by the overactivation of brain cells involved in pain processing. The neurotransmitter glutamate, which excites brain cells, is a prime suspect. ElectroCore turned to the vagus nerve as previous studies had shown that stimulating it in people with epilepsy releases neurotransmitters that dampen brain activity.

When the firm used a smaller version of ElectroCore's device on rats, it found it reduced glutamate levels and excitability in these pain centres. Other studies have shown that vagus nerve stimulation causes the release of inhibitory neurotransmitters which counter the effects of glutamate.

The big question is whether a non-implantable device can really trigger changes in brain chemistry in humans, or whether people are simply experiencing a placebo effect. "The vagus nerve is buried deep in the neck, and something that's delivering currents through the skin can only go so deep," says Mike Kilgard of the University of Texas at Dallas. As you turn up the voltage, there's a risk of it activating muscle fibres that trigger painful cramps, he adds.

Simon says that volunteers using the device haven't reported any serious side effects. He adds that ElectroCore will soon publish data showing changes in brain activity in humans after using the device. Placebo-controlled trials are also about to start.

Catherine has been using it for a year without ill effect. "I can now function properly as a human being again," she says.

The many uses of the wonder nerve

Coma, irritable bowel syndrome, asthma and obesity are just some of the disparate conditions that vagus nerve stimulation may benefit and for which human trials are under way.

It might also help people with tinnitus. Although people with tinnitus complain of ringing in their ears, the problem actually arises because too many neurons fire in the auditory part of the brain when certain frequencies are heard.

Mike Kilgard of the University of Texas at Dallas reasoned that if people were played tones that didn't trigger tinnitus while the vagus nerve was stimulated, this might coax the rogue neurons into firing in response to these frequencies instead. "By activating this nerve we can enhance the brain's ability to rewire itself," he says.

He has so far tested the method in rats and in 10 people with tinnitus, using an implanted device to stimulate the nerve. Not everyone noticed an improvement, but even so Kilgard is planning a larger trial. The work was presented at a meeting of the International Union of Physiological Sciences in Birmingham, UK, last month.

The technique is also being tested in people who have had a stroke.

"If these studies stand up it could be worth changing the name of the vagus nerve to the wonder nerve," says Sunny Ogbonnaya at Cork University Hospital in Ireland.

http://www.sciencedaily.com/releases/2013/08/130816125314.htm

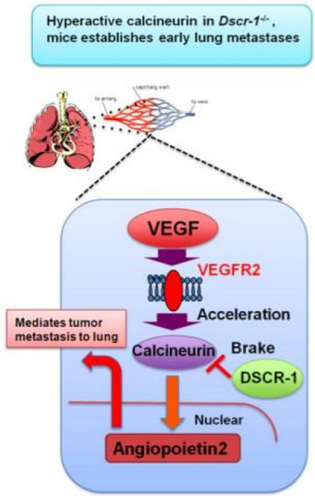
Tumors Form Advance Teams to Ready Lungs for Spread of Cancer

Cancer metastasis requires tumor cells to acquire properties that allow them to escape from the primary tumor site, travel to a distant place in the body, and form secondary tumors.

But first, an advance team of molecules produced by the primary tumor sets off a series of events that create a network of nurturing blood vessels for arriving primary tumor cells to set up shop.

In lung cancer, the formation of that niche likely involves immune cells and moderate levels of VEGF and other molecules that promote the formation of new blood vessels, or angiogenesis. But little is known about how the local lining, or endothelial, cells are activated at the niche.

Sandra Ryeom, PhD, assistant professor of Cancer Biology, Perelman School of Medicine, University of Pennsylvania, and colleagues, found that the signaling protein calcineurin upregulates another molecule, Ang-2 that promotes the needed angiogenesis. Hyperactivation of calcineurin in genetically altered mice that lack an inhibitior of calcineurin signaling leads to increased lung metastases. Conversely, inhibiting calcineurin or Ang-2 blocked metastases in lung cells of the mice. The findings are published this week in Cell Reports.



The findings may help shed light on the underpinnings of common cancer metastasis patterns, such as the tendency of prostate cancer to spread to the bones, or melanoma to the brain.

"We demonstrated that the calcineurin pathway is activated specifically in lung endothelium prior to the detection of tumor cells that preferentially and spontaneously metastasize to the lung from our experimental model of flank tumors in mice," says Ryeom.

Penn researchers found that the signaling protein calcineurin upregulates another molecule, Ang-2 that promotes necessary angiogenesis. Hyperactivation of calcineurin in genetically altered mice that lack an inhibitior of calcineurin signaling leads to increased lung metastases. Conversely, inhibiting calcineurin or Ang-2 blocked metastases in lung cells of the mice. The findings may help shed light on the underpinnings of common cancer metastasis patterns, such as the tendency of prostate cancer to spread to the bones, or melanoma to the brain. **(Credit: Sandra Ryeom, PhD, Perelman School of Medicine, University of Pennsylvania)**

Also, increased VEGF levels specifically in the lung, and not other organ microenvironments, trigger a threshold amount of calcineurin signaling that activates the Ang2 gene in lung endothelial cells. What's more, they showed that overexpression of the Ang-2 receptor prevents activation of the lung endothelium and inhibits lung metastases in their mouse models. "Our studies provide insights into the mechanisms underlying angiogenesis in the pre-metastatic niche and offer new targets for lung metastases," she says. Because calcineurin acts on the pathways that set up sites of metastasis away from the primary tumor sites, it could be a potential target for future cancer therapies; however it is also active in the immune system. In fact, calcineurin is inhibited by cyclosporine, which is used to combat transplant rejection, so using these types of drugs would be tricky for cancer unless they can be targeted specifically towards endothelial cells. Ongoing studies in the Ryeom lab are investigating whether calcineurin is important for metastases in other organs or whether this pathway is specific for lung metastases.

Co authors are Takashi Minami, Tatsuhiko Kodama, Jun-ichi Suehiro, Tsuyoshi Osawa, and Mai Miura, The University of Tokyo; Shuying Jiang, Makoto Naito, Nigata University, Japan; Yuichi Oike, Kumamoto University, Japan; and Keri Schadler, from Penn.

http://www.sciencedaily.com/releases/2013/08/130816153019.htm

Coffee and Tea May Contribute to a Healthy Liver

Surprise! Your morning cup of tea or coffee may be doing more than just perking you up before work.

An international team of researchers led by Duke-NUS Graduate Medical School (Duke-NUS) and the Duke University School of Medicine suggest that increased caffeine intake may reduce fatty liver in people with non-alcoholic fatty liver disease (NAFLD).

Worldwide, 70 percent of people diagnosed with diabetes and obesity have NAFLD, the major cause of fatty liver not due to excessive alcohol consumption. It is estimated that 30 percent of adults in the United States have this condition, and its prevalence is rising in Singapore. There are no effective treatments for NAFLD except diet and exercise.

Using cell culture and mouse models, the study authors -- led by Paul Yen, M.D., associate professor and research fellow, and Rohit Sinha, Ph.D of the Duke-NUS Graduate Medical School's Cardiovascular and Metabolic Disorders Program in Singapore -- observed that caffeine stimulates the metabolization of lipids

stored in liver cells and decreased the fatty liver of mice that were fed a high-fat diet. These findings suggest that consuming the equivalent caffeine intake of four cups of coffee or tea a day may be beneficial in preventing and protecting against the progression of NAFLD in humans.
The findings will be published in the September issue of the journal Hepatology.
"This is the first detailed study of the mechanism for caffeine action on lipids in liver and the results are very interesting," Yen said. "Coffee and tea are so commonly consumed and the notion that they may be therapeutic, especially since they have a reputation for being "bad" for health, is especially enlightening."
The team said this research could lead to the development of caffeine-like drugs that do not have the usual side effects related to caffeine, but retain its therapeutic effects on the liver. It could serve as a starting point for studies on the full benefits of caffeine and related therapeutics in humans.
In addition to Yen and Sinha, collaborators included Christopher Newgard, PhD, director of the Sarah W. Stedman Nutrition and Metabolism Center at Duke University School of Medicine, where the metabolomics analysis of the data was conducted.
The study was supported by funding from Singapore's Agency for Science, Technology, and Research; the Ministry of Health; and the Ministry of Education.
Rohit Anthony Sinha, Benjamin L. Farah, Brijesh K. Singh, Monowarul Mobin Siddique, Ying Li, Yajun Wu, Olga R. Ilkayeva, Jessica Gooding, Jianhong Ching, Jin Zhou, Laura Martinez, Sherwin Xie, Boon-Huat Bay, Scott A. Summers, Christopher B. Newgard, Paul M. Yen. Caffeine stimulates hepatic lipid metabolism via autophagy-lysosomal pathway. Hepatology, 2013; DOI: 10.1002/hep.26667

http://www.medscape.com/viewarticle/809593?src=rss

FDA: Don't Use Any Sterile Product From NuVision Pharmacy

In a statement issued today, the US Food and Drug Administration (FDA) reminds healthcare providers not to use any sterile products made by compounding pharmacy NuVision Pharmacy.

Megan Brooks

There continue to be "safety concerns with all sterile drug products made and distributed by NuVision Pharmacy of Dallas, Texas.
Health care providers should not administer any NuVision Pharmacy sterile products to patients because the products' sterility is not assured," the FDA said.
"NuVision Pharmacy has repeatedly declined to recall its sterile products," the FDA said today.
In a letter to NuVision dated July 26, 2013, the agency requested an immediate recall of all lots of sterile products produced at NuVision that have not passed their expiration dates.
In the letter, the FDA outlined poor sterile production practices observed by FDA investigators during an April 2013 inspection of NuVision's Dallas facility.
The FDA said those practices raised concerns about the lack of sterility assurance of NuVision's sterile drug products.
If a drug product marketed as sterile contains microbial contamination, "patients could be at risk for serious, potentially life-threatening infections," the FDA said.
NuVision responded to the letter by refusing to recall its sterile products.
"Under its authority, the FDA cannot require NuVision to undertake such a recall. Therefore the agency reminds health care providers not to use any sterile products from NuVision," the FDA said today.
In April, as reported by Medscape Medical News , NuVision recalled methylcobalamin injection and lyophilized injection products because of lack of sterility assurance and concerns associated with the quality control processes identified during an FDA inspection.
The FDA said today that it has received adverse event reports of fever, flu-like symptoms, and soreness at the injection site associated with the recalled methylcobalamin injection product.
On May 18, the FDA advised healthcare providers not to use any sterile product from NuVision Pharmacy because of concerns about a lack of sterility assurance, as reported by Medscape Medical News .
To report problems with these products, contact MedWatch, the FDA's safety information and adverse event reporting program, by telephone at 1-800-FDA-1088; by fax at 1-800-FDA-0178; online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm; with postage-paid FDA form 3500, available at http://www.fda.gov/MedWatch/getforms.htm; or by mail to MedWatch, 5600 Fishers Lane, Rockville, Maryland 20852-9787.

http://nyti.ms/19AO6El

Path to United States Practice Is Long Slog to Foreign Doctors

Thousands of foreign-trained immigrant physicians are living in the United States with lifesaving skills that are going unused because they stumbled over one of the many hurdles in the path toward becoming a licensed doctor here.

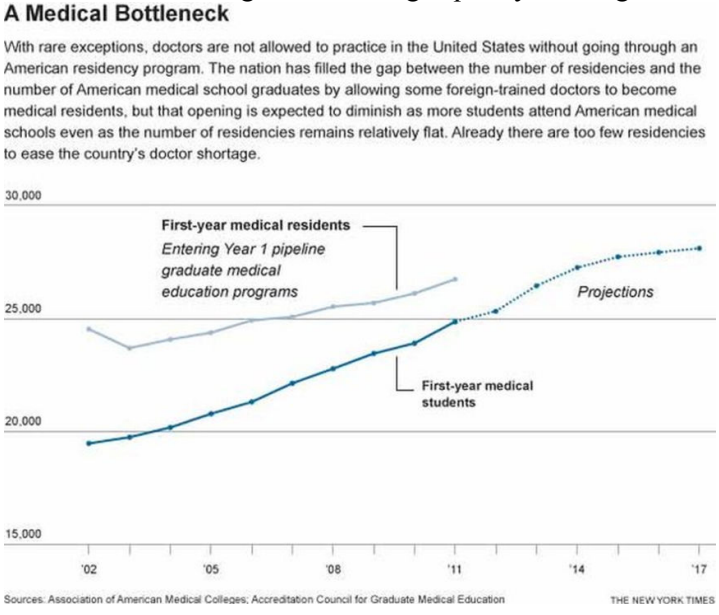
By CATHERINE RAMPELL

The involved testing process and often duplicative training these doctors must go through are intended to make sure they meet this country's high quality standards, which American medical industry groups say are unmatched elsewhere in the world. Some development experts are also loath to make it too easy for foreign doctors to practice here because of the risk of a "brain drain" abroad.

But many foreign physicians and their advocates argue that the process is unnecessarily restrictive and time-consuming, particularly since America's need for doctors will expand sharply in a few short months under President Obama's health care law. They point out that medical services cost far more in the United States than elsewhere in the world, in part because of such restrictions.

The United States already faces a shortage of physicians in many parts of the country, especially in specialties where foreign-trained physicians are most likely to practice, like primary care. And that shortage is going to get exponentially worse, studies predict, when the health care law insures millions more Americans starting in 2014.

The new health care law only modestly increases the supply of homegrown primary care doctors, not nearly enough to account for the shortfall, and even that tiny bump is still a few years away because it takes so long to train new doctors. Immigrant advocates and some economists point out that the medical labor force could grow much faster if the country tapped the underused skills of the foreign-trained physicians who are already here but are not allowed to practice. Canada, by contrast, has made efforts to recognize more high-quality training programs done abroad.



"It doesn't cost the taxpayers a penny because these doctors come fully trained," said Nyapati Raghu Rao, the Indian-born chairman of psychiatry at Nassau University Medical Center and a past chairman of the American Medical Association's international medical graduates governing council. "It is doubtful that the U.S. can respond to the massive shortages without the participation of international medical graduates. But we're basically ignoring them in this discussion and I don't know why that is."

Consider Sajith Abeyawickrama, 37, who was a celebrated anesthesiologist in his native Sri Lanka. But here in the United States, where he came in 2010 to marry, he cannot practice medicine.

Instead of working as a doctor himself, he has held a series of jobs in the medical industry, including an unpaid position where he entered patient data into a hospital's electronic medical records system, and, more recently, a paid position teaching a test prep course for students trying to become licensed doctors themselves.

For years the United States has been training too few doctors to meet its own needs, in part because of industry-set limits on the number of medical school slots available. Today about one in four physicians practicing in the United States were trained abroad, a figure that includes a substantial number of American citizens who could not get into medical school at home and studied in places like the Caribbean.

But immigrant doctors, no matter how experienced and well trained, must run a long, costly and confusing gantlet before they can actually practice here.

The process usually starts with an application to a private nonprofit organization that verifies medical school transcripts and diplomas. Among other requirements, foreign doctors must prove they speak English; pass three separate steps of the United States Medical Licensing Examination; get American recommendation letters, usually obtained after volunteering or working in a hospital, clinic or research organization; and be permanent residents or receive a work visa (which often requires them to return to their home country after their training).

The biggest challenge is that an immigrant physician must win one of the coveted slots in America's medical residency system, the step that seems to be the tightest bottleneck.

That residency, which typically involves grueling 80-hour workweeks, is required even if a doctor previously did a residency in a country with an advanced medical system, like Britain or Japan. The only exception is for doctors who did their residencies in Canada.

The whole process can consume upward of a decade — for those lucky few who make it through.

"It took me double the time I thought, since I was still having to work while I was studying to pay for the visa, which was very expensive," said Alisson Sombredero, 33, an H.I.V. specialist who came to the United States from Colombia in 2005.

Dr. Sombredero spent three years studying for her American license exams, gathering recommendation letters and volunteering at a hospital in an unpaid position. She supported herself during that time by working as a nanny. That was followed by three years in a residency at Highland Hospital in Oakland, Calif., and one year in an H.I.V. fellowship at San Francisco General Hospital. She finally finished her training this summer, eight years after she arrived in the United States and 16 years after she first enrolled in medical school.

Dr. Sombredero was helped through the process by the Welcome Back Initiative, an organization started 12 years ago as a partnership between San Francisco State University and City College of San Francisco. The organization has worked with about 4,600 physicians in its centers around the country, according to its founder, José Ramón Fernández-Peña.

Only 118 of those doctors, he said, have successfully made it to residency.

"If I had to even think about going through residency now, I'd shoot myself," said Dr. Fernández-Peña, who came to the United States from Mexico in 1985 and chose not even to try treating patients once he learned what the licensing process requires. Today, in addition to running the Welcome Back Initiative, he is an associate professor of health education at San Francisco State.

The counterargument for making it easier for foreign physicians to practice in the United States — aside from concerns about quality controls — is that doing so will draw more physicians from poor countries. These places often have paid for their doctors' medical training with public funds, on the assumption that those doctors will stay.

"We need to wean ourselves from our extraordinary dependence on importing doctors from the developing world," said Fitzhugh Mullan, a professor of medicine and health policy at George Washington University in Washington. "We can't tell other countries to nail their doctors' feet to the ground at home. People will want to move and they should be able to. But we have created a huge, wide, open market by undertraining here, and the developing world responds."

About one in 10 doctors trained in India have left that country, he found in a 2005 study, and the figure is close to one in three for Ghana. (Many of those moved to Europe or other developed nations other than the United States.)

No one knows exactly how many immigrant doctors are in the United States and not practicing, but some other data points provide a clue. Each year the Educational Commission for Foreign Medical Graduates, a private nonprofit, clears about 8,000 immigrant doctors (not including the American citizens who go to medical school abroad) to apply for the national residency match system. Normally about 3,000 of them successfully match to a residency slot, mostly filling less desired residencies in community hospitals, unpopular locations and in less lucrative specialties like primary care.

Over the last five years, an average of 42.1 percent of foreign-trained immigrant physicians who applied for residencies through the national match system succeeded. That compares with an average match rate of 93.9 percent for seniors at America's mainstream medical schools.

Mr. Abeyawickrama, the Sri Lankan anesthesiologist, has failed to match for three years in a row; he blames low test scores. Most foreign doctors spend several years studying and taking their licensing exams, which American-trained doctors also take. He said he didn't know this, and misguidedly thought it would be more expeditious to take all three within seven months of his arrival.

"That was the most foolish thing I ever did in my life," he says. "I had the knowledge, but I did not know the art of the exams here."

Even with inadequate preparation, he passed, though earning scores too low to be considered by most residency programs. But as a testament to his talents, he was recently offered a two-year research fellowship at the prestigious Cleveland Clinic, starting in the fall. He is hoping this job will give residency programs reason to overlook his test scores next time he applies.

"Once I finish my fellowship in Cleveland, at one of the best hospitals in America, I hope there will be some doors opening for me," he said. "Maybe then they will look at my scores and realize they do not depict my true knowledge."

The residency match rate for immigrants is likely to fall even lower in coming years. That is because the number of accredited American medical schools, and therefore United States-trained medical students, has increased substantially in the last decade, while the number of residency slots (most of which are subsizided by Medicare) has barely budged since Congress effectively froze residency funding in 1997.

Experts say several things could be done to make it easier for foreign-trained doctors to practice here, including reciprocal licensing arrangements, more and perhaps accelerated American residencies, or recognition of postgraduate training from other advanced countries.

Canada provides the most telling comparison. Some Canadian provinces allow immigrant doctors to practice family medicine without doing a Canadian residency, typically if the doctor did similar postgraduate work in the United States, Australia, Britain or Ireland. There are also residency waivers for some specialists coming from select training programs abroad considered similar to Canadian ones.

As a result, many (some estimates suggest nearly half) foreign-trained physicians currently coming into Canada do not have to redo a residency, said Dr. Rocco Gerace, the president of the Federation of Medical Regulatory Authorities of Canada.

In the United States, some foreign doctors work as waiters or taxi drivers while they try to work through the licensing process. Others decide to apply their skills to becoming another kind of medical professional, like a nurse practitioner or physician assistant, adopting careers that require fewer years of training. But those paths present barriers as well.

The same is true for other highly skilled medical professionals.

Hemamani Karuppiaharjunan, 40, was a dentist in her native India, which she left in 2000 to join her husband in the United States. She decided that going back to dentistry school in the United States while having two young children would be prohibitively time-consuming and expensive. Instead, she enrolled in a two-year dental hygiene program at Bergen Community College in Paramus, N.J., which cost her $30,000 instead of the $150,000 she would have needed to attend dental school. She graduated in 2012 at the top of her class and earns $42 an hour now, about half what she might make as a dentist in her area.

The loss of status has been harder.

“I rarely talk about it with patients,” she said. When she does mention her background, they usually express sympathy. “I’m glad my education is still respected in that sense, that people do recognize what I’ve done even though I can’t practice dentistry.”