http://bit.ly/1NUkpms

FDA OKs immunotherapy drugs for bladder, blood cancers

First drug for bladder cancer that harnesses the body's immune system

By LINDA A. JOHNSON

TRENTON, N.J. - U.S. regulators have approved the first drug for bladder cancer that harnesses the body's immune system, the first major advance in three decades against the most common type of bladder cancer.

Tecentriq won accelerated approval from the Food and Drug Administration for treating patients with advanced urothelial cancer after chemotherapy stops helping them — a point when most usually die within about six months.

Such conditional approval is granted based on promising initial test results for disorders where patients have few or no options. Testing on many more patients to confirm the early results, which is required to obtain full approval from the FDA, is in progress.

Tecentriq, developed by the Roche Group's Genentech unit, blocks a protein found on many tumor cells that deactivates T-cells, the key immune-system cells that hunt down and destroy cancer cells. A similar drug from Bristol-Myers Squibb Co., Opdivo, was approved by the FDA for treating Hodgkin lymphoma — the fourth cancer type for which it's been approved in the U.S.

Both drugs are part of a promising new class of injected cancer medicines that work with the patient's own immune system, helping it find and kill tumor cells that might otherwise multiply by using mechanisms to hide from immune-system sentinels. Drugmakers are racing to develop such drugs to fight a range of deadly cancers, and some of the new drugs have brought the first significant improvements in patient survival in decades. In many hard-to-treat cancers, new drugs that extend survival just a few months for some patients are considered a big advance.

Most bladder cancer patients for whom chemotherapy fails die within about six months on average, according to Dr. Daniel Chen, Genentech's head of development for so-called cancer immunotherapy drugs. Chen said in an interview that some patients given Tecentriq in clinical testing are alive as long as three years after starting treatment.

The tests on which Tecentriq's approval are based included 310 people with advanced urothelial cancer, which occurs in the bladder and sometimes in the ureter, urethra and pelvis. The testing found 15 percent of the patients had their tumors shrink, with that benefit lasting about 2 months to 14 months. In the subset of patients found to have high levels of the protein that Tecentriq targets, called PD-L1, 26 percent had their tumors shrink. Tumors completely vanished in nearly 6 percent of the patients tested, and in 12 percent of those with high levels of the PD-L1 protein. Those patients are still being followed, and many continue to do well.

Chen noted that unlike chemotherapy, which often causes disabling nausea and other serious side effects, patients suffered far less-severe side effects while on Tecentriq. Those ranged from various infections and fatigue to intestinal blockages and blood clots. "Many of these patients go back to work" during treatment, Chen said. "They're able to experience a normal quality of life." Chen said the additional study results also will be aimed at getting approval for using Tecentriq for newly diagnosed patients.

Bladder cancer is the fifth-most common type, and strikes far more men than women. There are about 77,000 new cases and 16,400 deaths per year in the U.S., according to the National Cancer Institute.

Tecentriq, known chemically as atezolizumab, has a list price of $12,500 per month, without insurance. It's a biologic drug, meaning it's manufactured in living cells rather than by missing chemicals in vats. Genentech said it will be available in one to two weeks.

Bristol-Myers Squibb's Opdivo also works by harnessing immune-system cells. The FDA granted accelerated approval based on patient tests showing that 7 percent of patients given Opdivo had their tumors disappear. Another 58 percent of patients had their tumors shrink or stop growing.

Opdivo already is approved for treating patients with advanced cases of melanoma, lung and kidney cancer. The drug's sales are growing rapidly with each additional approval and hit $704 million in the January-March quarter.

Opdivo has a list price of about $12,900 per month on average. That can vary because the dosage is based on the patient's weight. Bristol-Myers and Roche both provide financial assistance for patients who can't afford the drugs.

http://nyti.ms/1XEsuxj

Plant-Based, the Beyond Burger Aims to Stand Sturdy Among Meat

The Beyond Burger is sold alongside the case where beef, poultry, lamb and pork are sold

By STEPHANIE STROM MAY 22, 2016

For the handful of companies working to develop plant-based alternatives to meat, finding a hearty stand-in for the humble hamburger is the holy grail.

One of those companies, Beyond Meat, says it has come up with that burger. The company will begin selling the Beyond Burger on Monday at a Whole Foods in Boulder, Colo. — alongside the case where beef, poultry, lamb and pork are sold.

"This is what I had in mind when I started the company," said Ethan Brown, who founded Beyond Meat in 2009.

Companies making plant-based alternatives to a variety of animal proteins are popping up everywhere. Jars of Just Mayo, an eggless spread made by Hampton Creek, now sit near Hellmann's, and nut-based milks now account for almost 10 percent of the $20 billion milk market.

Sales of products incorporating plant proteins grew 8.7 percent from 2014 to 2015, while overall sales of food products grew 3.7 percent, according to Spins, which collects data on retail sales for the natural and specialty products industries.

Tom Rich, vice president of purchasing and distribution in the Denver region of Whole Foods Market where the Beyond Burger will first be sold, says there is a growing interest in alternative protein sources. The Beyond Burger, said Mr. Rich, a vegetarian, "tasted and felt and chewed like any other burger, and on some level, I just want to be able to eat the same way everyone else eats."

Caleb Bryant, a food service analyst at Mintel, said most consumers continued to think of a burger as meat-based, though he said he saw growing interest in plant-based alternatives among younger consumers. "This past year has been a big deal for vegetable burgers," Mr. Bryant said. He noted that the Superiority Burger, a vegetarian burger sold at the New York City restaurant that shares the same name, was nominated as a semifinalist for a James Beard Award.

Indeed, chefs like Dan Barber have been experimenting with veggie burgers. And a plant-based burger from Impossible Foods, a competitor to Beyond Meat, will soon be on the menu at "select" restaurants in New York, San Francisco and Los Angeles, according to the company's marketing.

Beyond Meat wants its burgers to go home via the grocery basket. At Whole Foods, where Mr. Brown will be, on and off, for the next couple of weeks, a package of two four-ounce Beyond Burgers will sell for $5.99. "I want as many people as possible to have access to our products," Mr. Brown said. "My goals go way beyond food."

Like many of the entrepreneurs developing new ways of extracting protein from plants, Mr. Brown said he was concerned about both nutrition and the environmental impact of large-scale animal farming and how the food industry will adequately feed the world's growing population.

Beyond Meat previously sold the Beast Burger as frozen burger patties among vegetarian burgers, such as those from MorningStar Farms and Amy's. The goal, however, was to develop a "fresh" burger that would sell in a refrigerated case alongside beef and other meat burgers.

The company had to solve a variety of issues. For one thing, it had to ensure that the middle of its burger would stay moist, pink and juicy as the exterior cooked to that distinct dark brown of a traditional hamburger. It had to "bleed" — thousands of beets were pulverized in the development process — and it had to emit the same smell as cooked beef.

"It's hard to reduce flavor and aroma to an equation, particularly when you need a solution that is simple and flexible," said Joseph Puglisi, a professor of structural biology at Stanford University whose research focuses on the shapes and forms of biological molecules.

The distribution of "fat" in the product was especially tricky, said Professor Puglisi, who serves as Beyond Meat's lead scientific adviser and helped the company assemble its team of young chemists, biologists and engineers. "We were able to get fat distributed throughout a patty — but in meat, fat is distributed in sheets," he said. "Plants don't have ligaments."

The goal was also to have no preservatives and all natural ingredients.

Mr. Brown said he spent months coaxing Whole Foods into selling the burgers in the meat section. At Whole Foods in Boulder, the burgers will be sold in the section where other meat alternatives are sold. Eventually, it will be sold in other Whole Foods stores in the region. It also will be on a new vegan menu in the store's cafe and available for takeout. And for two weeks, a team from Beyond Meat will be in the store, grilling Beyond Burgers and listening to customers' reactions. Next up, a T-bone steak? "That may be a long way off," Mr. Brown said. "But nothing's impossible."

http://www.eurekalert.org/pub_releases/2016-05/cp-ico051716.php

In changing oceans, cephalopods are booming

Climate change appears to have been goods far for cephalopod

Humans have changed the world's oceans in ways that have been devastating to many marine species. But, according to new evidence, it appears that the change has so far been good for cephalopods, the group including octopuses, cuttlefish, and squid. The study reported in the Cell Press journal Current Biology on May 23 shows that cephalopods' numbers have increased significantly over the last six decades.

This is a photograph of giant Australian cuttlefish (Sepia apama), Spencer Gulf, South Australia. **Scott Portelli**

"The consistency was the biggest surprise," says Zoë Doubleday of Australia's Environment Institute at the University of Adelaide. "Cephalopods are notoriously variable, and population abundance can fluctuate wildly, both within and among

species. The fact that we observed consistent, long-term increases in three diverse groups of cephalopods, which inhabit everything from rock pools to open oceans, is remarkable."

According to the researchers, there has been growing speculation that cephalopod populations were proliferating in response to a changing environment, based partly on trends in cephalopod fisheries. Cephalopods are known for rapid growth, short lifespans, and extra-sensitive physiologies, which may allow them to adapt more quickly than many other marine species.

To investigate long-term trends in cephalopod abundance, Doubleday and her colleagues assembled global time series of cephalopod catch rates (catch per unit of fishing or sampling effort) from 1953 to 2013. The study included 35 cephalopod species or genera representing six families. The data show that cephalopods, of many different types living all over the world, are on the rise.

The ecological and socio-economic ramifications associated with this increase in cephalopods are much less clear and are likely to be complex, according to the researchers.

"Cephalopods are voracious and adaptable predators and increased predation by cephalopods could impact many prey species, including commercially valuable fish and invertebrates," they write. "Conversely, increases in cephalopod populations could benefit marine predators which are reliant on them for food, as well as human communities reliant on them as a fisheries resource."

What may happen to cephalopod populations in the future is difficult to predict, particularly if fishing pressure continues to increase. Doubleday says that they are now investigating the factors responsible for cephalopods' proliferation.

"It is a difficult, but important, question to answer, as it may tell us an even bigger story about how human activities are changing the ocean," she says.

The research, funded by the Environment Institute at the University of Adelaide, was the result of a workshop involving researchers all over the world.

Current Biology, Doubleday et al.: "Global proliferation of cephalopods"
http://www.cell.com/current-biology/fulltext/S0960-9822(16)30319-0

http://www.eurekalert.org/pub_releases/2016-05/uor-dhi052216.php

Did human-like intelligence evolve to care for helpless babies?

A new study from the University of Rochester suggests that human intelligence might have evolved in response to the demands of caring for infants.

Steven Piantadosi and Celeste Kidd, assistant professors in brain and cognitive sciences, developed a novel evolutionary model in which the development of high levels of intelligence may be driven by the demands of raising offspring. Their study is available online in the Proceedings of the National Academy of Sciences' Early Edition.

"Human infants are born far more immature than the infants of other species. For example, giraffe calves are able to stand-up, walk around, and even flee from predators within hours of their births. By comparison, human infants cannot even support their own heads," said Kidd.

"Our theory is that there is a kind of self-reinforcing cycle where big brains lead to very premature offspring and premature offspring lead to parents having to have big brains. What our formal modeling work shows is that those dynamics can result in runaway pressure for extremely intelligent parents and extremely premature offspring," said Piantadosi.

In other words, because humans have relatively big brains, their infants must be born early in development while their heads are still small enough to insure a safe delivery. Early birth, though, means that human infants are helpless for much longer than other primates, and such vulnerable infants require intelligent parents. As a result, selective pressures for large brains and early birth can become self-reinforcing--potentially creating species like humans with qualitatively different cognitive abilities than other animals.

Piantadosi and Kidd tested a novel prediction of the model that the immaturity of newborns should be strongly related to general intelligence. "What we found is that weaning time--which acts as a measure of the prematurity of the infants--was a much better predictor of primate's intelligence than any of other measures we looked at, including brain size, which is commonly correlated with intelligence," said Piantadosi.

The theory may also be able to explain the origin of the cognitive abilities that make humans special. "Humans have a unique kind of intelligence. We are good at social reasoning and something called 'theory of mind'--the ability to anticipate the needs of others, and to recognize that those needs may not be the same as our own," said Kidd, who is also the director of the Rochester Baby Lab at the University of Rochester. "This is an especially helpful when taking care of an infant who is not able talk for a couple of years."

"There are alternative theories of why humans are so intelligent. A lot of these are based on factors like living in a harsh environment or hunting in groups," said Piantadosi. "One of the motivating puzzles of our research was thinking about those theories and trying to see why they predict specifically that primates or mammals should become so intelligent, instead of other species that faced similar pressures."

The key is live birth. According to the researchers, the runaway selection of intelligence requires both live birth of a single off spring and large brains, distinctive features of higher mammals.

"Our theory explains specifically why primates developed super intelligence but dinosaurs--who faced many of the same environmental pressures and had more time to do so--did not. Dinosaurs matured in eggs, so there was no linking between intelligence and infant immaturity at birth," said Kidd.

The research was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health.

http://www.eurekalert.org/pub_releases/2016-05/aafc-ici051916.php

Investigational CDK4/6 inhibitor abemaciclib is active against a range of cancer types

Abemaciclib showed durable clinical activity when given as continuous single-agent therapy to patients with breast cancer, non-small cell lung cancer (NSCLC), glioblastoma, and melanoma

Bottom Line: The investigational anticancer therapeutic abemaciclib, which targets CDK4 and CDK6, showed durable clinical activity when given as continuous single-agent therapy to patients with a variety of cancer types, including breast cancer, non-small cell lung cancer (NSCLC), glioblastoma, and melanoma, according to results from a phase I clinical trial.

Journal in Which the Study was Published: Cancer Discovery, a journal of the American Association for Cancer Research.

Senior authors: Amita Patnaik, MD, associate director of clinical research at South Texas Accelerated Research Therapeutics in San Antonio, Texas, and Geoffrey I. Shapiro, MD, PhD, director of the Early Drug Development Center at the Dana-Farber Cancer Institute in Boston.

Background: In February 2015, the U.S. Food and Drug Administration (FDA) approved the CDK4/6 inhibitor palbociclib (Ibrance) for use in combination with the aromatase inhibitor letrozole for treating postmenopausal women with estrogen receptor-positive, HER2-negative advanced breast cancer.

The oral CDK4/6 inhibitor abemaciclib is a very different molecule from palbociclib, with distinct attributes that contribute to its discrete therapeutic effects, in particular, its single-agent activity, according to Shapiro.

For example, abemaciclib has greater selectivity for CDK4 compared with palbociclib, which may explain why it does not affect white blood cell counts as severely, allowing it to be taken on a continuous schedule without treatment holidays, he said. Abemaciclib also penetrates the central nervous system, whereas palbociclib does not, raising the possibility that it could be used to treat primary or metastatic brain tumors, he added.

How the Study Was Conducted and Results: Patnaik, Shapiro, and colleagues enrolled 225 patients with a variety of types of advanced cancer in the phase I clinical trial designed to evaluate the safety and preliminary efficacy of abemaciclib. In the dose escalation phase, the researchers determined that the maximum tolerated dose was 200 milligrams (mg) every 12 hours; the dose-limiting toxicity was grade 3 fatigue.

In the expansion phase, single-agent abemaciclib was administered to 47 patients with breast cancer, 68 with NSCLC, 17 with glioblastoma, 26 with melanoma, and 15 with colorectal cancer. Among these patients, the most common treatment-related adverse events were fatigue, diarrhea, nausea, vomiting, anorexia, weight loss, kidney dysfunction, and decreased red and white blood cell counts.

Radiographic responses were observed for some patients with breast cancer, NSCLC, and melanoma.

Among the 36 patients with hormone receptor-positive breast cancer, 11 had a partial response, with four of the 11 responders having continued prior endocrine therapy, and an additional 18 patients had stable disease. Among the 68 patients with NSCLC, two had a partial response and 31 had stable disease; one patient who had a partial response and 12 who had stable disease were known to have KRAS-mutant NSCLC. Among the 26 patients with melanoma, one had a partial response and six had stable disease. Three of the 17 patients with glioblastoma had stable disease, with two of them continuing to receive treatment without disease progression for 19 and 23 cycles, respectively.

Author Comment: "These data show that abemaciclib is an oral drug that can be taken on a continuous schedule and achieve durable clinical activity against multiple tumors including breast and lung cancers," said Shapiro.

"The results of the trial supported the FDA decision to grant breakthrough therapy designation to abemaciclib (previously known as LY2835219) for patients with refractory hormone receptor-positive advanced or metastatic breast cancer," added Patnaik.

Limitations: Patnaik explained that because this study included 225 patients with different types of cancer, confirmatory clinical trials in specific patient populations are necessary to precisely define the role of abemaciclib in cancer care. Multiple clinical trials have already been initiated to evaluate abemaciclib as a treatment for certain groups of patients with breast cancer and NSCLC, as well as children with primary brain tumors and adults with brain metastases, she noted.

Funding & Disclosures: The study was funded by Eli Lilly and Company. Patnaik has received research funding from Lilly. Shapiro served on an advisory board for Lilly during the conduct of the study; reports receiving personal fees from Lilly, GI Therapeutics, Vertex Pharmaceuticals, and grants from Lilly for work other than reported here; and is an investigator on several trials using other CDK4/6 inhibitors, including palbociclib and ribociclib.

http://www.eurekalert.org/pub_releases/2016-05/cp-loy051816.php

Loss of Y chromosome is a risk factor for Alzheimer's disease

The loss of the Y chromosome in batches of blood cells over time continues to develop as one biological explanation for why men, on average, live shorter lives than women.

Researchers reporting May 23, 2016 in the American Journal of Human Genetics found that men with blood samples showing loss of chromosome Y developed Alzheimer's as often as people born with genes that put them at the most risk for the disease. The work will be presented at the annual conference of the European Society of Human Genetics.

"Most genetic research today is focused on inherited gene variants -- mutations that are inherited by the offspring, but what we're looking at are postzygotic mutations that are acquired during life," says senior author Lars Forsberg, a researcher in the Department of Immunology, Genetics, and Pathology at Uppsala University in Sweden. "Using new tools to analyze genetic variations that accumulate with age, we can help explain how sporadic diseases like cancer or Alzheimer's manifest," says first author Jan Dumanski.

One such postzygotic mutation found in the cells of biological males is the loss of the Y chromosome in a degree of blood cells. Loss of Y occurs in up to 17 percent of men and is more likely to be found in older men and men who smoke. This study expands on the idea that loss of Y, already a known risk factor for cancer (10.1038/ng.2966), could be a predictive biomarker for a wider range of poor health outcomes, specifically Alzheimer's. Why loss of Y can be linked to an increased risk for disease remains unclear, but the authors speculate it has to do with reduced immune system performance.

The researchers looked at over 3,000 men to ascertain whether there was any predictive association between loss of Y in blood cells and Alzheimer's disease. The participants came from three long-term studies that could provide regular blood samples: the European Alzheimer's Disease Initiative, the Uppsala Longitudinal Study of Adult Men, and the Prospective Investigation of the Vasculature in Uppsala Seniors. Across the datasets, those with the highest fraction of blood cells without a Y chromosome were consistently more likely to be diagnosed with Alzheimer's.

"Having loss of Y is not 100 percent predictive that you will have either cancer or Alzheimer's," Forsberg says, adding that there were men in the study who had the mutation and lived with no symptoms well into their 90s. "But in the future, loss of Y in blood cells can become a new biomarker for disease risk and perhaps evaluation can make a difference in detecting and treating problems early."

Forsberg, Dumanski, and colleagues will next investigate the effect of loss of Y in larger cohorts and explore in greater detail how it confers risk for specific types of cancers and disease. They also plan to look at the cellular changes caused by loss of Y and how it affects different types of blood cells.

The study was primarily funded by the Olle Enqvist Byggmästare Foundation, the European Research Council, the Swedish Cancer Society, the Swedish Research Council, the Swedish Heart-Lung Foundation, and Sci-Life-Lab-Uppsala

American Journal of Human Genetics, Dumanski et al.: "Mosaic loss of chromosome Y in blood is associated with Alzheimer's disease" http://www.cell.com/ajhg/fulltext/S0002-9297(16)30149-5

http://www.livescience.com/54839-food-additives-gut-bacteria.html

Why Processed Foods May Promote Gut Inflammation

Why Processed Foods May Promote Gut Inflammation

By Rachael Rettner, Senior Writer | May 23, 2016 02:13pm ET

SAN DIEGO – Certain food additives may interfere with your gut bacteria, causing changes that boost inflammation in the intestines and potentially promote the development of some chronic diseases, a new study suggests.

In the study, researchers looked at ingredients called emulsifiers, which are added to many processed foods, including ice cream and peanut butter, to improve those foods' texture and extend their shelf life.

The researchers used a special piece of lab equipment that's intended to simulate the human gut, including its bacteria, and consists of a series of pumps and glass containers. The scientists added two emulsifiers called carboxymethylcellulose (CMC) and polysorbate-80 (P80), to a simulation of normal gut contents.

Adding the emulsifiers led to a dramatic increase in a marker of gut inflammation, said study co-author Benoit Chassaing, an assistant professor of biomedical science at Georgia State University. Chassaing presented the study here on Saturday (May 21) at Digestive Disease Week, a scientific meeting focused on digestive diseases.

The researchers then took the altered community of gut bacteria out of the lab equipment and implanted it into mice that didn't have any gut bacteria of their own. These mice also developed intestinal inflammation and showed signs of metabolic syndrome, a cluster of conditions that includes obesity, high blood sugar and insulin resistance.

The study shows that emulsifiers directly affect gut bacteria, Chassaing said. However, the researchers still need to test whether emulsifiers have the same effect in people, and so the investigators are already planning a study, he told Live Science.

The new findings add to those of a 2013 study by the same group of researchers, which found that emulsifiers promote the development of inflammatory bowel disease (IBD) in mice that are genetically predisposed to the condition. The 2013 study also found that emulsifiers were linked with inflammation in normal mice (that were not genetically predisposed to gut diseases). However, at the time, the researchers didn't know if the emulsifiers directly affected the gut bacteria, or if they instead affected the mouse's own cells.

The new study was able to rule out any impact of the mouse's own cells, because the simulator used is a mechanical model of the gut, the researchers said.

In the upcoming study in people, the researchers will likely put participants on an emulsifier-free diet for a month, and then switch some of the participants back to a diet that includes emulsifiers, Chassaing said. The researchers will then examine whether the two groups show differences in gut inflammation and changes in bacteria, he said.

Emulsifiers are listed on ingredient labels, but the additives go by many different names, Chassaing said. This makes it hard to avoid emulsifiers simply by reading food labels. The best way to keep from eating emulsifiers is to avoid processed food, he said.

http://bit.ly/1RzNheu

Cask from the past: archaeologists discover 5,000-year-old beer recipe

Chinese find suggests barley was used for booze before being grown for food - and that beer could have played a role in the development of society

Chinese villagers could have been raising a pint 5,000 years ago, according to new research.

Archaeologists studying vessels unearthed in the Shaanxi province of China say they've uncovered beer-making equipment dating from between 3400 and 2900 BC - an era known as the late Yangshao period - and figured out the recipe to boot.

"China has an early tradition of fermentation and evidence of rice-based fermented beverage has been found from the 9000-year-old Jiahu site. However, to our knowledge, [the new discovery] is the first direct evidence of in situ beer making in China," said Jiajing Wang of Stanford University, first author of the new research.

The team examined residues in the vessels to reveal that the brew was made from a wide range of plants, including broomcorn millet (Panicum miliaceum), Job's tears (Coix lacryma-jobi) and barley. The discovery marks the earliest known evidence of barley being used in China, suggesting that the crop arrived in the country around 1,000 years earlier than previously thought.

That, archaeologists add, is intriguing since it suggests that the crop might have been used for making booze before it was grown for food, and that beer could have played a role in the development of society.

"The production and consumption of Yangshao beer may have contributed to the emergence of hierarchical societies in the Central Plain, the region known as 'the cradle of Chinese civilisation'," the authors say.

Writing in the Proceedings of the National Academy of Science, researchers from the US and China describe the analysis of a collection of complete funnels and pottery fragments from the Mijiaya site in the Shaanxi province of China whose shapes and styles, indicate that they were used for different stages of beer-making, a function backed up by analysis of residues within the vessels.

Wang and her colleagues unpicked the brew's recipe by examining these yellow residues and scrutinising the sizqe and shape of starch grains and phytoliths - tiny pieces of silica that form within plant cells.

Their analysis revealed that broomcorn millet, Job's tears, lily, yam, barley and even snake gourd root (Trichosanthes pilosa) went into the beer. What's more, they say, the type of damage to the starch grains, together with chemical analysis of the residues, suggests the drink was produced by methods familiar to modern brewers. "The beer was made by going through three processes, including malting, mashing, and fermentation," said Wang.

But despite cracking the beer's recipe, the archaeologists admit they can't say how its flavour would measure up to a modern pint. "I really have no idea," said Wang. "That is beyond our research methods."

http://bit.ly/1Wsi9pp

Breaking bad sniffles: Crystal meth made cold medicine rubbish

Blame meth

By Simon Oxenham

Cold medicine doing little to relieve your bunged up nose? That could be because a crack-down on chemicals that can be used to make crystal meth has meant some high-street cold medicines may be no better than placebo for relieving congestion.

Nine years ago, you could have walked into a shop on the UK high street and bought a packet of cold medicine that contained the decongestant pseudoephedrine. This drug has been used for decades, and works well, but in 2008 it was placed under tight controls when it became apparent that pseudoephedrine was being used for the illegal production of methamphetamine. Similar laws were introduced in the US in 2005.

Since then, pseudoephedrine has broadly been banished from shop shelves in the UK, the US and elsewhere. Today, you can only get products containing this compound either by obtaining a prescription, or asking a pharmacist for a packet

from behind the counter. Pharmacists are now legally obliged to look for suspicious purchases, and to limit the number of tablets sold.

Ineffective alternative

Drug companies have responded to the regulations by replacing the compound with phenylephrine, which has long been known to be far less effective. Confusingly, popular cold remedy Sudafed – which takes its name from pseudoephedrine – now comes in two forms: a shop version, containing phenylephrine, and a behind-the-counter pseudoephedrine version.

But pharmacists are now calling for phenylephrine to be banned after research has shown that popping a pill or taking a spoonful of the stuff is ineffective for relieving nasal decongestion. "The evidence is irrefutable – phenylephrine is no more effective than placebo" says Leslie Hendeles at the University of Florida.

In fact, there may never have been strong evidence that phenylephrine works. In 2006, cold expert Ronald Eccles at Cardiff University, UK, conducted a review of phenylephrine research and reported that he could not find any evidence that the drug works as a decongestant when taken orally – although it does seem to work as a nasal spray.

Less meth?

So we may all have blocked noses, but has the ingredient swap had any impact on crystal meth? Data from the US Drug Enforcement Administration suggests there was a decline in "meth lab incidents" after the Combat Methamphetamine Epidemic Act of 2005, which restricted access to pseudoephedrine. However, this decline was only short lived and may have been due to other factors such as increased training and awareness of the problem among law enforcement officers.

In the UK we don't have a crystal meth problem on anywhere near the scale of the US. Only 240 people sought help for methamphetamine problems in the UK last year so it's hard to tell what the effect of the intervention has been.

In the meantime, there may have been millions of people with perfectly treatable blocked noses, unknowingly taking what may well be little more than a placebo.

http://bit.ly/1shMZEr

How our modular brain pieces the world together

The brain processes different facial features separately, so how does it tie them together?

Bronson Harry

Picture a close friend. Imagine their face, the sound of their voice, their height, what they normally wear. You might be surprised to learn you have just used a host of different brain regions to recall this information.

Curiously, there is no single brain region that is involved in representing the people we know. Seeing a friend's face or hearing their voice activates different parts of the brain. This is because the brain is modular. It is made up of numerous regions that perform specific tasks.

The modular brain

The most striking example of modularity is the face perception network. Faces selectively activate a chain of distinct brain regions spanning the occipital and temporal lobes. Damage to this network profoundly impairs face recognition abilities, a condition called prosopagnosia.

A similar network of face regions is also found in monkeys and apes suggesting that a modular face network is an evolutionary adaptation. Possessing dedicated face processing hardware likely allowed us to quickly discern friend from foe, and such rapid identification would undeniably have helped our ancestors cope with the pressures of living in social groups.

Although important, faces are not the only source of information we use to identify people. It is possible to recognise someone simply by hearing their voice. Indeed, patients with damage to their face processing network can still recognise people from the sound of their voice or the way they dress.

However, there is no single brain network involved in analysing identity. Voices are processed by an area located in the auditory cortex, and body areas are anatomically distinct from regions that process faces. So how does the brain combine these different physical cues to generate the sense of a unique individual?

Putting it all together

Consider a comedian imitating a politician. Comedians can evoke a strong sense of another person's identity, even when they lack a clear physical resemblance to the person being imitated. Likewise, actors can create a diverse range of characters simply by changing their voice, posture and how they move.

If the regions that process faces, bodies and voices are anatomically distinct, then how is our unified sense of another person's identity formed? How do these different networks communicate with each other?

We recently explored this question in a brain imaging study that examined the spatial organisation of face and body networks. We used magnetic resonance imaging (MRI) to record brain activity while participants viewed images of faces, bodies and common household objects. We examined brain responses in two face areas, one in a region associated with memory and another in a region involved in vision.

In the visual region, responses to faces and bodies showed a modular organisation. We found that face and body selective areas were spatially distinct from each other. However, in the memory region, face and body selective responses were

similarly organised, so areas that preferred faces also showed a preference for bodies.

A group of MIT researchers who examined the brains of monkeys found similar results. In this study, monkeys were shown pictures of faces, headless bodies and images of whole bodies with the faces intact.

The results showed that the face area in the same memory region preferred images of whole bodies compared to either faces or bodies alone. Importantly, the response to whole bodies was greater than the combined response to isolated faces and bodies.

The binding power of memory

Together, these studies show that information from the face and body networks converge in parts of the brain that form memories. Previously, it was understood that these memory regions were associated with knowing whether a face was familiar.

This new evidence tells us that memory regions are also responsible for binding together different perceptual cues to create holistic, integrated representations of the people we encounter.

These findings illustrate how the brain uses different organisational schemes to help us understand our social world. A modular organisation affords fast, efficient extraction of important information about the people around us.

However, the brain must also bind the output from these various systems together to keep track of all the different people we interact with. Doing so helps us organise the complex web of friends, family, colleagues, Facebook acquaintances, public figures and celebrities that populate our increasingly social world.

http://bit.ly/1WRRjXn

A Plan to Prevent Gun Suicides

Firearm sellers have become unlikely allies of public health authorities in the effort to block people from killing themselves

By Nancy Shute on June 1, 2016

Ralph Demicco feels as though he has watched the 53-minute surveillance video 100 times, searching it for clues to preventing tragedy. He sees a young man walk into his gun shop in Hooksett, N.H. The man asks about buying a handgun. “He engaged the clerk in small talk, totally disarmed the clerk,” Demicco says. “No way in heck that clerk would suspect that three quarters of an hour after the conversation that person would take his life.”

And yet the 24-year-old man did kill himself, pulling the trigger soon after leaving the boxy beige building. Nor was he the only customer who did so. In one awful week in 2009, he and two other people came into the shop, which Demicco no longer owns, bought guns and used the purchases shortly thereafter to kill themselves.

The experience shook Demicco and prompted him to help found a movement that links members of the firearm community with public health experts to prevent suicides by raising awareness about gun safety, among other things. Its leaders are realists who accept that very strict, European-style gun control is not politically feasible in the U.S. and would, in any case, be a nonstarter for most gun sellers, who oppose such control.

But they also know that households that keep guns and ammunition in separate, locked locations and store their guns unloaded have much lower risks of accidental or intentional deaths from firearms. In addition, as a further safety measure, the group seeks to make it socially acceptable for relatives and friends to offer to hold on to a potentially suicidal gun owner's weapons until the crisis has passed.

The public safety campaign is admittedly modest so far, consisting mainly of distributing posters and brochures about suicide to gun shops. Still, its start in a state whose motto is “Live Free or Die” shows that the long-standing political stalemate over gun-control laws need not prevent progress from being made.

Evidence-Based Approach

The gun safety coalition is motivated by data as well as by the distressing stories of gun shop owners. In the case of guns, the impulsive nature of many suicides, combined with the lethal efficiency of firearms, creates an exceptionally deadly pattern.

Several studies now confirm that suicide is often a decision made suddenly. If the moment somehow passes safely, the evidence suggests, lives can be saved in the short and long term.

“There's a fair amount of research showing that the suicide crisis is time-limited,” says John Mann, a professor of translational neuroscience at Columbia University who studies suicide. Two thirds of those who survived a suicide attempt, according to one 1991 study, had started planning their course of action less than an hour beforehand.

Another study notes that almost half of the 82 people who attempted suicide said they had started thinking about their current attempt less than 10 minutes earlier. Moreover, in the case of guns especially, an investigation by the New Hampshire medical examiner's office showed that nearly one in 10 suicides by firearm from 2007 to 2009 involved a weapon that was purchased or rented the preceding week—often within just a few hours.

National data speak to the other half of this deadly combination. Although guns are not the most popular way that people try to take their life (this dubious

distinction belongs to pills), they are the most deadly. Statistics show that 85 percent of attempts with a gun are fatal, compared with 69 percent for hanging and 2 percent for self-poisoning. Mass shootings and murders dominate the news, but 21,334—or nearly two thirds—of the 33,599 gun deaths that occurred in the U.S. in 2014 were suicides. Another 10,945 were homicides.

Guns, then, take what is often an ambivalent decision and turn it into an irrevocable one.

Won't people who are stopped from killing themselves today just find another way to complete the act later? Some number will, unfortunately. Yet most who survive do not keep trying until they succeed. Instead, studies show, the majority of survivors die a natural death many years after failing to kill themselves. The period of greatest vulnerability seems to be in the first year after an attempt, a time when treatment for those who try to end their life is critically important, experts say.

Perhaps the best evidence for the strength of this survival instinct stems from pioneering research carried out by Richard Seiden in the 1970s. Then a clinical psychologist at the University of California, Berkeley, Seiden found that more than 90 percent of the 515 people who were prevented from jumping off the Golden Gate Bridge between the year it opened in 1937 and 1971 eventually lived long enough to die of nonviolent causes.

Indeed, Seiden's work spurred such a surge of scientific inquiry by other investigators who reached the same conclusion that state authorities finally agreed to install antisuicide netting underneath the famous span. Bidding to build the barrier is scheduled to finish sometime in 2016.

Lifesaving Restrictions

Figuring out ways to limit access to particularly lethal methods of committing suicide—whether they are bridges or guns—makes sense from a public health point of view. Yet it also made sense to Demicco and a few other gun shop owners in New Hampshire, who agreed to collaborate with mental health practitioners and researchers after that devastating rash of suicides in 2009.

When a public health researcher expressed surprise at the positive response from the firearm community, “a firearm instructor said, ‘I could be insulted by that,’” says Elaine Frank, who directs the Counseling on Access to Lethal Means project at Children's Hospital at Dartmouth-Hitchcock and is co-chair of the New Hampshire Firearm Safety Coalition. “‘Why do you think the firearm community would be less interested in preventing suicide than you would be?’”

In 2011 the group sent posters and brochures to New Hampshire's 65 retail gun shops. The goal was to encourage customers to become alert to signs of crisis in friends or household members and to make firearms inaccessible until the crisis had passed.

“Concerned about a family member or friend?” one poster asks. “Suicides in NH far outnumber homicides.” In the photograph, one gray-haired man rests his hand on the shoulder of another. A handgun lies on the kitchen table between them. “Hold on to their guns,” the poster continues. “Putting time and distance between a suicidal person and a gun may save a life.”

The leaders of the New Hampshire effort did not expect their social-marketing campaign to have a significant effect on the number of suicides right away—and it did not. But 48 percent of the gun shops throughout the state still had the handouts and other materials available for customers after the first year, according to a study published in 2015 in the journal Suicide and Life-Threatening Behavior. “That's actually a pretty incredible uptake, especially for a topic like suicide,” says Catherine Barber of the Harvard Injury Control Research Center, who is a co-author of the study, along with her colleague Mary Vriniotis, Frank, Demicco and the rest of the New Hampshire Firearm Safety Coalition. “Glancing at one poster isn't going to do the trick,” Barber says. “That's like one time seeing a poster about designated drivers. But hopefully it's lighting a match.”

Since the New Hampshire project's inception, the model has been adopted or adapted in more than a dozen states, each of which must tailor the concept to its political and legal realities. In Massachusetts, for example, only someone licensed to possess firearms could legally take a weapon for safekeeping, but attaching a trigger lock and giving the key to a trusted friend or relative would accomplish the same purpose.

Utah, which at 21 deaths per 100,000 people has one of the highest rates of suicide in the U.S., is training staff at hospitals and doctors' offices to screen patients for suicide risk and to intervene appropriately. Clark Aposhian, head of the influential Utah Shooting Sports Council, says his group is developing public service announcements aimed at encouraging friends and family of struggling loved ones to get some distance from firearms. “Go over to their house, kind of like a mini intervention at the door,” Aposhian suggests. “Put your arm around them and say, ‘Let me babysit your guns for a while.’”

It is still too early to know what impact these efforts have had in Utah or elsewhere. But research indicates that Aposhian, Demicco and fellow gun enthusiasts are taking the right steps. Perhaps, as is true of the movement that formed around the slogan “Friends don't let friends drive drunk,” championing the safeguarding of guns as a way to reduce suicides will pick up steam in the years ahead.

http://www.eurekalert.org/pub_releases/2016-05/nsfc-nss052416.php

NASA scientist suggests possible link between primordial black holes and dark matter

Dark matter may be made of black holes formed during the first second of our universe's existence

Dark matter is a mysterious substance composing most of the material universe, now widely thought to be some form of massive exotic particle. An intriguing alternative view is that dark matter is made of black holes formed during the first second of our universe's existence, known as primordial black holes. Now a scientist at NASA's Goddard Space Flight Center in Greenbelt, Maryland, suggests that this interpretation aligns with our knowledge of cosmic infrared and X-ray background glows and may explain the unexpectedly high masses of merging black holes detected last year.

"This study is an effort to bring together a broad set of ideas and observations to test how well they fit, and the fit is surprisingly good," said Alexander Kashlinsky, an astrophysicist at NASA Goddard. "If this is correct, then all galaxies, including our own, are embedded within a vast sphere of black holes each about 30 times the sun's mass."

In 2005, Kashlinsky led a team of astronomers using NASA's Spitzer Space Telescope to explore the background glow of infrared light in one part of the sky. The researchers reported excessive patchiness in the glow and concluded it was likely caused by the aggregate light of the first sources to illuminate the universe more than 13 billion years ago. Follow-up studies confirmed that this cosmic infrared background (CIB) showed similar unexpected structure in other parts of the sky.

In 2013, another study compared how the cosmic X-ray background (CXB) detected by NASA's Chandra X-ray Observatory compared to the CIB in the same area of the sky. The first stars emitted mainly optical and ultraviolet light, which today is stretched into the infrared by the expansion of space, so they should not contribute significantly to the CXB.

Yet the irregular glow of low-energy X-rays in the CXB matched the patchiness of the CIB quite well. The only object we know of that can be sufficiently luminous across this wide an energy range is a black hole. The research team concluded that primordial black holes must have been abundant among the earliest stars, making up at least about one out of every five of the sources contributing to the CIB.

The nature of dark matter remains one of the most important unresolved issues in astrophysics. Scientists currently favor theoretical models that explain dark matter as an exotic massive particle, but so far searches have failed to turn up evidence these hypothetical particles actually exist. NASA is currently investigating this issue as part of its Alpha Magnetic Spectrometer and Fermi Gamma-ray Space Telescope missions.

"These studies are providing increasingly sensitive results, slowly shrinking the box of parameters where dark matter particles can hide," Kashlinsky said. "The failure to find them has led to renewed interest in studying how well primordial black holes -- black holes formed in the universe's first fraction of a second -- could work as dark matter."

Physicists have outlined several ways in which the hot, rapidly expanding universe could produce primordial black holes in the first thousandths of a second after the Big Bang. The older the universe is when these mechanisms take hold, the larger the black holes can be. And because the window for creating them lasts only a tiny fraction of the first second, scientists expect primordial black holes would exhibit a narrow range of masses.

On Sept. 14, gravitational waves produced by a pair of merging black holes 1.3 billion light-years away were captured by the Laser Interferometer Gravitational-Wave Observatory (LIGO) facilities in Hanford, Washington, and Livingston, Louisiana. This event marked the first-ever detection of gravitational waves as well as the first direct detection of black holes. The signal provided LIGO scientists with information about the masses of the individual black holes, which were 29 and 36 times the sun's mass, plus or minus about four solar masses. These values were both unexpectedly large and surprisingly similar.

"Depending on the mechanism at work, primordial black holes could have properties very similar to what LIGO detected," Kashlinsky explained. "If we assume this is the case, that LIGO caught a merger of black holes formed in the early universe, we can look at the consequences this has on our understanding of how the cosmos ultimately evolved."

In his new paper, published May 24 in The Astrophysical Journal Letters, Kashlinsky analyzes what might have happened if dark matter consisted of a population of black holes similar to those detected by LIGO. The black holes distort the distribution of mass in the early universe, adding a small fluctuation that has consequences hundreds of millions of years later, when the first stars begin to form.

For much of the universe's first 500 million years, normal matter remained too hot to coalesce into the first stars. Dark matter was unaffected by the high temperature because, whatever its nature, it primarily interacts through gravity. Aggregating by mutual attraction, dark matter first collapsed into clumps called minihaloes, which provided a gravitational seed enabling normal matter to accumulate. Hot

gas collapsed toward the minihaloes, resulting in pockets of gas dense enough to further collapse on their own into the first stars. Kashlinsky shows that if black holes play the part of dark matter, this process occurs more rapidly and easily produces the lumpiness of the CIB detected in Spitzer data even if only a small fraction of minihaloes manage to produce stars.

As cosmic gas fell into the minihaloes, their constituent black holes would naturally capture some of it too. Matter falling toward a black hole heats up and ultimately produces X-rays. Together, infrared light from the first stars and X-rays from gas falling into dark matter black holes can account for the observed agreement between the patchiness of the CIB and the CXB.

Occasionally, some primordial black holes will pass close enough to be gravitationally captured into binary systems. The black holes in each of these binaries will, over eons, emit gravitational radiation, lose orbital energy and spiral inward, ultimately merging into a larger black hole like the event LIGO observed.

"Future LIGO observing runs will tell us much more about the universe's population of black holes, and it won't be long before we'll know if the scenario I outline is either supported or ruled out," Kashlinsky said.

Kashlinsky leads science team centered at Goddard that is participating in the European Space Agency's Euclid mission, which is currently scheduled to launch in 2020. The project, named LIBRAE, will enable the observatory to probe source populations in the CIB with high precision and determine what portion was produced by black holes.

Related video: 0:02 / 0:35 ***What the first LIGO detection would look like up close***

http://www.bbc.com/news/health-36367691

'Thousands miss out' on surgery for type-2 diabetes

Thousands of people with type-2 diabetes in the UK are missing out on obesity surgery that would slash blood sugars and even lead to remission in some cases, a team of experts say.

By Smitha Mundasad Health reporter

Leading surgeon Prof Francesco Rubino described the gut operation as "the closest thing to a cure" available. UK guidelines already recommend the surgery for some patients. But experts argue the guidance needs to be expanded and made more prominent, as most doctors do not offer it.

'Biggest changes'

About three million people in the UK have type-2 diabetes, which can lead to serious complications, including kidney failure, blindness and heart disease.

The team predict up to 100,000 obese diabetic patients - including those who are only mildly obese and have already tried medication and lifestyle changes - could benefit from the surgery, which involves removing part of the stomach or re-routing the gut. But they estimate fewer than 6,000 bariatric operations were carried out for type-2 diabetes last year.

They looked at a growing body of evidence that suggests the treatment - traditionally used for weight-loss - not only reduces weight but also alters gut hormones and the lining of the gut to get blood sugars under control.

This reduces the need for daily drugs or insulin injections and leads to a period of remission in more than a third of cases, experts say.

'I lost three stone'

Anne Mulvaney, aged 51, from London, said the surgery had given her a lifeline. She was diagnosed with type 2 diabetes four years ago and her weight climbed to 19 stone (120 kg). She tried to lose weight but she says it was nearly impossible. She was offered surgery in March, when taking anti-diabetic medication every day. Three months later she is now 15.6 stone (99kg) and though not yet what doctors would consider an ideal weight, she no longer has to take drugs to keep her blood sugar under control.

She said: "Before the operation I no energy and was thirsty all the time. "Now I have lots of energy, don't crave sugar anymore and can exercise without getting breathless as quickly. "But it is not a quick fix. You have to be dedicated and make changes. The whole process, including seeing a psychologist, took about two years. "It feels a bit like a corset that gets tight when you have a spoonful too much. "I don't eat as much as I used to now - but I don't get hungry. "I definitely don't regret it - it has given me a new lease of life."

Scientists argue the operations - which cost about £6,000 in established centres - would pay for themselves within two years, by cutting the cost of drugs and the expense of treating diabetic complications.

They say the National Institute for Health and Care Excellence (NICE) needs to make this option explicit in their diabetes guidance and to expand it to ensure long-term diabetics on the cusp of obesity are also considered.

'Needless barriers'

Prof Rubino, co-author of the report and a surgeon at King's College London, said: "Surgery represents a radical departure from conventional approaches to diabetes."The new guidelines effectively introduce, both conceptually and practically, one of the biggest changes for diabetes care in modern times."

Meanwhile Prof Mark Baker, at NICE, said the paper appeared to be broadly in line with the updated NICE guideline on obesity.

But Simon O'Neill at charity Diabetes UK, said: "Many people who stand to benefit from this potentially life-saving treatment are missing out due to needless barriers to obesity surgery services. "Even people who meet the criteria for the surgery are made to wait too long."

In a joint statement, endorsed by 45 international organisations and published in the journal Diabetes Care, experts put out a global call for surgery to be seen as a standard part of diabetes treatment in certain cases. The guidelines emerged at a summit organised by charity Diabetes UK, the American Diabetes Association, International Diabetes Federation, Chinese Diabetes Society and Diabetes India.

http://bit.ly/1sERJ6Z

New Obesity Treatment: Gas-Filled Balloons

A new obesity treatment that involves swallowing a capsule that contains a balloon may help people lose more weight than they would by just dieting, a new study suggests.

By Rachael Rettner, Senior Writer | May 24, 2016 12:55pm ET

SAN DIEGO – For the treatment, people swallow a small capsule that contains a balloon, which a doctor then inflates with nitrogen-based gas through a catheter attached to the capsule. Once the balloon is inflated, it is slightly larger than a standard 8-ounce (237 milliliters) cup, and helps people feel fuller sooner, said the researchers, who presented the study here today (May 24) at Digestive Disease Week, a scientific meeting focused on digestive diseases.

In the study, 185 obese people (with a body mass index of 30 to 40), received the balloon treatment, called the Obalon 6-Month Balloon System. This involved swallowing a total of three balloons (a new one every three weeks), and then removing all the balloons after three months. A separate group of 181 people received a "sham" procedure, in which they swallowed sugar pills that doctors pretended to fill with gas, so that participants wouldn't know if they had received the real treatment.

Both groups also saw a dietician to help them lose weight. After six months, participants in the balloon group lost an average of 6.8 percent of their body weight, compared to an average of 3.5 percent in the sham group.

"Our research shows that the studied balloon system can help patients lose almost twice as much weight compared with lifestyle changes alone," study co-author Dr. Shelby Sullivan, director of bariatric endoscopy at Washington University School of Medicine in St. Louis, Missouri, said in a statement. "This is important because weight loss is very difficult, and a significant number of people are not successful in achieving their weight loss goals with diet changes and exercise."

The study also found that that 64 percent of people who received the balloon treatment lost at least 5 percent of their body weight, whereas only 32 percent of the control group met that benchmark.

Side effects of the balloon treatment included abdominal cramping and nausea, but nearly all participants said these side effects were mild or moderate, according to the researchers.

Currently, the Obalon balloon system is not approved by the U.S. Food and Drug Administration (FDA), so the treatment is not yet available in the United States. However, it is approved in several European countries and in Mexico. Sullivan received funding from Obalon Therapeutics, Inc., to conduct this research.

Another balloon system for weight loss, called ReShape Dual Balloon System, was approved by the FDA in 2015. Unlike the Obalon balloon, ReShape requires a doctor to insert the balloon through the mouth using a device called an endoscope. And ReShape is filled with liquid, not gas. Both ReShape and Obalon need to be removed by a doctor through the mouth.

Yet another balloon system for weight loss, called Ellipse, is also working toward FDA approval. Like Oblaon, Ellipse comes in the form of a capsule that patients swallow. However, Ellipse is filled with liquid, and it deflates on its own after four months, so it can pass through the digestive tract at the end of treatment.

A small study of Ellipse, involving 34 people, found that patients with Ellipse lost an average of 9.5 percent of their body weight, or 22 lbs. (10 kilograms), after four months of use.

Sullivan noted that because the three Oblaon balloons are given in stages, the system gives the stomach time to adjust to having the balloons in place; each time another balloon is added, it takes up more space.

http://www.eurekalert.org/pub_releases/2016-05/uoca-ssa051816.php

Study shows area undamaged by stroke remains so, regardless of time stroke is left untreated

No evidence of time dependence on damage outcomes for undamaged tissue

CINCINNATI -- Radiological imaging is being used more often to evaluate stroke diagnosis and outcomes, with penumbra, or tissue that is at risk of progressing to dead tissue but is still salvageable if blood flow is returned, as a potential target for therapy.

However, there have been few studies about what happens to the penumbra without treatment to restore blood flow through the blocked arteries, known as reperfusion treatment.

A study led by Achala Vagal, MD, associate professor at the University of Cincinnati (UC) College of Medicine and a UC Health radiologist, looked at a group of untreated acute stroke patients and found that there was no evidence of time dependence on damage outcomes for the penumbra but rather an association with collateral flow--or rerouting of blood through clear vessels.

These findings are being presented at the American Society of Neuroradiology's annual meeting May 25 in Washington, DC.

Vagal says their sample size was small--only 110 patients--so larger studies are needed to examine how treatment may differ in a stroke with a delayed or unknown onset time.

"Using a large, multicenter stroke registry, we analyzed all untreated acute stroke patients who received baseline CT angiogram, an X-ray that uses a dye and camera (fluoroscopy) to take pictures of the blood flow in an artery, and CT perfusion, to show which areas of the brain were getting blood, within 24 hours of the onset of stroke, and follow-up CT angiogram or MR angiogram within 48 hours," she says. "Baseline CT angiogram results were reviewed for artery blockages and rerouting of blood flow, and follow-up imaging was reviewed to determine if blood flow was restored."

Vagal adds that CT perfusion was used to determine baseline numbers for the penumbra and that dead tissue was measured on follow up CT and MR imaging.

Results showed that there was no significant correlation between salvaged penumbra and time; however, there was a correlation between salvaged penumbra and the amount of collateral blood flow, meaning the blood flow that was rerouted.

"Larger studies are needed to understand the natural history of penumbra that could lead to future trials and have treatment implications particularly in delayed or unknown onset time," she says.

This research was funded by a National Institutes of Health Center for Clinical and Translational Science and Training (CCTST) KL2 Research Scholar Mentored Career Development Award. Vagal's mentoring team for this scholar award included Pooja Khatri, UC Department of Neurology, Max Wintermark, MD, University of Stanford, and Thomas Tomsick, MD, UC Department of Radiology.

http://www.eurekalert.org/pub_releases/2016-05/sri-sfs052516.php

Scripps Florida scientists show commonly prescribed painkiller slows cancer growth

Celecoxib slows the growth rate of a specific kind of cancer

JUPITER, FL - Scientists from the Florida campus of The Scripps Research Institute (TSRI) have found that one of the most widely prescribed pain and anti-inflammation drugs slows the growth rate of a specific kind of cancer in animal models and suggests the medication could have the same effect on other types of tumors. The new study, published online ahead of print by the journal Cancer Research, focused on the effects of celecoxib (Pfizer's Celebrex®).

Celebrex® targets an enzyme called "cyclooxygenase-2" (COX-2), which is linked to pain and inflammation. This enzyme is also critical in the creation of prostaglandins, compounds that act like hormones and play a role in promoting tumor growth. COX-2 expression is typically low in normal tissue, but high in multiple types of cancers.

"We were actually interested in determining what a particular signaling pathway does in cancer," said TSRI Associate Professor Joseph Kissil, who led the study. "In the process, we found that it activates genes that promote survival of tumor cells and that they do so by turning on enzymes involved in inflammation, including COX2, which anti-inflammatory drugs like Celebrex® inhibit."

The researchers went on to conduct animal studies tracking the effects of celecoxib on the growth of cancer cells from a tumor type known as neurofibromatosis type II (NF2). In humans, NF2 is a relatively rare inherited form of cancer caused by mutations in the anti-tumor gene NF2, which leads to benign tumors of the auditory nerve.

Animals received a daily dose of the drug, and tumor growth was followed by imaging. Analysis of the results showed a significantly slower tumor growth rate in celecoxib-treated models than in controls. Using various approaches, the new study also showed that a signaling cascade known as the Hippo-YAP pathway is involved in these results and that the protein YAP is required for the proliferation and survival of NF2 cells and tumor formation.

"Our study shows that COX2 inhibitors do have an effect on the tumor cells," said TSRI Research Associate William Guerrant, the study's first author. "They also have an impact on inflammatory responses that play a role in tumor growth. It's possible that in other cancers these effects might actually be stronger because of the drug's impact on inflammation."

In addition to Kissil and Guerrant, other authors of the study, "YAP Mediates Tumorigenesis in Neurofibromatosis Type 2 by Promoting Cell Survival and Proliferation through a COX-2-EGFR Signaling Axis," are Smitha Kota, Scott Troutman, Vinay Mandati and Mohammad Fallahi of TSRI; and Anat Stemmer-Rachamimov of Massachusetts General Hospital.

The work was supported by the National Institutes of Health (grants NS077952 and CA124495). Guerrant is also a recipient of a Young Investigator Award from the Children's Tumor Foundation.

http://nyti.ms/25q4G2V

Could Alzheimer's Stem From Infections? It Makes Sense, Experts Say

Could it be that Alzheimer's disease stems from the toxic remnants of the brain's attempt to fight off infection?

By GINA KOLATA MAY 25, 2016

Provocative new research by a team of investigators at Harvard leads to this startling hypothesis, which could explain the origins of plaque, the mysterious hard little balls that pockmark the brains of people with Alzheimer's.

It is still early days, but Alzheimer's experts not associated with the work are captivated by the idea that infections, including ones that are too mild to elicit

symptoms, may produce a fierce reaction that leaves debris in the brain, causing Alzheimer's. The idea is surprising, but it makes sense, and the Harvard group's data, published Wednesday in the journal Science Translational Medicine, supports it. If it holds up, the hypothesis has major implications for preventing and treating this degenerative brain disease.

The Harvard researchers report a scenario seemingly out of science fiction. A virus, fungus or bacterium gets into the brain, passing through a membrane — the blood-brain barrier — that becomes leaky as people age. The brain's defense system rushes in to stop the invader by making a sticky cage out of proteins, called beta amyloid. The microbe, like a fly in a spider web, becomes trapped in the cage and dies. What is left behind is the cage — a plaque that is the hallmark of Alzheimer's.

So far, the group has confirmed this hypothesis in neurons growing in petri dishes as well as in yeast, roundworms, fruit flies and mice. There is much more work to be done to determine if a similar sequence happens in humans, but plans — and funding — are in place to start those studies, involving a multicenter project that will examine human brains.

"It's interesting and provocative," said Dr. Michael W. Weiner, a radiology professor at the University of California, San Francisco, and a principal investigator of the Alzheimer's Disease Neuroimaging Initiative, a large national effort to track the progression of the disease and look for biomarkers like blood proteins and brain imaging to signal the disease's presence.

Dr. David Holtzman, a professor and the chairman of neurology at the Washington University School of Medicine in St. Louis, was also intrigued. "It is obviously outside the box," he said. "It really is an innovative and novel study."

The work began when Robert D. Moir, of Harvard Medical School and Massachusetts General Hospital, had an idea about the function of amyloid proteins, normal brain proteins whose role had long been a mystery.

The proteins were traditionally thought to be garbage that accumulates in the brain with age. But Dr. Moir noticed that they looked a lot like proteins of the innate immune system, a primitive system that is the body's first line of defense against infections.

Elsewhere in the body, such proteins trap microbes — viruses, fungi, yeast and bacteria. Then white blood cells come by and clear up the mess. Perhaps amyloid was part of this system, Dr. Moir thought.

He began collaborating with Rudolph E. Tanzi, also at Harvard Medical School and Massachusetts General Hospital, in a study funded by the National Institutes of Health and the Cure Alzheimer's Fund. The idea was to see if amyloid trapped microbes in living animals and if mice without amyloid proteins were quickly ravaged by infections that amyloid could have stopped.

The answers, they reported, were yes and yes.

In one study, the group injected Salmonella bacteria into the brains of young mice that did not have plaques.

"Overnight, the bacteria seeded plaques," Dr. Tanzi said. "The hippocampus was full of plaques, and each plaque had a single bacterium at its center."

For years, researchers had been fixated on the idea of plaques as a sort of trash that gathered in the brain. Few had asked if there might be some other explanation.

As Dr. Samuel E. Gandy, a professor of neurology and psychiatry at the Icahn School of Medicine at Mount Sinai Hospital in New York, explained, there was a long and persuasive body of research laying out the Alzheimer's pathway: Plaques form and set off the formation of tangled threadlike tau proteins. Then, as tangles of tau kill nerve cells, the brain becomes inflamed, resulting in the killing of many more nerve cells.

There were a few puzzling clues that something else might be going on, but they did not make much sense.

For example, Dr. Weiner said, some investigators reported that people who had developed Alzheimer's had higher levels of antibodies to herpes, an indicator of a previous infection, than people who did not have the disease.

"The suggestion that herpes was causative seemed a bit far-fetched," he said.

The new paper, Dr. Gandy and Dr. Weiner said, provides a plausible explanation.

Dr. Berislav Zlokovic, the director of the Zilkha Neurogenetic Institute at the University of Southern California, said his studies of the blood-brain barrier also fit well with the new hypothesis. When he discovered that the barrier started to break down with aging, he noticed that the leakiest part was the membrane that protects the hippocampus, the site of learning and memory. That is also where Alzheimer's plaques form.

Dr. Tanzi and Dr. Moir's hypothesis, he said, "is very hypothetical at this point, but it does make sense."

Of course, there must be more to Alzheimer's than the brain's innate immune system. What about people who have a mutated gene that guarantees they will develop the disease at an early age?

For them, Dr. Tanzi says, the problem is that they vastly overproduce beta amyloid. There is so much that it clumps on its own, without the presence of microbes.

Not everyone who has had a brain infection develops Alzheimer's, though. Why would some be more vulnerable than others? According to the new theory, it probably has to do with the brain's ability to clear out the balls of beta amyloid

after they have killed microbes, Dr. Tanzi said. For example, it is known that people with a gene called ApoE2 have brains that are good at sweeping out plaque, and have a low risk of Alzheimer's in old age. Those with a different version, ApoE4, are inefficient in removing plaque and have a high risk of Alzheimer's.

Recent data suggests that the incidence of dementia is decreasing. It could be because of better control of blood pressure and cholesterol levels, staving off ministrokes that can cause dementia. But could a decline in infections also be part of the picture? "That's a possibility," Dr. Weiner said.

At this point, the Harvard researchers have what many say is an intriguing hypothesis, but they readily acknowledge that much work lies ahead.

The Cure Alzheimer's Fund is starting a large collaborative project that will use gene sequencing technology to carefully look for microbes in brains from people who had Alzheimer's and those who did not. Researchers will also look for microbes in plaques found in human brains.

That, though, "is a big, big second step," Dr. Tanzi said. "First, we need to ask whether there are microbes that may sneak into the brain as we age and trigger amyloid deposition." "Then," he said, "we can aim at stopping them."

http://rsc.li/1TGDXaY

Crawling chemical system acts as if it's alive

Crawling across a glass surface, the larger vesicle consumes smaller ones on its path

Kathryn Gempf

They crawl. They eat. They excrete. So you'd be forgiven for thinking these globules created by a team Japan were alive – but they're not.

Discovering life-like motion in non-living systems fascinates Akihisa Shioi, from Doshisha University. He and his team are constantly combining new chemicals to investigate the idea.

They already knew that droplets of didodecyldimethylammonium bromide (DDAB), a cheap surfactant, react with iodide ions, then scoot around and leave chemical traces, like miniature turbo-snails. Unlike snails though, these vesicles shrank, and collapsed after a few seconds. They needed feeding. Oleic acid and calcium ions proved the missing link.

Together, DDAB, oleate and calcium, form globules, called vesicles, with intriguing life-like movement. The vesicles crawl around on a glass slide by reacting with iodide ions, ingest smaller vesicles to maintain their size and energy, and leave behind waste; just like a living system.

Despite having an inkling that this combination of chemicals would be an interesting mix, Shioi was surprised to see the vesicles acting this way.

'This system is a demonstration of the potential of vesicles as hypothetical precursor compartment structures of the first cells, in how they can offer much more than a simple "bag" separating internal and external environments,' says Peter Walde, an expert in these kinds of materials at Swiss Federal Institute of Technology (ETH) in Zurich, Switzerland. He hopes scientists will explore the concepts displayed here within the context of complex chemical systems from which the first forms of life evolved.

'Reconstructing life-like systems in the laboratory not only refers to the long-age dream of the scientist making life from non-living, but can help in understanding the principles of life from a physico-chemical perspective,' adds Pasquale Stano, a systems chemist from Roma Tre University, Italy.

Direction control and alternative globule materials, which are biocompatible, are Shioi's next steps for his chemical creations. Progress with these goals, could lead to exciting applications in micropatterning, drug delivery, or as scavengers to clean blood vessel walls.

However, Pier Luigi Luisi, a specialist in synthetic biology at Roma Tre University, warns that phenomena like this mechanical motion are generally 'due to a very particular context of environmental conditions.' Therefore, changing any aspect of the experiment could lose the particles their movement.

Shioi recently demonstrated his research to a class of children, and they were hooked. Seeing the vesicles scuttling around and gobbling up smaller ones, we all instinctively ask, as the children did, 'Are they alive?!'

This article is open access M Nakada et al, Mol. Syst. Des. Eng., 2016, DOI: 10.1039/C5ME00012B

http://bit.ly/1sj1zLR

Neanderthals built mystery underground circles 175,000 years ago

Smallish stalagmites vaguely discernible as arranged in a jumbled ring on a limestone cave floor

By Colin Barras

They worked by torchlight, following the same procedure hour after hour: wrench a stalagmite off the cave floor, remove the tip and base, and carefully lay it with the others.

Today we can only guess as to why a group of Neanderthals built a series of large stalagmite structures in a French cave – but the fact they did provides a rare glimpse into our extinct cousin's potential for social organisation in a challenging environment.

Gone are the days when we thought of Neanderthals as crude and unintelligent. Archaeological evidence now suggests they were capable of symbolic thought,

had a basic knowledge of chemistry, medicine and cooking, and perhaps some capacity for speech. They may even have taught modern humans new artisanal skills when the two species met and interbred.

Made by Neanderthals – but what were they for? **Etienne Fabre/SSAC**

A reassessment of evidence from Bruniquel cave, near Toulouse in south-west France, suggests even more Neanderthal sophistication. In one chamber, 336 metres from the cave entrance, are enigmatic structures – including a ring 7 metres across – built from stalagmites snapped from the cave floor.

Natural limestone growths have begun to cover parts of the structure, so by dating these growths a team led by Jacques Jaubert at the University of Bordeaux could work out an approximate age for the stalagmite constructions.

They are roughly 175,000 years old, which means they easily predate the arrival of modern humans in Europe. They were built at a time when Neanderthals were the only hominins in the region.

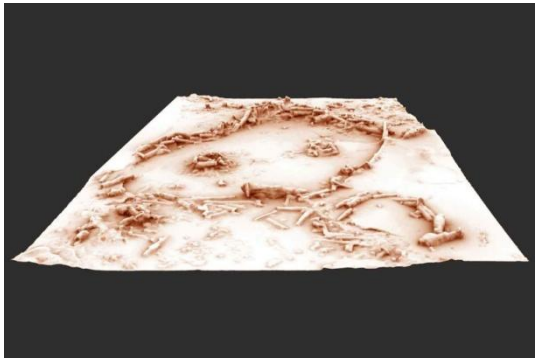
The stalagmite structures are 50 centimetres high in places, says Jaubert. They are built from around 400 individual stalagmites with a combined weight of about 2 tonnes.

"That must take time [to shift]," he says – although exactly how long it took the Neanderthals to build the structures isn't clear. "As often in prehistory, measuring time is not easy."

What we do know is that the structures were built in dark, challenging conditions and the builders had no natural light to help them. Indeed, Jaubert's team found traces of fire at several points around and on the structures.

The simplest explanation is that the structures served as some sort of shelter or refuge – perhaps the stalagmite "walls" supported a roof of perishable wood, for example – but there are no other artefacts and very few signs of domestic activity in the chamber beyond the presence of one charred bone fragment that possibly belonged to a bear or large herbivore.

That draws comparisons with much later cave sites such as Chauvet, a 30,000-year-old site of modern human occupation that is rich in cave art but contained a mere handful of artefacts. So perhaps Bruniquel – like Chauvet – served some ritual role. If so it would provide more evidence for the Neanderthal's capacity for symbolic thought.



A 3D reconstruction of the structures in Bruniquel cave Xavier Muth **- Get in Situ, Archéotransfert, Archéovision -SHS-3D, base photographique Pascal Mora**

Paola Villa at the University of Colorado in Boulder has previously called for Neanderthals to be considered on the same sort of intellectual plane as modern humans. She says the new paper lends weight to her argument.

Villa points out that the Bruniquel cave was actually discovered and studied in the 1990s. Even then, it seemed likely that Neanderthals had arranged the stalagmites, because carbon dating of the single charred bone found at the site suggested the site predated the arrival of modern humans in Europe. But until now few researchers were really aware of the structures' existence.

This is partly because the previous work wasn't published in the international scientific literature, but Villa thinks there was another reason the Bruniquel finds were overlooked in the late 90s and early 2000s: mainstream scientific thinking at the time simply rejected the idea of Neanderthals as intelligent and sophisticated.

"[It] ran against the prevailing and damning views of Neanderthal inferiority compared to modern humans," Villa says.

http://www.eurekalert.org/pub_releases/2016-05/asa-sdm052316.php

Study dispels myth about millionaire migration in the US

New study dispels the common myth about U.S. millionaires moving from high to low tax states

WASHINGTON, DC - The view that the rich are highly mobile has gained much political traction in recent years and has become a central argument in debates about whether there should be "millionaire taxes" on top-income earners. But a new study dispels the common myth about the propensity of millionaires in the United States to move from high to low tax states.

"The most striking finding in our study is how little elites seem willing to move to exploit tax advantages across state lines," said Cristobal Young, an assistant professor of sociology at Stanford University and the lead author of the study. "Millionaire tax flight is occurring, but only at the margins of significance."

In any given year, Young and his fellow researchers found that roughly 500,000 individuals file tax returns reporting incomes of $1 million or more (constant 2005 dollars). From this population, only about 12,000 millionaires change their state each year. The annual millionaire migration rate is 2.4 percent, which is lower than the migration rate of the general population (2.9 percent). The highest rates of migration are seen among low-income tax filers: migration is 4.5 percent among people who earn around $10,000 a year.

"There is a widely held perception that elites are extremely mobile -- that they are more attached to money than to place, and with money you can live anywhere you want," said Young, who noted that millionaires are no less likely to live in states with high income taxes (e.g., New Jersey or California) than in states with low or zero income taxes (e.g., Texas or Florida). "We tend to think of migration as a form of freedom and one of the privileges enjoyed by the rich. In practice, migration comes with high social and economic costs -- uprooting one's family, breaking away from one's social networks, and restarting in a new place."

The study finds that family responsibilities are a key factor that limit migration among top-income earners. "Very affluent people are much more likely to be married and to have school-age children, which makes moving more difficult," Young said.

Young also noted that most millionaires today are "the working rich" and do not live off inherited wealth, but instead rely on earnings from employment. "They work as lawyers, doctors, managers, and financial executives," he said. "They are at the peak of their careers and typically earn million-dollar incomes only for several years. People avoid potentially disruptive moves when they are performing at the very top of their game."

Titled, "Millionaire Migration and Taxation of the Elite: Evidence from Administrative Data," the study, which appears in the June issue of the American Sociological Review, relies on federal income tax returns from all U.S. tax filers who earned $1 million or more in any year between 1999 and 2011. This resulted in a dataset of 45 million tax records from 3.7 million unique tax filers over 13 years. For comparison, Young and his co-authors, Charles Varner, a sociologist and an associate director of the Center on Poverty and Inequality at Stanford University, and Ithai Z. Lurie and Richard Prisinzano, both financial economists at the Office of Tax Analysis at the U.S. Department of Treasury, also drew a 1 percent sample of the total population of tax filers, giving them an additional 24 million tax records from 2.6 million unique filers across the income distribution. The researchers tracked the income and residency of all of the filers over the entire study period.

"Previous studies on elite tax flight have struggled with data limitations either by using narrow segments of the millionaire population, such as professional athletes, or by analyzing limited geographic regions, such as one or two states," Young said. "This study includes every tax record filed by every U.S. millionaire over more than a decade."

According to the study, in the average state, which has an annual population of more than 9,000 individual millionaires, a one percent tax increase on this population would result in an expected loss of 23 of these economic elites. "Yes, a handful of top earners would leave," Young said. "But, more notably, virtually all of the millionaire population would stay."

While millionaire migration is extremely limited, there is a grain of truth in the worries about millionaire tax flight, the study finds. "When millionaires do migrate, they are more likely to move to a state with a lower tax rate, and that state is almost always Florida," Young said.

There are nine states without a state income tax, but only Florida disproportionally attracts millionaires from higher tax states, Young said. The other states, such as Texas, Nevada, and New Hampshire, do not.

"My guess is that if Florida established a 'millionaire tax,' elites would still find Florida appealing because of its climate and geography -- and patterns of elite migration wouldn't really change," Young said.

In fact, the millionaire migration that does occur has so little to do with tax differences that Young and his co-researchers estimate that if all states had the same tax rate -- so there were no tax incentives to move -- there would only be approximately 2.2 percent or about 250 fewer millionaire migrations between states each year.

The study also looked at the millionaire population along the borders between states with different tax rates. "In these narrow geographic regions, you would expect millionaires to cluster on the low tax side of the border, but we see very weak evidence of this," Young said.

As for policy implications, Young said "millionaire taxes" result in minimal tax flight among millionaires and help states raise revenue to improve education, infrastructure, and public services, while reducing inequality.

"Our research indicates that 'millionaire taxes' raise a lot of revenue and have very little downside," Young said.

http://www.eurekalert.org/pub_releases/2016-05/acos-fcp052516.php

Free colonoscopy program for uninsured detects cancer at earlier stage and is cost neutral

Successful colon cancer screening program expands to all hospitals in Louisville and provides a model for statewide implementation in Kentucky

CHICAGO - For uninsured patients who are at a high risk for colorectal cancer (CRC), performing free screening colonoscopies can identify cancer at an earlier stage and appears to be cost neutral from a hospital system perspective, according to study results published online in the Journal of the American College of Surgeons ahead of print publication.

In the United States, the impact of CRC totaled $7.49 billion in 2000 and is expected to increase to $14.03 billion by 2020.* Even after expansion of insurance coverage from the Affordable Care Act, some Americans and unregistered residents will still not receive health care coverage and will be unable to access resources for better health, which ultimately leads to worse outcomes and higher total costs for these patients if the disease is detected at a later stage. To help prevent this scenario, a research team led by surgeons from the University of Louisville (Kentucky) School of Medicine sought to determine if it would be cost-effective to provide free screening colonoscopies to a group of uninsured patients.

Lead study author Erica Sutton, MD, FACS, assistant professor surgery at the Hiram C. Polk Jr. Department of Surgery at the University of Louisville, said her team partnered with two groups, the Kentucky Colon Cancer Prevention Project and Surgery on Sunday Louisville, Inc., to conduct this study. Patients were referred to these non-profit organizations by free clinics in Louisville or primary care doctors, and those considered at high risk for CRC were offered free screening colonoscopies. Patients were considered at increased risk if they had a positive family history, a history of inflammatory bowel disease, or visible blood in the stool.

"Our community wanted to address how we fight and prevent colon cancer," Dr. Sutton said. "This approach is compassionate, but we also wanted to look at the cost or cost savings that we can expect to see from conducting a program like this for the uninsured."

The investigators collected patient data from these colonoscopies over a 12-month period. During the study period, 682 uninsured patients between the ages of 24 and 77 were screened. Nine cancers were identified: three patients were found to have stage I tumors, two patients had stage II, three had stage III, and one had stage 0.

The incidence of CRC, which was 1.3 percent, was compared with a control group of uninsured patients from the Surveillance, Epidemiology, and End Results (SEER) registry, a U.S. cancer surveillance system designed to track cancer incidence and survival. Researchers used published estimates from SEER-Medicare data of health expenditures by CRC stage during the initial phase of care. Health care costs included all Medicare payments, private insurer payments, and patient copayments and deductibles for covered services. To compare overall costs between patients in the study and the SEER database, the average initial cost of care (up to one year) was weighted by the stage-specific incidence in each group.

Compared with patients in the SEER-Medicare database, the study's cohort included more early stage cancers, and subsequently had a marginally lower estimated per patient initial cost ($43,126 vs. $43,736), which suggests the program is cost neutral from a system perspective.

"From strictly a payer standpoint, we found that this program did not cost more than what we currently do without it," Dr. Sutton said. She added the patients with cancer continued to get annual screenings through the program and free follow-up treatments.

Since the team started this study in 2013, Dr. Sutton said, they have been able to expand the free screenings to all the hospitals in Louisville. She said the team wanted to provide a model to hospitals in other parts of the state, and those hospitals have expressed interest as well. The team hopes this study's findings can begin a more wide-reaching national conversation about improving access to health care services in areas of ongoing disparity.

"If we don't want colon cancer to exist, we need to set up controlled screening programs, and we aren't going to bankrupt our system by preventing cancer in this way," Dr. Sutton said.

Other study authors are Samuel Walling, BE; Charles Kimbrough, MD, MPH; Nikhil Borkhetaria, MD; Whitney Jones, MD; and Brad Sutton, MD, MBA.

Yabroff KR, Mariotto AB, Feuer E, Brown ML. Projections of the costs associated with colorectal cancer care in the United States, 2000-2020. Health Economics 2008;17:947-959.
"FACS" designates that a surgeon is a Fellow of the American College of Surgeons.
Citation: Cost Analysis of Free Colonoscopies in an Uninsured Population at Increased Risk for Colorectal Cancer. Journal of the American College of Surgeons

http://bit.ly/1qU7khQ

New meta-analysis shows ketamine effective against persistent post-surgical pain and could provide major cost-savings globally

Cheap and safe drug may have the potential to save health systems billions of dollars globally

A new meta-analysis showing the effectiveness of ketamine for dealing with persistent post-surgical pain (PPSP) is to be presented at Euroanaesthesia 2016 (London, May 27-30). Ketamine, a cheap and safe drug, may have the potential to save health systems billions of dollars globally by being used in place of other drugs to prevent PPSP.

In this new study, Dr Philip Peyton (Austin Hospital & University of Melbourne, Department of Anaesthesia, Melbourne, Australia) and colleagues evaluated the evidence around ketamine for prevention of PPSP. Around 1 in 8 patients report PPSP after major surgery, and one third of these rate their pain as severe. A number of drugs and interventions have been studied to reduce this risk, including N-methyl D-aspartate (NMDA) receptor antagonists (such as ketamine), lidocaine and gabapentinoids (for example pregabalin (also known as Lyrica®). However, a recent Cochrane Review concluded that ketamine was the only agent with current evidence of a potential benefit in preventing PPSP. Ketamine is a non-selective potent NMDA antagonist commonly used as a second or third line agent to treat refractory acute postoperative pain.

Peyton and colleagues recently finished a pilot study of 80 patients for a proposed large phase 3/4 multicentre randomised trial of ketamine for PPSP, and then performed an updated meta-analysis including data from these 80 patients. A systematic PubMed literature review was performed of papers reporting randomised clinical studies using placebo control that investigated the effect of intravenous ketamine at standard analgesic doses, either given during or during and after surgery, on the incidence of long term postsurgical pain, as either a primary or secondary trial endpoint.

Incidence of PPSP was confirmed if the pain was still present 3-6 months after surgery and was rated at 3 or higher on a 10-point scale, or required ongoing use of painkillers. A total of 8 studies with 563 participants were found (including Peyton and colleagues' pilot study) and incorporated in a random effects meta-analysis. They found patients given ketamine were half as likely to experience PPSP compared with those given placebo (actual risk ratio 0.49 for ketamine versus placebo).

Dr Peyton says: "A large multicentre randomised trial of the effectiveness of perioperative intravenous ketamine is warranted. Demonstration of clinical effectiveness would promote widespread change in clinical anaesthesia practice and major benefits to patients and the community."

He concludes: "Developed countries spend billions of dollars on treatment of persistent post-surgical pain. Should further studies confirm our findings on ketamine, healthcare systems will have a cheap and effective means to treat this condition, allowing huge cost savings."

http://bit.ly/1WsScGa

Why It's OK to Let Babies 'Cry It Out'

New study finds that leaving a little one to "cry it out" may actually lead him or her to get more shut-eye

By Laura Geggel, Senior Writer | May 26, 2016 05:21pm ET

It can be difficult to listen to a baby wail in his or her crib at nighttime, but a new study finds that leaving a little one to "cry it out" does not raise the baby's stress level, and may actually lead him or her to get more shut-eye over time.

The findings may give sleep-deprived parents more insight into which parenting strategies could work best for their babies, the researchers said.

However, they cautioned that the study was small and included mostly higher-income, well-educated families. Therefore, more research is needed to see whether the findings apply to other groups, they said.

In the study, the researchers randomly placed 43 infants, ages 6 to 16 months old, who had trouble falling and staying asleep at night, into one of three groups. In one group, parents tried "graduated extinction," in which they didn't respond to the babies' cries immediately but would eventually comfort the child briefly without picking him or her up or turning on the lights. If the baby cried again, the parents would wait a little longer before they went to comfort the baby, and so on until the baby fell asleep.

In the second group, the parents tried "bedtime fading," which meant that if the babies had trouble falling asleep the night before, parents would put them to bed later the next night. But the parents still comforted the child as they normally would at night. In the third group, which acted as the control group, parents simply received educational information about sleep strategies for babies, and no specific instructions.

The first two methods are controversial, largely because of the belief that letting a baby cry can be stressful for both infants and parents, and may increase their

levels of the stress hormone cortisol, the researchers said. To measure the stress levels of the babies in the study, the researchers analyzed the babies' cortisol levels from cotton swabs of their saliva that the parents collected in the mornings and afternoons.

Stressed babies?

The study found that, within three months, the 14 babies in the graduated-extinction group (the ones who were left to cry) and the 15 babies in the bedtime-fading group (the ones who were put to bed later the following night) started falling asleep faster at night compared with the 14 babies in the control group. Moreover, those in the graduated-extinction group woke up fewer times during the night than the babies in the control group did at the three-month mark, the researchers found.

The results also showed that the afternoon cortisol levels in the babies in the two sleeping intervention groups dropped more over time than those of the babies in the control group, indicating less stress, the researchers said.

It's possible that these methods work because the babies learn to soothe themselves, stop crying and go to sleep, the researchers said.

One year after the intervention started, the mothers assessed their children, looking for any emotional or behavioral problems, and underwent a test evaluating parent-child attachment. There were no differences among the groups in terms of the children's behavioral and emotional temperaments, the researchers said.

The study also found that the mothers' moods improved over time in all three groups, but that this improvement was especially strong for those in the bedtime-fading group, the researchers found.

The new study provides pediatricians and parents with solid evidence about which sleep methods work best for babies, said Dr. David Gozal, an expert in pediatric sleep and a professor of pediatrics at the University of Chicago who was not involved with the study.

"For young infants, it has been our usual recommendation to teach the baby to self-soothe through a process of graduated extinction, very similar to the one implemented in this study," Gozal told Live Science. However, parents who want results need to persevere, he said.

"Perseverance and determination to succeed are key, since different infants will require different periods of time before they 'get with the program,'" he said. "If, however, after a reasonable period of truly trying [a method] things are not improved, switching to another method is always an option."

The study was published in the May issue of the journal Pediatrics.

http://bit.ly/24eByJA

Mongol hordes gave up on conquering Europe due to wet weather

It has mystified historians ever since. After a string of major victories, the Mongol army suddenly retreated from central Europe in 1242.

By Conor Gearin

Do we have a wet-weather plan? **Bridgeman images**

Some scholars claim Mongolian politics forced the withdrawal, while others credit the strength of fortified towns in present-day Hungary and Croatia. But Europe could have been rescued by its own bad weather, an analysis of tree rings and historical documents concludes.

The Mongol cavalry fed its horses on the grass of the Eurasian steppe, says Nicola Di Cosmo of Princeton University, one of the study's authors. A warm climate in the early 1200s helped make the grasslands lush and this, in turn, helped the Mongols extend their empire into Russia, he says.

In 1241, the Mongol army reached the plains' western limit in Hungary. Led by Genghis Khan's grandson Batu, the Mongols crushed the Polish and Hungarian armies on open, flat terrain that suited their mobile warfare tactics. "They were familiar with that environment," says Di Cosmo. "What they didn't know is how prone to flooding that particular area was."

Huge swamp

Compared with the rest of the steppe, Hungary has a high water table so it floods easily. Analysing tree rings in the region, Di Cosmo and his colleagues found that Hungary had a cold, wet winter in early 1242. This probably turned Hungary's central plain into a huge swamp.

Historical documents the team studied back up this claim, recording, for example, that melting snows kept the Mongol army from attacking a Hungarian castle surrounded by marshes. Lacking pasture for its horses, the Mongols fell back to drier highlands and then to Russia in search of better grass. While climate wasn't the only factor in the reteat, it would be a mistake to ignore it, says Di Cosmo. "It's like saying the winter in Russia had no effect on Napoleon's army," he says.

Michael Mann of Pennsylvania State University, University Park, says the study is interesting, but he warns against over-interpreting the influence of climate on

historic events. “I’m sceptical that such ‘climate determinism’ holds nearly as universally as some authors seem to think,” he says. The changes in weather the study reported seemed “modest”, he says.

But Aaron Putnam of the University of Maine in Orono says that the study steered clear of determinism, taking into account all potential factors. “I think it’s convincing,” he says. “The previous explanations of the Mongol withdrawal didn’t add up.”

Horse logistics limited the Mongols, Putnam says. “They were incredibly technologically savvy, but they got into a place where horses just didn’t do well.”

Putnam says that natural weather records like tree rings have much more to tell us about the history of premodern civilisations, which depended heavily on environmental conditions. “It’s just an incredible archive.”

Journal reference: Scientific Reports, DOI: 10.1038/srep25606

http://nyti.ms/1sFpCo4

Infection Raises Specter of Superbugs Resistant to All Antibiotics

American military researchers have identified the first patient in the United States to be infected with bacteria that are resistant to an antibiotic that was the last resort against drug-resistant germs.

By SABRINA TAVERNISE and DENISE GRADY MAY 26, 2016

The patient is well now, but the case raises the specter of superbugs that could cause untreatable infections, because the bacteria can easily transmit their resistance to other germs that are already resistant to additional antibiotics. The resistance can spread because it arises from loose genetic material that bacteria typically share with one another.

“Think of a puzzle,” said Dr. Beth Bell, of the Centers for Disease Control and Prevention. “You need lots of different pieces to get a result that is resistant to everything. This is the last piece of that puzzle, unfortunately, in the United States. We have that genetic element that would allow for bacteria that are resistant to every antibiotic.”

The bacteria are resistant to a drug called colistin, an old antibiotic that in the United States is held in reserve to treat especially dangerous infections that are resistant to a class of drugs called carbapenems. If carbapenem-resistant bacteria, called CRE, also pick up resistance to colistin, they will be unstoppable.

“This is huge,” said Dr. Lance Price, a researcher at George Washington University. “We are one step away from CRE strains that cannot be treated with antibiotics. We now have all the pieces in place for it to be untreatable.”

The gene for resistance to colistin was first found in China, where the drug is used in pig and poultry farming. Researchers reported its discovery there in November. It has also been found in the intestine of one pig in the United States.

CRE is still relatively rare, causing just 600 deaths a year, but by 2013, researchers had identified it in health care facilities in 44 states. Dr. Thomas R. Frieden, director of the Centers for Disease Control and Prevention, often calls it the “nightmare superbug” because it is resistant to all but one antibiotic — colistin.

“We risk being in a post-antibiotic world,” Dr. Frieden said during a gathering for journalists in Washington on Thursday. “That wouldn’t just be urinary tract infections or pneumonia — that could be for the 600,000 patients a year who need cancer treatment.”

He added: “The medicine cabinet is empty for some patients.”

The colistin resistance in the United States came to light when a 49-year-old woman, who Dr. Bell said was “connected to the military,” was treated for a urinary infection at a military clinic in Pennsylvania. Because her urine culture had unusual results, the sample was sent to the Walter Reed National Military Medical Center, which identified the drug resistance. The bacteria, though resistant to colistin and some other antibiotics, were not resistant to carbapenems. Doctors there published a report on the case in a medical journal.

Patrick McGann, a scientist at the Walter Reed Army Institute of Research and lead author of the paper, said researchers had only started analyzing samples a few weeks ago. They tested samples from six patients, and one of them was the woman’s.

Dr. Bell said researchers did not know how the patient contracted the resistant bacteria. The microbes have been found in people in Asia and Europe, but the patient had not traveled during the past five months. It is possible that she contracted the bacteria from food, or from contact with someone else who was infected, Dr. Bell said.

Public health workers will interview the woman and will probably test her family members and other close contacts for the bacteria, Dr. Bell said.

Infectious disease doctors have long warned that overuse of antibiotics in people and in animals put human health at risk by reducing the power of the drugs, some of modern medicine’s most prized jewels. About two million Americans fall ill from antibiotic-resistant bacteria every year and at least 23,000 die from those infections. The Obama administration has elevated the issue, laying out a strategy for how to bring the problem under control.

The CRE germs usually strike people receiving medical care in hospitals or nursing homes, including patients on breathing machines or dependent on catheters. Healthy people are rarely, if ever, affected. But the bugs attack broadly, and the infections they cause are not limited to people with severely compromised immune systems. CRE was believed to be the cause of infections from improperly

cleaned medical scopes that led to the death of two people at Ronald Reagan U.C.L.A. Medical Center in California last year.

The Department of Defense, in a blog post about the discovery of the gene in the United States, said it gave “a new clue into the antibiotic resistance landscape.”

But the gene is rare: The blog pointed out that federal health researchers had searched for the gene in 44,000 samples of salmonella and 9,000 samples of E. coli/shigella, taken from people and retail meat, and did not find it.

http://www.bbc.com/news/science-environment-36397034

DNA 'tape recorder' to trace cell history

Researchers have invented a DNA "tape recorder" that can trace the family history of every cell in an organism.

By Roland Pease BBC Radio Science Unit

The technique is being hailed as a breakthrough in understanding how the trillions of complex cells in a body are descended from a single egg. "It has the potential to provide profound insights into how normal, diseased or damaged tissues are constructed and maintained," one UK biologist told the BBC. The work appears in Science journal.

The human body has around 40 trillion cells, each with a highly specialised function. Yet each can trace its history back to the same starting point - a fertilised egg. Developmental biology is the business of unravelling how the genetic code unfolds at each cycle of cell division, how the body plan develops, and how tissues become specialised. But much of what it has revealed has depended on inference rather than a complete cell-by-cell history.

"I actually started working on this problem as a graduate student in 2000," confessed Jay Shendure, lead researcher on the new scientific paper.

"Could we find a way to record these relationships between cells in some compact form we could later read out in adult organisms?"

Overcoming failure

The project failed then because there was no mechanism to record events in a cell's history. That changed with recent developments in so called CRISPR gene editing, a technique that allows researchers to make much more precise alterations to the DNA in living organisms.

The molecular tape recorder developed by Prof Shendure's team at the University of Washington in Seattle, US, is a length of DNA inserted into the genome that contains a series of edit points which can be changed throughout an organism's life.

Each edit records a permanent mark on the tape that is inherited by all of a cell's descendants. By examining the number and pattern of all these marks in an adult cell, the team can work back to find its origins.

Developmental biologist James Briscoe of the Crick Institute, in London, UK, calls it "a creative and exciting use" of the CRISPR technique. "It uniquely and indelibly marks cells with a 'barcode' that is inherited in the DNA. This means you can use the barcode to trace all the progeny of barcoded cells," he said.

Jay Shendure collaborated with molecular biologist Alex Schier of Harvard University to prove the technique on a classic lab organism - the zebrafish.

Not only did they show the technique works, they could trace the lineage of hundreds of thousands of cells in mature fish. They also showed it has the power to change perceptions about biological development.

"We can look at individual organs - say the left eye or the right eye, or the gills or the heart," Prof Shendure explained in an interview with the BBC's Science in Action radio programme, "and the real surprise was that in every organ we looked at, the majority of the organ came from just a handful of progenitor cells."

For example, although they identified over a thousand cell lineages within one of their fish, it took only five of them to create most of the blood cells. The surprise is evident in the published paper, which includes a few suggested explanations. James Briscoe also finds the discovery remarkable.

"It's striking that a barcode found in one organ was rarely found in another," he wrote in an e-mail, adding that in the early embryo, cells are often mobile and so a richer mix could be expected. An unexpectedly small group of "founder cells" would be one explanation.

Or "there could be many founding cells, from different lineages (barcodes), at early embryonic stages, but many of these lineages die off as the tissue develops."

Further experiments with the technique could unwrap the details. But the fact that a simple, profound question was immediately thrown up by the new technique shows just how powerful it is.

And the technique does not have to be limited to healthy development.

"Cancers develop by a lineage, too," Alex Schier told the BBC. "Our technique can be used to follow these lineages during cancer formation - to tell us the relationships of cells within a tumour, and between the original tumour and secondary tumours formed by metastasis."

And Prof Shendure points out that many inherited diseases develop because of faulty genetic programming. "Many of these may well have their basis in the skewing of the cell lineage," he explained.

The technique comes with the somewhat tortured acronym GESTALT - the German for "shape". It is easy to use, and could easily be improved, says Jay Shendure. James Briscoe is already thinking of ways to use it with his experimental animals - mice.

For developmental biology, GESTALT could be the shape of things to come.

http://apne.ws/1sFvBt3

Dr. Heimlich, 96, uses his maneuver to save choking woman

The 96-year-old retired chest surgeon credited with developing the namesake Heimlich maneuver has used it to save a woman choking on food at his senior living center.

By Lisa Cornwell with Dan Sewell

CINCINNATI (AP) - Dr. Henry Heimlich was in the dining room at the Deupree House in Cincinnati, where he lives, when an 87-year-old woman sitting next to him began choking Monday night.

The dining room maitre d', Perry Gaines, told The Cincinnati Enquirer that Heimlich dislodged a piece of hamburger from the woman's airway and she quickly recovered.

Heimlich said he was having dinner when he looked over at the woman sitting next to him and could see that her face was growing pink and she was obviously choking. He said he got up behind her and began the technique.

"As soon as I did the Heimlich maneuver, a piece of meat with a bone in it immediately popped out," he said.

Choking victim Patty Ris said Friday that she couldn't breathe and Heimlich rushed over to stand her up and dislodge the food.

"I definitely would have died right then and there," said Ris, who said she felt fine Friday and had no after-effects. "There was no doubt about it."

Ris said that after she regained her breath Heimlich explained to her what he had done. She told him afterward: "God put me in this seat next to you."

Heimlich said in interviews Friday that it was the first time he'd used his maneuver, and his son Phil Heimlich said he believed that was accurate.

But the doctor said in at least one previous account, a 2003 interview he did with BBC News Online, that he had applied his emergency technique three years earlier.

The Heimlich maneuver involves abdominal thrusts applied to a choking person in an effort to lift the diaphragm and force air from the lungs to dislodge any object.

Heimlich has said he developed the maneuver after reading accounts of people choking in restaurants, with many of them dying.

Through the years, he appeared on radio and television shows including "Tonight Show Starring Johnny Carson" to discuss and demonstrate the technique.

Heimlich's views on how and when the maneuver should be used have put him at odds with some people in the health field.

http://www.eurekalert.org/pub_releases/2016-05/du-aca052716.php

Appalachian coal ash richest in rare earth elements

Concentrations are highest in coal from the Appalachian Mountains

DURHAM, N.C. -- A study of the content of rare earth elements in U.S. coal ashes shows that coal mined from the Appalachian Mountains could be the proverbial golden goose for hard-to-find materials critical to clean energy and other emerging technologies.

In the wake of a 2014 coal ash spill into North Carolina's Dan River from a ruptured Duke Energy drainage pipe, the question of what to do with the nation's aging retention ponds and future coal ash waste has been a highly contested topic.

One particularly entrepreneurial idea is to extract so-called "critical" rare earth elements such as neodymium, europium, terbium, dysprosium, yttrium and erbium from the burned coal. The Department of Energy has identified these globally scarce metals as a priority for their uses in clean energy and other emerging technologies. But exactly how much of these elements are contained in different sources of coal ash in the U.S. had never been explored.

Researchers from Duke University measured the content of rare earth elements in samples of coal ash representing every major coal source in the United States. They also looked at how much of these elements could be extracted from ash using a common industrial technique.

The results, published online on May 26 in the journal Environmental Science and Technology, showed that coal from the Appalachian Mountains contains the most rare earth elements. However, if extraction technologies were cheap enough, there are plenty of rare earth elements to be found in other sources as well.

"The Department of Energy is investing $20 million into research on extraction technologies for coal wastes, and there is literally billions of dollars' worth of rare earth elements contained in our nation's coal ash," said Heileen Hsu-Kim, the Mary Milus Yoh and Harold L. Yoh, Jr. Associate Professor of Civil and Environmental Engineering at Duke.

"If a program were to move forward, they'd clearly want to pick the coal ash with the highest amount of extractable rare earth elements, and our work is the first comprehensive study to begin surveying the options," Hsu-Kim said.

The researchers took coal ash samples from power plants located mostly in the American Midwest that burn coal sourced from all over the country, including the three largest sources: the Appalachian Mountains, southern and western Illinois, and the Powder River Basin in Wyoming and Montana. The content of rare earth elements was then tested using hydrofluoric acid, which is much stronger and more efficient than industrial methods, but is too hazardous to use on a large scale.

The results showed that ash collected from Appalachian Mountain coal has the highest amount of rare earth elements at 591 milligrams per kilogram (or parts per million). Ash from Illinois and the Powder River Basin contain 403 mg/kg and 337 mg/kg, respectively.

The researchers then used a common industrial extraction technique featuring nitric acid to see how much of the rare earth elements could be recovered. Coal ash from the Appalachian Mountains saw the lowest extraction percentages, while ash from the Powder River Basin saw the highest. Hsu-Kim thinks this might be because the rare earth elements in the Appalachian Mountain coal ash are encapsulated within a glassy matrix of aluminum silicates, which nitric acid doesn't dissolve very well.

"One reason to pick coal ash from the Appalachian Mountains would be for its high rare earth element content, but you'd have to use a recovery method other than nitric acid," said Hsu-Kim, who also holds an appointment in Duke's Nicholas School of the Environment. "For any future venture to begin an extraction program, the recovery method will need to be tailored to the specific chemistry of the coal ash being used."

The Duke researchers also tried "roasting" the coal ash with an alkali agent before dissolving it with nitric acid. Even though the process hadn't been optimized for recovery purposes, the tests showed a marked improvement in extraction efficiency.

"The reagents we used are probably too expensive to use on an industrial scale, but there are many similar chemicals," said Hsu-Kim. "The trick will be exploring our options and developing technologies to drive the costs down. That way we can tap into this vast resource that is currently just sitting around in disposal ponds."

This work was supported by the National Science Foundation (CBET-1510965, OISE-12-43433), the Environmental Research and Education Foundation and the American Coal Ash Association.

The study is available free online at http://dx.doi.org/10.1021/acs.est.6b00085.

"Trends in the Rare Earth Element Content of U.S.-Based Coal Combustion Fly Ashes," Ross K. Taggart, James C. Hower, Gary S. Dwyer and Heileen Hsu-Kim. Environmental Science & Technology, May, 26 2016. DOI: 10.1021/acs.est.6b00085

http://www.eurekalert.org/pub_releases/2016-05/tuom-ti052716.php

Telling irregularities

New procedure uses the heart rate to estimate the life expectancy of infarct patients

The heart rate may be an indicator of a person's life expectancy. A research team at the Technical University of Munich (TUM) has to this end analyzed an effect which at first seems paradoxical: Minor irregularities in the heartbeat are indicative of a healthy body. A clinical study confirmed a strong correlation between this phenomenon and the survival prospects of heart attack patients. The new methods of measurement may soon be applied in medical practice.

A healthy person's heart will beat slightly faster upon inhalation and slow down again upon exhalation. The reason for this is that inhaling dampens an effect that will normally regulate the heart rate down to the at rest rate of approximately 60 beats per minute. This phenomenon is called respiratory sinus arrhythmia, which may be translated as a "breathing-induced irregularity in the sinus node, the bundle of nerve fibers controlling the heart beat".

The phenomenon has been known since the 19th century. A body weakened by a heart attack will show a clearly smaller difference between heart rates during the exhaling and inhaling cycles. Therefore, several attempts at using arrhythmia characteristics to draw conclusions about the life expectancy of patients were made in the past.

Thus far, however, the data taken on its own yielded no conclusions as to the life expectancy of a patient. This, however, is precisely what the scientists working with Prof. Georg Schmidt, head of the Biosignal Processing team at the University Hospital Klinikum rechts der Isar, have now achieved.

Breathing cycle and heart rate: The decisive moment

Whilst in the majority of earlier studies the full breathing cycle was correlated to the heart rate, the TUM team now focused on exhaling and specifically on the moment when the heart rate would normally be reduced again. "With our approach, you might say we are surgically selecting the moment when the decisive events take place," says Georg Schmidt.

In the analysis of the heart rate data, an algorithm Schmidt and his team proposed in an article published in the Lancet in 2006 has proven useful. The method renders the respiratory sinus arrhythmia measurable by - to put it simply - extracting other sources of heart rhythm variation from the data collected over a certain period. The algorithm calculates an average from the data, which may then be graphed.

"Our method produces a far more specific picture of the functional condition of the body," says Dr. Daniel Sinnecker, primary author of the study. "There is no other method as yet to isolate the vagal function as specifically as this."The vagal function, i.e. the activity of the vagus nerve, is responsible, among other, for reducing the heart rate of healthy persons as described above. Although the vagus nerve affects many other bodily processes, its activity is not directly measurable.

More than 900 patients examined

Within the framework of the study, published in the Journal of the American College of Cardiology, breathing cycles and heart beat rhythms of close on 950

heart attack patients were measured shortly after a heart attack. The data was analyzed to find respiratory sinus arrhythmia. The test persons were re-examined every six months over a five-year period. The result: Heart attack patients with less pronounced arrhythmia had a higher risk of dying within the period of observation. Examined persons with only minor arrhythmia were five times more at risk of dying over the five-year period than people with higher breathing-related fluctuations.

Two further clinical studies are currently under way with TUM participation, examining the respiratory sinus arrhythmia in different groups of persons. One of the studies (EU-Cert-ICD) examines different treatment strategies in people with pacemakers, whilst the other (INVADE) monitors elderly people with and without heart disease. Schmidt and his team are confident that the results of these studies will confirm that their method, taken on its own, will be a reliable indicator of risk.

Everyday application imminent

The developers are confident that the new method may soon be widely deployed. "We are quite close to everyday application since, by and large, the development of the method is complete," says Georg Schmidt. The technical hurdles are few: Since it is no longer necessary these days to measure breathing rate in addition to heart beat, a modern ECG unit would basically suffice.

"Even the general practitioner could therefore within ten minutes record sinus arrhythmic activity."

The method may be fruitfully applied in more than 80 percent of the cases, says Schmidt. Irrespective whether the examined patients had recently suffered a heart attack, it could be used in combination with other indicators to assess the health risk. Hidden risks may in this way be detected in some persons and possibly mitigated with an implantable defibrillator, for instance.

"In addition to that, the cost of treatments could be reduced by avoiding unnecessary procedures," says Georg Schmidt.

A next step might be to apply this method to examine the efficacy of different strategies for treatment. Should a patient's characteristics improve in the course of treatment, it is likely that the applied therapy was appropriate.

D. Sinnecker, M. Dommasch, A. Steger, A. Berkefeld, P. Hoppmann, A. Müller, J. Gebhardt, P. Barthel, K. Hnatkova, K. M. Huster, K. Laugwitz, M. Malik, G. Schmidt, Expiration-Triggered Sinus Arrhythmia Predicts Outcome in Survivors of Acute Myocardial Infarction, Journal of the American College of Cardiology 2016;67(19). DOI: 10.1016/j.jacc.2016.03.484.

A. Bauer, J. Kantelhardt, P. Barthel, R. Schneider, T. Mäkikallio, K. Ulm, K. Hnatkova, A. Schömig, H. Huikuri, A. Bunde, M. Malik, G. Schmidt, Deceleration capacity of heart rate as a predictor of mortality after myocardial infarction: cohort study, The Lancet Volume 367 , Issue 9523 , 2006. DOI: http://dx.doi.org/10.1016/S0140-6736(06)68735-7

http://nyti.ms/22sRtoj

Report Warns of Climate Change Disasters That Rival Hollywood's

Stonehenge eroding under the forces of extreme weather. Venice slowly collapsing into its canals. The Statue of Liberty. gradually flooding.

By JONAH BROMWICH MAY 26, 2016

Stonehenge, Salisbury, England. **Andrew Testa for The New York Times**

Images like these, familiar from Hollywood climate-catastrophe thrillers, were evoked by a joint report, released on Thursday by Unesco, the United Nations Environment Program and the Union of Concerned Scientists, that detailed the threat climate change could pose to World Heritage sites on five continents.

(The Australian continent was originally included in the report, but that its government requested it be removed because of concerns that the information would hurt its tourism industry.)

Adam Markham, the deputy director for climate and energy at the Union of Concerned Scientists and the report's lead author, said that while many of the sites were bound to be affected by factors including a rise in sea levels, intense storms and wildfires, planning could go a long way toward protecting them.

"It is a very tough challenge, but if we recognize the scale of the problem — and I don't think most people realize how big it is or how fast the changes are coming — then I think there is a lot we can do," he said.

The report highlights 31 sites in 29 countries that have already felt some impact from climate change, including well-known tourist destinations like Easter Island and Yellowstone National Park. It was drawn from peer-reviewed science literature, technical reports and local experts, as well as domestic evaluations of the sites prepared for the World Heritage Committee.

Venice's Grand Canal. **Andrea Wyner for The New York Times**

Though the report emphasizes the importance of the recent Paris climate accord, Mr. Markham said that emissions already affecting the climate are likely to create "a lot of change and impact."

"We don't have enough resources to save every threatened asset," he said. "Can we save every lighthouse that is on an eroding cliff? Probably not. So there are going to have to be hard choices made in every country."

Thirteen listed heritage sites were examined in comprehensive case studies intended to demonstrate the way climate change has already had an impact. In a study of the Statue of Liberty, for instance, the effects of Hurricane Sandy, which scientists have shown were exacerbated by a rise in the sea level, are explored at length.

Rebecca Beavers, the coastal adaptation coordinator of the National Park Service who helps the agency plan for the impact of climate change, and was an adviser on the report, said the damage to the facilities and infrastructure at the Statue of Liberty from the 2012 storm had precipitated a new focus on how best to contend with extreme weather.

"I think that it's important to recognize that adaptation is continuous change," Ms. Beavers said. "It's not isolated action, it's not a single step. It really is a process."

The report includes a series of recommendations for government agencies, the tourism industry and heritage site managers. It emphasizes that the sites themselves represented a trove of historical information on human responses to extreme weather, and that the archaeological data they held could help guide policy makers.

On Its Second Try, NASA Adds Space to Station

Mr. Markham, who is British, said he personally was very upset about what was happening to Skara Brae, a 5,000-year-old Neolithic settlement that is one of many sites off the coast of Scotland at risk from coastal erosion.

"This is the famous one, which I've never seen and I want to be able to see, but I care about all of those sites," Mr. Markham said. "For me, that is my cultural heritage, disappearing into the ocean."

http://nyti.ms/25tWp1r

On Its Second Try, NASA Adds Space to Station

NASA inflated a new experimental room at the International Space Station on Saturday.

By The Associated Press May 28, 2016

CAPE CANAVERAL, Fla. — NASA successfully inflated a new experimental room at the International Space Station on Saturday, producing the world's first pump-up compartment for astronauts.

The operation took much longer than expected, stretching over three days.

The astronaut Jeffrey Williams spent seven hours on Saturday opening and closing an air valve to expand the compartment. Enough air finally seeped inside so that the puffy white pod could stretch to its full size of 13 feet in length and 10.5 feet in diameter, which is equivalent to a small bedroom. Internal air tanks provided the final pressurization to complete the job.

Mr. Williams and his five crewmates will now have to wait a week before entering the pod. NASA wants to make certain the chamber is airtight before opening the door.

It was NASA's second attempt to inflate the Bigelow Expandable Activity Module, or BEAM, named for the aerospace company that created it as a precursor to potential moon and Mars habitats, and orbiting tourist hotels.

The BEAM barely expanded during Thursday's inflation attempt. Experts believe the soft-sided compartment was tightly packed for so long before its launch last month that its fabric layers had trouble unfolding.

Pressure inside the chamber was relieved on Friday to ease the friction among the multiple layers. By Saturday, the cubicle had swelled an additional six feet in length, and looked more like a giant beach ball with every pulse of air.

In all, Mr. Williams opened the valve 25 times on Saturday for a total of 2.5 minutes' worth of air flowing from the space station into the chamber.

Popping noises could be heard as pressure built inside the BEAM. Officials said it was the sound of internal straps releasing as the pod swelled in both length and girth.

NASA insisted on a slow inflation to avoid a sudden pressurization of the BEAM that could stress the connecting parts of the space station.

NASA paid $17.8 million to Bigelow Aerospace for this version of the BEAM, which could lead to a bigger inflatable room being constructed at the space station.

The company's founder, Robert Bigelow, is developing a pair of private inflatable space stations that could fly in a few years. Mr. Bigelow, a longtime hotel entrepreneur, sees inflatables as the future of spaceflight.

Because expandable spacecraft can be compressed for launch, the saved space allows rockets to carry more cargo. The standard aluminum rooms that currently make up the space station cannot be larger than what fits into a rocket.

The BEAM — which sits empty except for sensors — will remain attached to the orbiting lab for two years as engineers measure temperature, radiation levels and resistance to impact from space debris. Given its experimental status, the compartment will be off limits to astronauts most of the time.

SpaceX, formally known as Space Exploration Technologies Corporation of Hawthorne, Calif., delivered the BEAM early last month, and the compartment was installed on the outside of the 250-mile-high outpost. Launch delays had kept it grounded an extra six months.