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Male and female mice respond differently to inflammation

New research published in the Journal of Leukocyte Biology suggests that the inflammatory response in female mice differs from males mice in type and number of white blood cells recruited to the site of inflammation

New research published in the Journal of Leukocyte Biology shows that male and female mice respond differently to inflammation at the cellular level. Specifically, in male mice the spleen acts as a source of white blood cells, while in females this is not the case. This discovery suggests that human studies are necessary to determine if current medical practices, which treat men and women generally the same, should be altered to reflect sex-specific differences.

"The principal implication of this study is that it highlights the importance of sex differences in complex biological processes such as inflammation," said James Whiteford, Ph.D., a researcher involved in the work from the Centre for Microvascular Research at the William Harvey Research Institute, Barts and the London School of Medicine and Dentistry at Queen Mary University of London, in London, England. "This is particularly relevant as to how we design and interpret our experiments and how we evaluate the potential efficacy of anti-inflammatory therapeutics."

To make this discovery, Whiteford and colleagues used male and female mice and exposed them to zymozan in a peritonitis reaction and compared the numbers of different types of white blood cells to the peritoneal cavity and the blood. They found that higher levels of neutrophils and monocytes were recruited to the blood and peritoneal cavity in males than in females. They also compared the production and expression of a diverse spectrum of chemokines and cytokines and their receptors and found that males and females were similar.

"Sex differences in immune-related diseases have long been known. Autoimmunity, for example, is much more common in women, a bias often linked to immune cell types called B and T cells," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "These new findings highlighted important potential sex differences in how more primitive or 'innate' immune cells including neutrophil and monocytes operate. These new data will influence how we design and interpret clinical trials and also may provide new therapeutic opportunities for diseases that differentially affect men and women."

published by the Society for Leukocyte Biology.

Details: Emma Kay, Lorena Gomez-Garcia, Abigail Woodfin, Ramona S. Scotland, and James R. Whiteford. Sexual dimorphisms in leukocyte trafficking in a mouse peritonitis model. J. Leukoc. Biol. November 2015; 98:805-817; doi: 10.1189/jlb.3A1214-601RR; http://www.jleukbio.org/content/98/5/805.full

http://www.eurekalert.org/pub_releases/2015-11/uog-sdm110215.php

Swedish diagnostic method for Alzheimer's becomes international standard

Researchers at Gothenburg University have developed a reference method for standardized measurements that diagnose Alzheimer's disease decades before symptoms appear.

The method has now formally been classified as the international reference method, which means that it will be used as the standard in Alzheimer's diagnostics worldwide. Everyone naturally builds the beta amyloid protein in his or her brain. The protein's normal function is not completely mapped, but one theory is that it participates in the formation and removal of synapses, which is vital in enabling the brain to form new memories.

Remain in the brain

Beta amyloid built by healthy people is quickly transported out to the spinal fluid and blood. But with Alzheimer's, the beta amyloids remain in the brain, where they clump together and begin to damage the synapses, which leads to brain, nerve cell death. This process can begin in middle age and continue unnoticed for decades until the nerve cells are so damaged that symptoms take the form of a memory disorder and impaired cognitive abilities. At that point, the disease is felt to be too advanced to be treated, so intensive worldwide research is underway to find methods that diagnose Alzheimer's sooner.

Exact measure

After decades of research, Henrik Zetterberg and Kaj Blennow at Sahlgrenska Academy, Gothenburg University, were able to develop a method that measures the exact amount of beta amyloid in spinal fluid and diagnose Alzheimer's ten to thirty years before the disease becomes symptomatic. "If the concentration of beta amyloid in the spinal fluid is abnormally low, it indicates that the protein is sticking in the brain, which is the earliest sign of Alzheimer's disease," says Henrik Zetterberg.

Global reference

The Gothenburg researchers' pioneering studies have gained wide international recognition since the measurement method they developed was approved as the global reference method. "This means that the method will be used as the norm for standardizing beta amyloid measurements around the world. With the help of the standard, people who are worried about Alzheimer's disease can be tested, and get the same results regardless of whether it is done in San Francisco, Sao Paolo, London, Gothenburg or Cape town," says Kaj Blennow.

"We put a lot of effort into this project and it has been initiated and conducted, and now completed by us at Gothenburg within the framework of a global cooperation project that we head," says Henrik Zetterberg.

Promising result for drug candidates

This major advance coincides with recent studies that show promising results for different drug candidates that attack Alzheimer's disease and target beta amyloids.

"These new drugs will likely prove most effective for persons who have just begun to accumulate beta amyloids in their brain. Then a well-proven and standardized method becomes crucial, as it ensures that these people are identified in a diagnostically safe and precise manner," says Kaj Blennow.

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Study led by Temple researchers reveals new link between Down syndrome and Alzheimer's

Study led by researchers at Lewis Katz School of Medicine at Temple University raises hope for new treatments

Philadelphia, PA - Individuals with Down syndrome who survive into adulthood face the additional challenge of early-onset dementia, in which toxic amyloid plaques build up in the brain. The condition is strikingly similar to Alzheimer's disease, and as new work led by researchers at the Lewis Katz School of Medicine at Temple University (LKSOM) shows, dementia in Down syndrome involves defects in a regulatory enzyme known as γ-secretase activating protein (GSAP), which also happens to malfunction in Alzheimer's disease.

In the field of Down syndrome research, the new findings are groundbreaking, and according to Domenico Praticò, MD, Professor in the Departments of Pharmacology and Microbiology and the Center for Translational Medicine at LKSOM and senior investigator on the study, the work could soon lead to the development of a specific GSAP-targeted therapy that is capable of safely mitigating dementia in Down syndrome. Previous γ-secretase inhibiting drugs failed in patients because of their high intrinsic toxicity.

The study, which appeared online in the Annals of Neurology, is the first to draw a connection between GSAP hyperactivity and excess processing of the Aβ precursor protein (APP) - the protein responsible for the final formation of amyloid beta - in Down syndrome. Dr. Praticò and colleagues made the discovery after examining donated tissue from the brains of deceased Down syndrome patients. Relative to postmortem brain tissue from healthy subjects, the samples from individuals with Down syndrome showed substantially elevated levels of both GSAP protein and its activity.

Dr. Praticò's team also found that GSAP hyperactivity was associated with abnormalities in the GATA1 transcription factor, which controls GSAP production. They demonstrated that when GATA1 activity was silenced in neurons that overexpressed APP, both GSAP levels and amyloid beta peptide levels increased. Overexpression of GATA1, on the other hand, produced the opposite effect.

In Down syndrome, APP overexpression is extreme, reaching levels in the brain that are four to five times higher than normal. Its excess levels are a direct consequence of the triplicate copy of the 21st chromosome, which not only causes the syndrome in the first place but also houses the APP gene.

"The higher levels of APP in Down syndrome patients causes increased formation of amyloid beta peptides which then precipitate in the amyloid plaques in the brain much earlier in life," Dr. Praticò explained. "Amyloid plaques begin to form in the brain of Down syndrome patients in the late teens and early 20s." Symptoms of dementia emerge in the following years.

The new findings could mark a turning point for Down syndrome survivors. "We've shown that GSAP inhibition reduces amyloid production, and because GSAP is specific to the formation of amyloid, without affecting other pathways, it should be a safe alternative to other strategies of a direct γ-secretase inhibition," Dr. Praticò said.

Dr. Praticò and colleagues already have access to a GSAP inhibitor. They plan next to investigate the effects of the agent in preclinical studies in mice. "We are very optimistic that our animal models will work," he said. "If they do, we will move to a clinical trial, where we hope to be able to reduce amyloid production safely and effectively."

Other researchers contributing to the new work include Dr. Jin Chu in the Department of Pharmacology and Center for Translational Medicine at LKSOM; and Dr. Thomas Wisniewski in the Departments of Neurology, Psychiatry and Pathology, and Center for Cognitive Neurology at the New York University School of Medicine, New York.

The research was funded by National Institutes of Health grant AG08051 and by the Alzheimer Art Quilt Initiative and the Wanda Simone Endowment for Neuroscience.

You can read the entire Annals of Neurology study at http://onlinelibrary.wiley.com/doi/10.1002/ana.24540/pdf.

http://www.eurekalert.org/pub_releases/2015-11/si-ms110215.php

Molecular 'brake' stifles human lung cancer

By testing over 4,000 genes in human tumors, a Salk team uncovered an enzyme responsible for suppressing a common and deadly lung cancer

LA JOLLA--Scientists at the Salk Institute have uncovered a molecule whose mutation leads to the aggressive growth of a common and deadly type of lung cancer in humans.

This enzyme, called EphA2, normally polices a gene responsible for tissue growth. But when EphA2 is mutated, the Salk team discovered, cellular systems can run amok and quickly develop tumors. The new work, published the week of November 2, 2015 in PNAS, suggests that EphA2 could be a new target for a subset of lung cancer, which affects nonsmokers as well as smokers, and is the leading cause of cancer-related deaths worldwide.

"Sometimes there are hundreds of mutations in the genes of a patient's tumors, but you don't know whether they are drivers of the disease or byproducts," says senior author Inder Verma, professor of genetics and holder of Salk's Irwin and Joan Jacobs Chair in Exemplary Life Science. "We found a new way by which to identify cancer suppressor genes and understand how they could be targeted for therapies."

Two gene mutations in particular are known to spur the growth of human tumors: KRAS and p53. Though both genes have been heavily studied, they are difficult to therapeutically target, so the Salk team decided to look at genes that might police KRAS and p53 instead.

The researchers narrowed in on the 4,700 genes in the human genome related to cellular signaling--specifically, genes that have the ability to tamp down cell growth and proliferation. Then the team adapted a genetic screening technique to quickly and efficiently test the effect of these thousands of genes on tumor development. In animal models, the Salk team found that 16 of these cell-signaling genes produced molecules that had a significant effect on KRAS- and p53-related tumors.

Of these 16 molecules, one especially stood out: the EphA2 enzyme, originally discovered in the lab of another Salk scientist, Tony Hunter. Previously, EphA2's significance in lung cancer was unclear, but the team discovered that its absence let KRAS-associated tumors grow much more aggressively.

"With a mutation in KRAS, a tumor forms in 300 days. But without EphA2, the KRAS mutation leads to tumors in half the time, 120 to 150 days," says Verma, who is also an American Cancer Society Professor of Molecular Biology. "This molecule EphA2 is having a huge effect on restraining cancer growth when KRAS is mutated." Mutated KRAS is a common culprit in approximately 10 to 20 percent of all cancers, particularly colon cancer and human lung cancer.

"Since activating EphA2 led to the suppression of both cell signaling and cell proliferation, we believe that the enzyme might serve as a potential drug target in KRAS-dependent lung adenocarcinoma," says Narayana Yeddula, a Salk research associate and first author of the paper.

A 10-year national project called the Cancer Genome Atlas mapped the genomes of hundreds of patients for over 20 different cancers and uncovered a number of related genetic mutations, though the role of these mutations has not been well understood in lung cancer (especially adenocarcinoma, which makes up almost a quarter of all lung cancers). From the Cancer Genome Atlas data, the Salk team found that genetic alterations of EphA2 were detected in 54 out of 230 patients with adenocarcinoma. The team also found, surprisingly, that the loss of EphA2 activated a pathway commonly associated with cancer (dubbed Hedgehog) that promotes tumor growth.

"Oddly, among human lung cancer patients with EphA2 mutations, around 8 percent of patients actually have high EphA2 expression. So, in some instances, EphA2 is not suppressing tumors and may be context-dependent. Therefore, we need to carefully evaluate the molecule's function when designing new therapeutics," adds Yifeng Xia, a Salk staff researcher involved in the work.

Other authors on the paper were Eugene Ke of the Salk Institute and Joep Beumer of the Salk Institute and the Hubrecht Institute in the Netherlands.

This work was supported in part by an NIH grant, a Salk Cancer Center Core grant, Ipsen, the H.N. and Frances C. Berger Foundation, and the Leona M. and Harry B. Helmsley Charitable Trust.

http://bit.ly/1kcJhYU

Molten metal storms rage on orphan planet that lost its star

We just found weather on a lost world. Changes in the brightness of a planet adrift in space could be caused by clouds of molten metal passing in and out of view.

The starless planet, PSO J318.5-22, was discovered in the Pan-STARRS survey in 2013. At about eight times the mass of Jupiter, it's much more like the giant planets we see orbiting other stars than the small, failed stars called brown dwarfs.

That means it probably formed around a star and was somehow shot out of its orbit into lonely deep space (see artist's impression, above). That also makes this planet much easier to study than those that are almost lost in the dazzle from the stars they circle.

MPIA/V. Ch. Quetz

"You have to work really hard to even see them, whereas this object is just by itself," says Beth Biller at the University of Edinburgh, UK. Biller's team measured the planet's brightness and found that it could vary by up to 10 per cent in just a few hours. The explanation, they say, could lie in its weather systems.

Stormy spots

"If you think about the Great Red Spot on Jupiter, it would be stormy spots like that," Biller says. Both worlds have similar rotation periods: 10 hours for Jupiter, and between 5 and 10 hours for the lone planet.

But unlike Jupiter, which has cooled from a hot start over the long life of our solar system, this planet retains a scorching surface temperature of about 1100 kelvin – maintained by internal heat since it has no star.

Those conditions mean that any clouds it has should be molten, containing liquid metals where on Earth we would have water. "These are likely hot silicates and iron droplet clouds," Biller says. "This makes Venus look like a nice place."

Caroline Morley, who models exoplanet atmospheres at the University of California, Santa Cruz, thinks the finding may mean that similar planets – whether orbiting stars or not – might show the same behaviour. "It strongly suggests that these objects should be variable [in brightness]," Morley says. "We really want to be able to look at this variability and then connect it to storm systems."

Biller's team is already trying to tease out a similar analysis from observations of a star called HR 8799, which has planets closely resembling this lone world.

That makes this an exciting time to be looking for exo-weather, Morley says. "People have been saying for years that we [should] look at brown dwarfs because they're like planets, and we can make these connections," she says. "But now we're actually starting to do that." *Reference: arxiv.org/abs/1510.07625*

http://bit.ly/1PpBGSf

Russia Wants to Send Monkeys to Mars and Women to the Moon

The Russian space agency has announced plans for space missions through 2029

By Danny Lewis

It looks like the space race is back on. Over the last few months, space agencies around the world have announced plans to send all sorts of missions back to the Moon and out towards Mars. Now Russia is getting in on the game, announcing a timeline of operations spanning the next 15 years that includes sending trained monkeys to Mars in 2017 and testing a women-only crew for a future Moon mission in 2029.

Roscosmos, the Russian space agency, has had a busy few weeks, first announcing a new partnership with the European Space Agency to send a lunar rover to search for water at the Moon's south pole by 2020. But now, Roscosmos has announced it wants to go a bit further first by sending a team of trained rhesus monkeys to the red planet, Julienne Roman reports for *Tech Times*. Right now, a squad of future monkey cosmonauts are training three hours a day at the Institute of Biomedical Problems in Moscow, learning how to operate controls and solve simple math problems. "What we are trying to do is to make them as intelligent as possible so we can use them to explore space beyond our orbit," lead trainer Inessa Kozlovskaya tells Victoria Woollaston for *The Daily Mail*.

Scientists prize rhesus monkeys for their intelligence and because they can live for up to 25 years, Kozlovskaya and her team hope that their furry students will quickly learn how to survive a six-month-long mission to Mars. She also hopes that their current students will be able to recruit other monkeys to their squad and pass along what they learn from the scientists.

Russian scientists are training rhesus monkeys like these for a mission to Mars in 2017.
Martin Siepmann/imageBROKER/Corbis

It's no secret that animals have a long and deadly connection to the early days of spaceflight. To see if they could survive the journey, scientists sent a menagerie into space—fruit flies, mice, chimps and dogs to name a few.

The first monkey in space was named Albert II, who blasted 83 miles above the ground in an American-built V-2 rocket on June 4, 1949. He survived leaving the atmosphere, but died during the return trip to Earth when his parachute failed. It wasn't until 10 years later that a pair of monkeys named Abel and Baker became the first animals to return from space alive, Karl Tate wrote for Space.com in 2013.

While Kozlovskaya works on training her monkeys for Mars, a crew of six Russian women are spending this week locked inside a mock spaceship to see how well a team of all-female astronauts might handle the upcoming Moon mission in 2029. The test spaceflight is the first of its kind to study a crew entirely made up of women, Shaun Walker reports for *The Guardian*:

The experiment is expected to be psychologically taxing, but is less daunting by far than another experiment launched in 2010 in Moscow to simulate a potential mission to Mars. That saw six male volunteers spend 520 days in a capsule. A similar mixed-sex experiment in 2000 ended in disaster when two male crew members got into a fight and one tried to kiss a female crew member.

The six women will be released from their mock capsule next Thursday. If successful, they could be on the path to becoming the first women to walk on the Moon, following in the footsteps of Valentina Tereshkova, the Soviet cosmonaut who became the first woman to travel through space.

http://bit.ly/1RXQTZR

The Spice That Built Venice

The story of an import so prized, royals were literally rolling in it

By Jack Turner

In the year 1173 a bankrupt Venetian merchant by the name of Romano Mairano went looking for a way out of financial ruin.

Over a trading career spanning several decades, Mairano had seen his share of ups and downs—latterly, more downs than ups. He could count himself lucky to be alive: Two years earlier, he had escaped a massacre of his compatriots in Constantinople, fleeing as his ships and goods were burned or confiscated.

Scores of different spices, including these colorful peppercorns, are available at the Drogheria Mascari, a family-owned store that opened on the Ruga dei Spezieri ("street of the spice merchants") in Venice in 1948. **(Fabrizio Giraldi)**

Back in Venice, safe but not sound—at least not in any financial sense—he was desperate. He decided to orchestrate a risky trade that could help him pay off his loans and restore his wealth, a trade for one of the most valuable commodities of the day: pepper.

Discover Venice anew, from its rich history and many cultural quirks to its delightful, present-day customs and excursions.

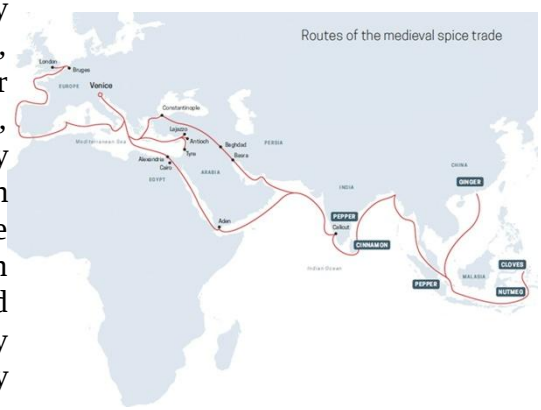
Mairano was bold but not crazy. Such schemes had enriched Venetian merchants for generations. Since well before the millennium, his forebears had sailed to Alexandria, the ancient Egyptian trading town at the head of the Nile Delta.

By virtue of its access to the Red Sea trade routes leading to Arabia and beyond, Alexandria was the chief entrepôt between East and West, the point where fine luxuries such as silks, perfumes, gems, and, above all, spices arrived from the most remote parts of Asia. For the Venetian merchant courageous or lucky enough, Alexandria was the gateway to riches.

But if the rewards were great, so too were the dangers. Merchants ran the risk of attacks by pirates, and they were at the mercy of the volatile, violent politics of the age. No insurer backed their cargoes; no coast guard patrolled the seas. They had to outmaneuver Venice's perennial enemies and competitors, the Genoese. And Mairano would be doing business in a Muslim country nominally at war with Europe—its ruler none other than Saladin, who would later defeat the Crusaders.

On this occasion, the gods of commerce smiled on Mairano. With money borrowed from a wealthy friend, he shipped a cargo of lumber to Alexandria, and in return he brought back spices. He was finally able to repay his creditors—not in cash, but in pepper. The remainder of the spices he sold in Venice at many times the purchase price.

To understand how Venice became such a glorious city, it pays to look south and east, just as Mairano did. Over the course of a long career, Mairano, like countless other traders, had a stake in many deals: for timber, slaves, textiles, wine, ships, grain, metals, and more. But for reasons of simple economic alchemy, spices were the marquee good. As they moved between the jungles of South and Southeast Asia, where they were harvested, to their final points of sale in Europe, the value of spices mounted exponentially. They were small, readily transferable, durable—and immensely desirable.



Spices harvested in the jungles of Asia were a symbol of wealth and status in medieval Europe. As often as not, the pepper that appeared on a king's table was sold at some point by a Venetian trader. **(David Griffin)**

Medieval high society had an insatiable appetite for spiced sauces, sweets, wine, and ale—not, as was long believed, to cover the taste of old and rotting meat, for spices were far too expensive for that. No less than in our day—indeed far more so, given the acutely hierarchical nature of medieval life—eating was as much about making an impression as enjoying flavor. And of all the spices, pepper was far and away the most important, for its consumers and Venice alike.

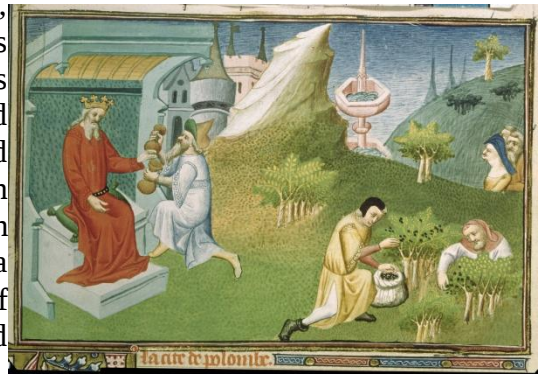
In Mairano's era, Venetian traders in London sold a pound of pepper for a sum equivalent to a week's work for an unskilled laborer. Cost alone ensured that pepper was as much an attribute of high rank as castles and coats of arms. Kings and wealthy prelates cured their ailments with pepper. They carried peppery pomanders to ward off pestilence, and went to their graves embalmed in myrrh and pepper.

The most eminent medical authorities of the time insisted that pepper could revive flagging libidos. Around the year 1100, one Duke William of Aquitaine boasted of a week-long ménage à trois, claiming his exertions (188, no less) were fueled by a hearty dose of the spice.

Once spices arrived in Venice, they were unloaded for distribution across Europe. Some were resold directly to merchants arriving from the north. Others were shipped on barges up the Po Valley, and carried on mules across the Alpine passes to Germany and France. Venetian galleys sailed past the Strait of Gibraltar and onward to London and Bruges.

As often as not, the cinnamon in a duke's pomander or the ginger in an abbot's medicine chest or the pepper appearing on a king's table was at some point freighted and sold by a Venetian.

As with any successful business, location was key. By virtue of Venice's ties to Byzantium, from the city's earliest days Venetian merchants had had privileged access to the overland trade routes to Asia. When the French saint Gerald of Aurillac passed through the northern Italian town of Pavia around 894, he met a small group of Venetian merchants selling cloths and spices from Byzantium.



A king is offered the fruits of a pepper harvest in this 15th-century illustration. **(From the Livre des Merveilles du Monde, Bibliothèque Nationale, Paris, Bridgeman Images)**

In due course Byzantium's energies faltered, and the relationship with Venice became increasingly hostile. By the year 1000, Venice opened another route to the Orient by concluding treaties with the Muslim rulers of Egypt and the Levant, safeguarding the position of its merchants in Islamic lands.

As the medieval European economy grew, the spice trade grew with it. The largely ad hoc voyages of Mairano's day gave way to a regular system of convoys known as the *muda*, or state-subsidized galleys auctioned out to the highest bidder. No spices were allowed in the cogs, round ships, or carracks that were the workhorses of maritime trade. Rather, they were whisked across the sea in armed fleets carrying up to 300 metric tons of spice, defended by a contingent of marines, and sped on their way by banks of rowers, swift enough to outrun any pursuer.

Pirates and other raiders were not the only obstacles, however. Venice's dealings with Muslim rulers sat uneasily with the Roman Catholic powers of Europe and particularly the papacy, which remained, with varying degrees of ardor, wedded to the ideal, if not necessarily the practice, of Crusade.

So it was that in 1322 a papal envoy arrived with the news that many of Venice's leading citizens had been excommunicated as punishment for having violated papal bans on trading with the infidel.

The sequel to this story nicely illustrates the Venetians' gift for navigating the tricky shoals of religion, geopolitics, and finance. While vigorously protesting the excommunication, the signoria complied with the papal diktat, halting direct voyages to Alexandria. Yet trade was simply diverted to the Armenian port of Lajazzo, a tiny Christian enclave tucked into the angle formed by Anatolia and the Levantine coast. Here the Venetians could acquire the very same spices they had previously purchased directly from the sultan, knowing full well that Lajazzo's spices had been subjected to the same taxes, tolls, and levies imposed by the region's Islamic rulers. No matter. Any moral peril was neatly transferred to the Armenians.

Business was business, and Venice's papal problem was neatly defused. In due course, a few decades after the pope's envoy had dropped his bombshell, the Venetian galleys were once again loading their precious cargoes of spice at Alexandria. No one was seriously inconvenienced—no one, that is, beyond Europe's consumers, who for a time paid a little more for their pepper.

At the Drogheria Mascari, aromatics are kept in special drawers to preserve their fragrance. **(Fabrizio Giraldi)**

Bad news came in 1501, however, when word reached Venetian merchants that the Portuguese navigator Vasco da Gama had sailed around Africa to India, bypassing the Mediterranean and—so it was feared—diverting the flow of pepper away from Venice. As it happened, it would be another century or so before the rivers of spice would finally run dry, during which time the city became increasingly forgetful of the traffic that had once bankrolled its beauty. In some of the majestic, sun-drenched canvases of Canaletto, you might glimpse merchant galleys in the background, but the 18th-century painter showed no interest in the cargo they bore.

Yet even today in one of the city's bakeries you might find a *peverino*, a type of peppered cookie, relative of the better-known *panpepato* and *panforte*—spiced, honeyed confections that date to the Middle Ages. Or take a walk down the elegant colonnades of the Ruga dei Spezieri, the "street of the spice merchants." There in the bustling market, among the tourists and Venetian vendors happily pocketing their money, you may hear the faintest of echoes of the commercial energies that once helped build a glorious city.

http://bit.ly/1RXQTZR

Rice was domesticated three times across Asia, not once in China

So good, they tamed it thrice?

New evidence suggests that sticky rice hails from southern China, but that other modern types like basmati can trace their history back to two other domestication events, one in the shadow of the Himalayas and the other in the Indian subcontinent.

The claim challenges the favoured theory of Asian rice's origins – that it was domesticated in China's Yangtze Valley. It was thought that this gave rise to all the modern varieties of *Oryza sativa* we eat today.

Now Peter Civáň of the University of Manchester, UK, and his team are challenging this theory. By comparing DNA from 1083 varieties of modern rice with 446 samples of wild rice taken from all over southern Asia, they have traced the plant's history back to three distinct types of rice.

The sticky variety, favoured in Japan, belongs to the *japonica* group, which the team traced back to the middle of the Yangtze Valley in southern China. Other research has traced this as the single ancestor of all of today's *O. sativa* rice varieties, but the team identified two further origins.

The team traced the *indica* group of long, dry grains back to the Brahmaputra River valley which drains the Himalayas, while the *aus* group of drought-tolerant rice hails from the region that is now India and Bangladesh.

Rice rice baby

"We show that there were not one, not two, but three domestications of rice in Asia," says Civáň. "Aromatic varieties, like basmati, arose out of hybrids between *japonica* and *aus* rice."

The work places the domestication events between 9000 and 10,000 years ago, but we do not know whether hunter-gatherers or early farmers were responsible for each case.

"It shows that the question of the domestication history of rice remains open, with different approaches reaching different conclusions," says Michael Purugganan of New York University, whose team proposed in 2011 that rice was domesticated only once. He argues that the regions of DNA that were analysed by Civáň's team might present a distorted history of the plant, and that studying more neutral genetic stretches may tell a different story.

"Our knowledge is never definitive," says Civáň, whose team is hoping to identify gene variants that could make new tastier and hardier varieties of cultivated rice.

"It will be interesting to see if other types of genetic data confirm our conclusions or provide even deeper insights into rice's domestication history," he says.

Journal reference: Nature Plants, DOI: 10.1038/nplants.2015.164

http://www.bbc.com/news/health-34697408

Pet dogs 'may help children avoid asthma'

Young children who have a pet dog in the home are less likely to go on to develop asthma, a large Swedish study has found.

By Michelle Roberts Health editor, BBC News online

Exposure to a dog in the first year of life was linked to a 13% lower risk of asthma in later childhood among the 650,000 children the authors tracked. The findings, in JAMA Pediatrics, support the idea that pets can bolster the immune system and prevent allergy. More evidence is still needed - past studies have found conflicting results. Certainly, for a child who is already allergic to dogs, buying a puppy would not be a good idea, say the Swedish researchers.

Man's best friend?

Pets are a common cause of allergy, with half of all asthmatic children allergic to cats and 40% allergic to dogs, according to the charity Allergy UK. When animals groom themselves, they lick. Skin cells covered in saliva - animal dander - are shed along with loose fur. It's the dander to which some people become sensitised.

The findings of this latest study suggest exposure to dog dander in infancy might actually be beneficial. Children who had grown up with a dog in their home were less likely to have asthma at the age of seven than children without dogs. Living on a farm with lots of animals seemed to confer even more protection, cutting the risk of asthma by about 50%.

Lead scientist Prof Tove Fall, from Uppsala University in Sweden, said: "Our results confirmed the farming effect and we also saw that children who grew up with dogs had about 15% less asthma than children without dogs."

She said this fits with the hygiene hypothesis which favours exposure to dust and dirt to improve our tolerance of common allergens. The findings should also provide some reassurance for parents. "That's important information for parents who are pregnant or are planning to have a baby, that they should not worry about getting a dog or a puppy if they would like to. "But if you have an allergic child you should not get a dog to cure your child. It won't work and will probably make the allergy worse."

If you are allergic and live with pets, there are things you can do to cut your risk of having an allergic reaction.

Asthma UK advises:

Try to keep pets out of your bedroom and where possible living area

Regular grooming and bathing of cats and dogs can help

You could try using air filters and an efficient vacuum cleaner. This might be helpful for people who have cat allergies; however the evidence on the benefit of these remains unclear

No breed of dog is completely "non-allergic" because they all shed dander

Amena Warner of Allergy UK said: "There have been a few studies that have alluded to this but not such a longitudinal study with so many children so from that point of view this is quite a powerful study. It's very welcome." Erika Kennington of Asthma UK, said more research was needed to better understand the effects so that it could be turned into practical advice for parents of young children.

http://nyti.ms/1OqT2iQ

Death Rates Rising for Middle-Aged White Americans, Study Finds

Something startling is happening to middle-aged white Americans. Unlike every other age group, unlike every other racial and ethnic group, unlike their counterparts in other rich countries, death rates in this group have been rising, not falling.

By GINA KOLATA NOV. 2, 2015

That finding was reported Monday by two Princeton economists, Angus Deaton, who last month won the 2015 Nobel Memorial Prize in Economic Science, and Anne Case. Analyzing health and mortality data from the Centers for Disease Control and Prevention and from other sources, they concluded that rising annual death rates among this group are being driven not by the big killers like heart disease and diabetes but by an epidemic of suicides and afflictions stemming from substance abuse: alcoholic liver disease and overdoses of heroin and prescription opioids.

Angus Deaton with his wife, Anne Case, right, last month after he won the 2015 Nobel Memorial Prize in Economic Science. Together, they wrote a study analyzing mortality rates. **Ben Solomon for The New York Times**

The analysis by Dr. Deaton and Dr. Case may offer the most rigorous evidence to date of both the causes and implications of a development that has been puzzling demographers in recent years: the declining health and fortunes of poorly educated American whites. In middle age, they are dying at such a high rate that they are increasing the death rate for the entire group of middle-aged white Americans, Dr. Deaton and Dr. Case found.

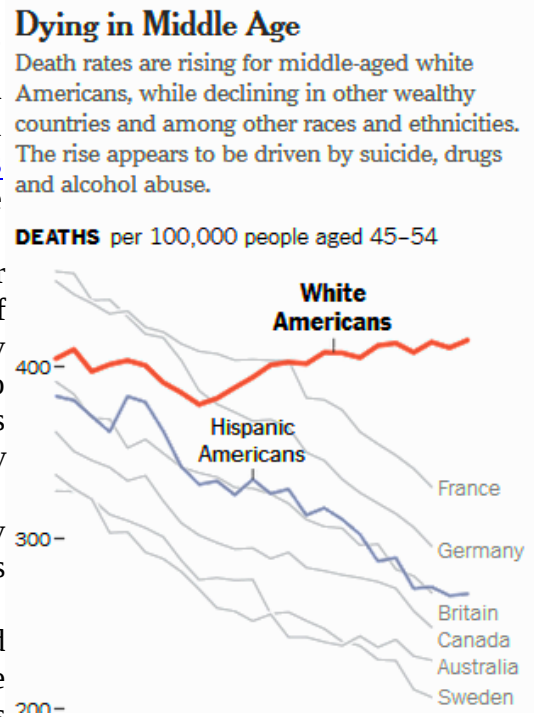
The mortality rate for whites 45 to 54 years old with no more than a high school education increased by 134 deaths per 100,000 people from 1999 to 2014.

"It is difficult to find modern settings with survival losses of this magnitude," wrote two Dartmouth economists, Ellen Meara and Jonathan S. Skinner, in a commentary to the Deaton-Case analysis to be published in Proceedings of the National Academy of Sciences.

"Wow," said Samuel Preston, a professor of sociology at the University of Pennsylvania and an expert on mortality trends and the health of populations, who was not involved in the research. "This is a vivid indication that something is awry in these American households."

Dr. Deaton had but one parallel. "Only H.I.V./AIDS in contemporary times has done anything like this," he said.

In contrast, the death rate for middle-aged blacks and Hispanics continued to decline during the same period, as did death rates for younger and older people of all races and ethnic groups. Middle-aged blacks still have a higher mortality rate than whites — 581 per 100,000, compared with 415 for whites — but the gap is closing, and the rate for middle-aged Hispanics is far lower than for middle-aged whites at 262 per 100,000.



David M. Cutler, a Harvard health care economist, said that although it was known that people were dying from causes like opioid addiction, the thought was that those deaths were just blips in the health care statistics and that over all everyone's health was improving. The new paper, he said, "shows those blips are more like incoming missiles." Death rates are rising for middle-aged white Americans, while declining in other wealthy countries and among other races and ethnicities. The rise appears to be driven by suicide, drugs and alcohol abuse.

Dr. Deaton and Dr. Case (who are husband and wife) say they stumbled on their finding by accident, looking at a variety of national data sets on mortality rates and federal surveys that asked people about their levels of pain, disability and general ill health.

Dr. Deaton was looking at statistics on suicide and happiness, skeptical about whether states with a high happiness level have a low suicide rate. (They do not, he discovered; in fact, the opposite is true.) Dr. Case was interested in poor health,

including chronic pain because she has suffered for 12 years from disabling and untreatable lower back pain.

Dr. Deaton noticed in national data sets that middle-aged whites were committing suicide at an unprecedented rate and that the all-cause mortality in this group was rising. But suicides alone, he and Dr. Case realized, were not enough to push up overall death rates, so they began looking at other causes of death. That led them to the discovery that deaths from drug and alcohol poisoning also increased in this group.

They concluded that taken together, suicides, drugs and alcohol explained the overall increase in deaths. The effect was largely confined to people with a high school education or less. In that group, death rates rose by 22 percent while they actually fell for those with a college education.

It is not clear why only middle-aged whites had such a rise in their mortality rates. Dr. Meara and Dr. Skinner, in their commentary, considered a variety of explanations — including a pronounced racial difference in the prescription of opioid drugs and their misuse, and a more pessimistic outlook among whites about their financial futures – but they say they cannot fully account for the effect.

Dr. Case, investigating indicators of poor health, discovered that middle-aged people, unlike the young and unlike the elderly, were reporting more pain in recent years than in the past. A third in this group reported they had chronic joint pain over the years 2011 to 2013, and one in seven said they had sciatica. Those with the least education reported the most pain and the worst general health.

The least educated also had the most financial distress, Dr. Meara and Dr. Skinner noted in their commentary. In the period examined by Dr. Deaton and Dr. Case, the inflation-adjusted income for households headed by a high school graduate fell by 19 percent.

Dr. Case found that the number of whites with mental illnesses and the number reporting they had difficulty socializing increased in tandem. Along with that, increasing numbers of middle-aged whites said they were unable to work. She also saw matching increases in the numbers reporting pain and the numbers reporting difficulty socializing, difficulty shopping, difficulty walking for two blocks.

With the pain and mental distress data, Dr. Deaton said, “we had the two halves of the story.” Increases in mortality rates in middle-aged whites rose in parallel with their increasing reports of pain, poor health and distress, he explained. They provided a rationale for the increase in deaths from substance abuse and suicides.

Dr. Preston of the University of Pennsylvania noted that the National Academy of Sciences had published two monographs reporting that the United States had fallen behind other rich countries in improvements in life expectancy. One was on mortality below age 50 and the other on mortality above age 50. He coedited one of those reports. But, he said, because of the age divisions, the researchers analyzing the data missed what Dr. Deaton and Dr. Case found hiding in plain sight. “We didn’t pick it up,” Dr. Preston said, referring to the increasing mortality rates among middle-aged whites.

Ronald D. Lee, professor of economics, professor of demography and director of the Center on Economics and Demography of Aging at the University of California, Berkeley, was among those taken aback by what Dr. Deaton and Dr. Case discovered.

“Seldom have I felt as affected by a paper,” he said. “It seems so sad.”

http://www.eurekalert.org/pub_releases/2015-11/agu-scl110315.php

Some chemicals less damaging to ozone can degrade to long-lived greenhouse gas

Some substitutes for ozone-damaging chemicals being phased out worldwide under international agreements are themselves potent greenhouse gases and contribute to warming.

WASHINGTON, DC -- Now, a new study published Nov. 2 in Geophysical Research Letters, a publication of the American Geophysical Union, shows for the first time how some of those replacement chemicals can break down in the atmosphere to form a greenhouse gas that can persist for millennia, much longer than the substitute chemicals themselves.

Specifically, when some chemicals widely used as refrigerants break down in the stratosphere -- a layer in the middle atmosphere -- under some conditions, they can form a potent greenhouse gas that lasts for up to 50,000 years, according to scientists from the Cooperative Institute for Research in Environmental Sciences (CIRES) at the University of Colorado Boulder and the NOAA Earth System Research Laboratory (ESRL) in Boulder.

"This compound, carbon tetrafluoride or CF_4, essentially lasts forever because there aren't any known removal mechanisms in the atmosphere," said James Burkholder, a research chemist at NOAA ESRL and lead author of the study.

Burkholder's colleague Aaron Jubb, a CIRES scientist working at NOAA ESRL and now at Oak Ridge National Laboratory, did the laboratory work showing how CF_4 can be made from some halocarbons, chemicals that include hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) and are substitutes for the more ozone-damaging chemicals that have largely been phased out. Jubb started with trifluoroacetyl fluoride -- a compound produced in the atmosphere when some halocarbons breaks down -- exposed it to short-

wavelength UV radiation, and looked at the reaction products that formed. CF_4 was one of those breakdown products.

The amount of CF_4 produced by this photochemical process was shown to be a small fraction of atmospheric CF_4; industrial sources are much larger emitters of CF_4. Still, identifying this particular source of such a potent and lasting greenhouse gas is important, particularly since its production could continue to grow depending on which "parent" products are used by industry.

"We really need to understand the chemistry of the compounds we use," Jubb said. "Even as we move towards shorter-lived halocarbons for industrial use, during atmospheric degradation they can produce a long-lived atmospheric effect."

This work was supported in part by NOAA's Atmospheric Chemistry, Carbon Cycle, and Climate (AC4) Program and NASA's Atmospheric Composition Program.

Authors of "An atmospheric photochemical source of the persistent greenhouse gas CF4" are Aaron Jubb (Cooperative Institute for Research in Environmental Sciences and NOAA Earth System Research Laboratory (ESRL) Chemical Sciences Division, now at Oak Ridge National Laboratory), Max McGillen (Cooperative Institute for Research in Environmental Sciences and NOAA ESRL Chemical Sciences Division), Robert W. Portmann (NOAA ESRL Chemical Sciences Division), John S. Daniel (NOAA ESRL Chemical Sciences Division), and James B. Burkholder (NOAA ESRL Chemical Sciences Division).

CIRES is a partnership of NOAA and CU-Boulder.

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http://www.eurekalert.org/pub_releases/2015-11/thuo-amb110315.php

Alzheimer's may be a collection of diseases that should be treated separately

'It is essential to carefully characterize and classify the mechanisms that underlie Alzheimer's disease, in order to allow for the development of novel therapies that can be prescribed according to the patient's relevant disease sub-type.'

Deciphering the mechanism that underlies the development of Alzheimer's disease in certain families but not in others, researchers at the Hebrew University of Jerusalem's Faculty of Medicine have proposed that the malady is actually a collection of diseases that probably should be treated with a variety of different approaches.

Neurodegenerative diseases are incurable and debilitating conditions that result in degeneration or death of cells in the nervous system. Conditions such as prion disorders (the most famous of which is "Mad Cow Disease"), Alzheimer's Disease and Parkinson's Disease share two key features: they emerge as a result of aberrant protein folding and aggregation, and their onset is late in life. These maladies emerge either sporadically or as familial, mutation-linked illnesses (certain prion disease can be also infectious).

Most sporadic cases are diagnosed during the patient's seventh decade of life or later, while familial cases typically manifest during the fifth or sixth decade. Despite their relative rareness, mutation-linked cases are very important, as they provide hints that can help decipher the mechanisms that underlie the development of the disease.

The late onset feature typical to distinct neurodegenerative diseases, and the common temporal emergence patterns of these maladies, raise key questions: first, why do individuals who carry disease-linked mutation show no clinical signs until their fifth or sixth decade of life? In addition, why do apparently distinct disorders share a common temporal emergence pattern?

One possible explanation is that as people age, the efficiency of the mechanisms that protect younger people from the toxic aggregation of proteins declines, thus exposing them to disease. Indeed, previous studies clearly indicate that the aging process plays key roles in enabling neurodegenerative disorders to onset late in life.

These finding raised the question of what mechanisms are negatively regulated by aging, allowing the emergence of neurodegeneration in the elderly.

Since neurodegenerative disorders stem from aberrant protein folding, an international research team, led by Prof. Ehud Cohen and Dr. Tziona Ben-Gedalya at The Institute for Medical Research Israel - Canada (IMRIC) in the Hebrew University's Faculty of Medicine, postulated that an aging-associated decline in the activity of proteins that assist other proteins to fold properly, may be one mechanism that exposes the elderly to neurodegeneration.

To identify such mechanisms, they searched for similar mutational patterns in different proteins that are linked to the development of distinct neurodegenerative disorders. Their research showed that the development of Alzheimer's disease in certain families, and of a familial prion disorder in other families, originate from very similar mutational patterns.

Based on this discovery, they identified that the malfunction of the protein "cyclophilin B," which helps nascent proteins to attain their proper spatial

structures, is responsible for the manifestation of both maladies. They also comprehensively characterized the mechanism that underlies the development of Alzheimer's disease in individuals who carry these mutations, and found that it has no relevance to the emergence of the disease in patients who carry other Alzheimer's-linked mutations.

According to Prof. Ehud Cohen: "This study provides important new insights: first, it shows that the development of distinct neurodegenerative disorders stems from a similar mechanism. More importantly, it indicates that Alzheimer's disease can emanate from more than one mechanism, suggesting that it is actually a collection of diseases that should be classified."

The new insights derived from this study may reinforce the efforts to develop novel therapies to the different subtypes of Alzheimer's disease, providing new hope to those who suffer from this incurable disorder and to their families.

Prof. Ehud Cohen added: "Our study proposes that the failure to develop efficient Alzheimer's therapy emanates from the pooling, in clinical experiments, of patients who suffer from distinct disorders that eventually lead to Alzheimer's symptoms. Therefore it is essential to carefully characterize and classify the mechanisms that underlie Alzheimer's disease, in order to allow for the development of novel therapies that can be prescribed to the individual patient according to their relevant disease subtype."

The paper's co-authors include researchers at the Institute for Dental Sciences, Faculty of Dental Medicine, Hebrew University of Jerusalem; Dept. of Physiology and Pharmacology at the Sackler Faculty of Medicine at Tel Aviv University; Dept. of Biochemistry and Molecular Biology, Wise Faculty of Life Sciences, Tel Aviv University; and Bone and Extracellular Matrix Branch, NICHD, National Institutes of Health (NIH), USA.

The study was supported by the Rosalinde and Arthur Gilbert Foundation (AFAR), the European Research Council, the National Institute for Psychobiology in Israel (NIPI), and the Israel Science Foundation.

http://www.eurekalert.org/pub_releases/2015-11/uovh-blm110315.php

Baffling lab mystery leads to potential new anemia treatment

Researchers can trigger production of oxygen-carrying cells on demand

A bizarre result of a routine lab experiment has led researchers at the University of Virginia School of Medicine to an unexpected new way to trigger the production of red blood cells. This could represent a significant step forward in the battle against anemia, benefitting people with diabetes, people with kidney disease or cancer, and older people for whom anemia can become a chronic problem.

While more work needs to be done before the method could be used in people, the possibilities are tantalizing. For example, the approach could:

allow doctors to turn on red blood cell production whenever necessary;

be used on the battlefield to triage wounded soldiers until they could receive a blood transfusion; and

be used to treat people who cannot receive blood transfusions because of religious beliefs.

About Anemia

People with anemia - the most common blood disorder - lack sufficient red blood cells, which transport oxygen. People with anemia often experience fatigue and lack energy because their cells aren't getting enough oxygen. There are many causes, including iron deficiency, vitamin deficiencies and diseases such as kidney disease and cancer. Anemia is particularly prevalent in older adults.

The UVA researchers, however, were not investigating anemia when they made their discovery. Instead, Thomas J. Braciale, MD, PhD, and his team members were looking into the role of dendritic cells in the lungs. Dendritic cells have traditionally been thought to be sensors of infection and inflammation, but a lab test involving the flu virus produced a bizarre effect in mice that ultimately revealed an entirely new aspect to the cells' function.

Strange Effect

After injecting mice with the flu virus and an antibody that blocked a certain molecule expressed by dendritic cells, the researchers discovered that the experiment had an unexpected effect: The mice's spleens enlarged massively. The researchers were baffled, so they repeated the experiment, only to get the same results.

"We did it again and I didn't believe it, and we did it again and I didn't believe it," Braciale recalled. "I asked whether you needed to flu infect the mice when you injected this antibody. So the postdoc [a lab member] did the experiment, and he just injected the antibody without flu injecting the mice. Giant spleens. After much consultation, after talking with my colleagues in Pathology, we decided we were inducing stress erythropoiesis."

Stress erythropoiesis is when the body produces red blood cells because of injury or other stress. In discovering an unexpected molecular trigger for the process, Braciale had found a switch he could flip to prompt red blood cell production.

"In the very basic way, what we've discovered is that the process of regulating stress in the body is mediated - certainly in part, at least - by these dendritic cells," he explained. "And stress can be a variety of different stresses. It doesn't have to be infection, it doesn't have to be inflammation. It can be anemia. It can be hemorrhage. And these cells act to initiate this response that, until this report, there's been really no evidence that these [dendritic] cells ever participate in making red blood cells."

Findings Published

Braciale has more work to do before researchers can begin testing the approach in people. However, he's optimistic, based on his findings so far. "We're very excited to see where this goes. We know that the same things can be done in humans in the following sense. There are mice called humanized mice. These are mice that are engineered so they have a human blood system. And if you inject these mice with this antibody, they'll make red blood cells." The discovery has been described in an article in the Journal of Clinical Investigation written by Taeg S. Kim, Mark Hanak, Paul C. Trampont and Braciale.

http://www.eurekalert.org/pub_releases/2015-11/mc-so1110315.php

Study: Only 1 in 5 US pancreatic cancer patients get this key blood test at diagnosis

CA 19-9 tumor marker test especially important for early-stage patients, Mayo finds

NAPA, Calif. -- Only 1 in 5 U.S. pancreatic cancer patients receive a widely available, inexpensive blood test at diagnosis that can help predict whether they are likely to have a better or worse outcome than average and guide treatment accordingly, a Mayo Clinic study shows. People who test positive for elevated levels of a particular tumor marker tend to do worse than others, but if they are candidates for surgery and have chemotherapy before their operations, this personalized treatment sequence eliminates the elevated biomarker's negative effect, researchers found. The findings will be presented at the Western Surgical Association annual meeting Nov. 7-10 in Napa.

"This is another argument for giving chemotherapy before surgery in all pancreatic cancer patients and ending the old practice of surgery followed by chemo," says senior author Mark Truty, M.D., a gastrointestinal surgical oncologist at Mayo Clinic in Rochester, Minn. "The study answers an important clinical question and applies to every pancreatic cancer patient being considered for surgery."

The Mayo study, which used the National Cancer Data Base, is the first on the subject based on national data and is the largest of its kind, Dr. Truty says.

Researchers analyzed outcomes for 97,000 patients. The tumor marker whose impact they studied is known as CA 19-9. It is associated with several cancers, including pancreatic cancer, and can be measured in the blood of most people: 10 percent do not produce it. Pancreatic cancer patients who didn't secrete CA 19-9 were also studied.

Pancreatic cancer patients whose blood showed higher-than-normal CA 19-9 levels tended to have worse outcomes than others at the same stage of cancer, the study found. Surprisingly, the elevated tumor marker's negative effect on survival was most pronounced in patients diagnosed at an early stage, the researchers wrote. "When we looked at how these patients did after surgical removal of their cancers, the only treatment sequence that completely eliminated the increased risk posed by CA 19-9 elevation was chemotherapy followed by surgical removal of the tumor," Dr. Truty says.

Another key finding was that only 19 percent of pancreatic cancer patients nationally have their CA 19-9 checked at diagnosis, far fewer than anticipated, he says. The CA 19-9 blood test has been standard for pancreatic cancer patients at Mayo Clinic for years. Failing to test for and address elevated CA 19-9 means that many patients with above-normal levels may undergo significant surgeries that may not be as beneficial long term as anticipated, Dr. Truty says.

About 50,000 people are diagnosed with pancreatic cancer each year in the U.S. Historically, only about 7 percent of pancreatic cancer patients have lived at least five years after diagnosis. But advances such as the CA 19-9 test and improved chemotherapy, radiation and surgical techniques are improving survival odds for many patients, Dr. Truty says.

"Our conclusion is that every patient should have a CA 19-9 test at diagnosis. This is a simple, cheap and widely available test that allows personalization of pancreatic cancer treatment," Dr. Truty says, noting that the test costs about $170 -- pennies on the dollar relative to the overall cost of a patient's cancer care. "Further, patients with any elevation of CA 19-9 should be considered for preoperative chemotherapy to eliminate this risk."

Mayo Clinic funded the study. The first author is Mayo Clinic resident John Bergquist, M.D., a physician and researcher.

http://www.eurekalert.org/pub_releases/2015-11/uok-eed110315.php

Endurance expert: Drugs could help 'lazy' people exercise

In what has been described as 'doping for lazy people' a Kent endurance expert advocates psychoactive drugs to encourage sedentary people to exercise

Endurance expert suggests drugs could help 'lazy people' exercise In what has been described as 'doping for lazy people' a University of Kent endurance expert has advocated the use of psychoactive drugs to encourage sedentary people to exercise.

Together with lack of time, physical exertion is one of the main perceived barriers to exercise. This is not surprising because humans evolved to be 'lazy', i.e. to conserve energy. Professor Samuele Marcora suggests that reducing perception of effort during exercise using caffeine or other psychoactive drugs (e.g. methylphenidate and modafinil) could help many people stick to their fitness plans.

Whilst acknowledging that such an intervention is both drastic and controversial, Professor Marcora points out that perception of effort is one of the main reasons why most people choose sedentary activities for their leisure time. Compared to watching television (zero effort), even moderate-intensity physical activities like walking require considerable effort. He says finding a way that makes people with very low motivation to do even moderate exercise, like walking, could be particularly useful. Similarly, a reduction in perception of effort would be very helpful to the many people who find exercise difficult because they are overweight and/or exercise after work in a state of mental fatigue.

Professor Marcora also states that whilst there is no strong ethical opposition to the use of psychoactive drugs to help quit smoking (nicotine) or treat obesity (appetite suppressants), the negative perception of doping in sport may prevent the use of stimulants and other psychoactive drugs to treat physical inactivity.

Given that physical inactivity is responsible for twice as many deaths as obesity, he hopes that psychopharmacological treatment for physical inactivity will be considered fairly and seriously rather than immediately rejected on the basis of unrelated ethical considerations about doping in sport.

Professor Samuele Marcora is Director of Research at the University of Kent's School of Sport and Exercise Sciences. His paper Can Doping be a Good Thing? Using Psychoactive Drugs to Facilitate Physical Activity Behaviour has been published in the journal Sports Medicine.

http://www.eurekalert.org/pub_releases/2015-11/uops-pmb110315.php

Penn Medicine: Brain's hippocampus is essential structure for all aspects of recognition memory

PHILADELPHIA - The hippocampus, a brain structure known to play a role in memory and spatial navigation, is essential to one's ability to recognize previously encountered events, objects, or people - a phenomenon known as recognition memory - according to new research from the departments of Neurosurgery and Psychology in the Perelman School of Medicine at the University of Pennsylvania. Their work is published in PNAS.

Recognition memory is composed of two processes: recollection, or recognizing something along with vivid details of the initial encounter; and familiarity, a general sense of having previously encountered something. These processes often break down as a result of aging, neurodegenerative disorders (e.g. Alzheimer's disease), or traumatic brain injury, and the new findings provide a roadmap to examine strategies to improve these functions.

"There has been a longstanding debate in the field of recognition memory about how the human hippocampus contributes to our ability to recognize," said lead author Maxwell Merkow, MD, Neurosurgery Chief Resident at the Hospital of the University of Pennsylvania. "One segment of the scientific literature contends that neural activity in the hippocampus only contributes to recollection, whereas some believe hippocampal activity supports both recollection and familiarity. Our study aimed to get to the bottom of this."

The Penn team hypothesized that the hippocampus supported both recollection and familiarity, the twin processes believed to underlie recognition memory. Showing a clear link between hippocampal activity and recognition memory performance in general has previously proven elusive, having been documented in just a few earlier studies. This paper is the first to also record a link between hippocampal activity and both the processes of recollection and familiarity.

Merkow and colleagues studied 66 patients who were already undergoing intracranial monitoring of their hippocampus for epilepsy. Using these direct electrical recordings, the team was able to test the level of high frequency neuronal activity (a marker of neurons firing) in this region, a very precise measure which captures activity tied to cognition processes lasting mere hundreds of milliseconds.

The team administered a memory task in which participants were shown and asked to remember a series of words. Patients were then tested by being shown a second series of words, some of which they had seen before, and some that were new. Patients had to determine whether or not each word had been part of the group they had learned initially. While all of this was going on, the team recorded electrical data directly from the patient's hippocampus.

They found elevated high frequency activity during those trials in which the patient correctly identified a word they had previously seen. This was opposed to lower activity during trials where they either failed to recognize an old word or in which they saw a new word, whether or not they correctly identified it as new.

Another major finding was that the strength of hippocampal activity predicted behavioral performance, thereby directly linking the hippocampus to recognition memory. Crucially, both the recollection and familiarity components of recognition correlated with hippocampal activity. These data show that the cognitive processes we use for recognition memory are both supported by actions within the hippocampus.

"This work directly addresses the issue of where in the brain recognition takes place," Merkow said. "We now need to focus our efforts on how these processes occur." The team plans to use the same high frequency recordings from smaller electrodes to answer this question. This work brings science one step closer to understanding how brain activity supports memory and potentially improving memory through future interventions.

Additional Penn authors include John F. Burke and Michael J. Kahana
This work was supported by the National Institutes of Health (MH055687)

http://www.eurekalert.org/pub_releases/2015-11/uobc-urt110315.php

UBC researchers transform humble blood cells into 'Franken-platelets'

Faculty of Medicine scientists have created a "Franken-platelet" - a supercharged blood cell - that might be capable of healing major wounds, busting clots or blocking inflammation.

Named for their disk-like shape, platelets stop bleeding by adhering to a rupture in blood vessels, plugging the hole, and secreting proteins that trigger the formation of blood clots. Despite their importance, platelets are relatively simple - unlike most cells, they lack a nucleus, and thus don't have DNA.

Assistant Professor Christian Kastrup, in the Department of Biochemistry and Molecular Biology and the Michael Smith Laboratories, and graduate students Vivienne Chan and Stefanie Novakowski injected platelets with DNA and other ingredients needed to make RNA - the crucial molecules that transform DNA's code into the multitude of proteins that carry out a cell's many activities.

The resulting RNA, the first-ever produced inside a platelet, didn't endow the cells with any new powers. But the RNA, when extracted from the platelets and immersed in a soup of cellular biochemicals, performed as predicted, producing proteins that glowed when exposed to certain types of light.

The experiments, described in an article this week in the German chemistry journal Angewandte Chemie International Edition, point the way to fortifying platelets with more useful genes. One possibility is making platelets even better at blood clotting. These supercharged platelets would be programmed to release more coagulation enzymes, enabling them to seal ruptures that would prove too large for normal platelets.

But the researchers' breakthrough also raises the possibility of endowing platelets with powers they don't currently have. For example, they could release RNA or proteins that decrease inflammation - the natural response by injured or infected tissues that, when unchecked, leads to such diseases as artherosclerosis or arthritis. Platelets might even be programmed to "go against type," releasing proteins that degrade clots near the heart or brain, where they can cause heart attacks or stroke.

"This technology could be used to make platelets that go beyond their present capabilities," says Dr. Kastrup, a member of the UBC Centre for Blood Research. "Platelets are a basic component of blood, so they make an excellent way to deliver therapies to people with uncontrollable internal bleeding, or inflammatory diseases, or dangerous clots. We've gotten platelets to make their own RNA; our next step is getting them to make therapeutic RNA, or therapeutic proteins."

http://www.eurekalert.org/pub_releases/2015-11/cp-ne102815.php

'Odometer neurons' encode distance traveled and elapsed time

Grid cells integrate information about time and distance to support memory and spatial navigation, even without visual landmarks

Animals navigate by calculating their current position based on how long and how far they have traveled and a new study on treadmill-running rats reveals how: neurons called grid cells integrate information about time and distance to support memory and spatial navigation, even in the absence of visual landmarks. The findings, published November 4 in the journal Neuron, challenge currently held views of the role of grid cells in the brain.

"Space and time are ever-present dimensions by which events can be organized in memory," says senior study author Howard Eichenbaum, a psychologist and neuroscientist at Boston University. "These findings support the view that memory evolved as a common function in mammals using circuits that organize events in space, time, and potentially many other dimensions of experience."

Past research has shown that grid cells receive information from other cells about the direction traveled. But until now, there was no direct evidence showing that grid cells signal distance or time, leaving its role in path integration merely speculative. In the new study, Eichenbaum and first author Benjamin Kraus of Boston University addressed this question by placing rats on treadmills while recording the activity of grid cells. The researchers kept either the run duration or distance fixed while varying the speed to disentangle the influence of these factors on cell firing.

During treadmill running, 92% of grid cells fired at specific moments or distances while the rats ran in place. For example, one cell would fire 8 seconds into the run, regardless of the speed or distance, while another cell would fire after the rat ran 400 centimeters, regardless of the speed or duration. About half of the cells were influenced by time, another half by distance, and 41% were affected by both time and distance.

"The major current view is that grid cells are dedicated to coding locations in space," Eichenbaum says. "Our findings reflect the discovery that, when location is held constant, grid cells also encode time and distance, suggesting a much broader role for the medial entorhinal cortex than solely mapping space."

In particular, the findings suggest that grid cells are capable of supporting path integration, even without visual cues such as landmarks and optic flow. However, the cells' grid patterns were larger and further spaced during treadmill running compared with foraging in an open field with a stable visual landmark. This observation suggests that visual information may help to calibrate the activity of grid cells to improve the accuracy of animals' spatial representation of their

environment. Moreover, the same time- and distance-keeping mechanism could be important for organizing the temporal flow of experiences in memory as well as that in spatial routes.

Eichenbaum believes the studies so far are just the beginning of explorations about how time information is represented in the memory system. "We need to understand how the hippocampus and entorhinal cortex interact to support memory for the flow of events. We need to know the sources of temporal information to this system. And we need to know how sequential events are linked to the representation of time," he says. "We believe that knowledge about the brain circuits that support memory will eventually lead to new directions for treatment or prevention of memory and cognitive disorders."

This work was supported by the National Institute of Mental Health and Office of Naval Research.

Neuron, Kraus et al.: "During running in place, grid cells integrate elapsed time and distance run" http://dx.doi.org/10.1016/j.neuron.2015.09.031

http://www.eurekalert.org/pub_releases/2015-11/acs-rdm103015.php

Requiring drug makers to take back unused pharmaceuticals

About $5 billion worth of unused prescription drugs get flushed down toilets, tossed in the trash or left in medicine cabinets across the U.S. each year.

These practices can contribute to a host of problems, including water pollution and drug abuse. To address these issues, some local governments are starting to intervene, according to an article in Chemical & Engineering News (C&EN), the weekly newsmagazine of the American Chemical Society.

Katharine Gammon, a contributing editor at C&EN, reports that medication that washes down the drain or ends up in landfills can wind up in rivers, streams and aquifers. This contamination could affect the health of wildlife and, ultimately, humans. As for prescriptions that sit unused in medicine cabinets, public health advocates say these drugs are in danger of getting into the wrong hands. Currently, national efforts to prevent these various scenarios involve one-day events during which people can drop off leftover drugs at police and sheriffs' stations. But, say some experts, these programs are not convenient, and many people feel anxious about turning in drugs to law enforcement.

In the absence of a more effective national approach to collecting pharmaceuticals, some local governments are crafting programs of their own. At least a few counties on the West Coast passed ordinances that require drug companies to install take-back containers at pharmacies and incinerate what they collect. The pharmaceutical industry mounted a legal challenge to the first rule passed in 2012 by Alameda County, California, but it was defeated. The county is now implementing its program, and more could be coming soon.

http://www.eurekalert.org/pub_releases/2015-11/uoq-sfm110315.php

Scarlet fever making a comeback

An international study led by University of Queensland (UQ) researchers has tracked the re-emergence of a childhood disease which had largely disappeared over the past 100 years.

Researchers at UQ's Australian Infectious Diseases Centre have used genome sequencing techniques to investigate a rise in the incidence of scarlet fever-causing bacteria and an increasing resistance to antibiotics.

UQ School of Chemistry and Molecular Biosciences researcher Professor Mark Walker said the disease had re-emerged in parts of Asia and the United Kingdom.

"We have not yet had an outbreak in Australia, but over the past five years there have been more than 5000 cases in Hong Kong (a 10-fold increase) and more than 100,000 cases in China.

"And an outbreak in the UK has resulted in 12,000 cases since last year," he said.

Scarlet fever, which mainly affects children under 10, is spread by Group A Streptococcus (strep throat bacteria) known as GAS. Symptoms include a red rash on the skin, sore throat, fever, headache and nausea. Serious illness can be treated with antibiotics.

UQ School of Chemistry and Molecular Biosciences researcher Dr Nouri Ben Zakour said the research results were "deeply concerning". "We now have a situation which may change the nature of the disease and make it resistant to broad-spectrum treatments normally prescribed for respiratory tract infections, such as in scarlet fever. She said penicillin continued to provide an excellent treatment for patients who were not allergic to it.

Dr Ben Zakour said the rise in scarlet fever could pre-empt a future rise in rheumatic heart disease, which causes permanent heart damage. "With this heightened awareness, we can now swiftly identify scarlet fever-associated bacteria and antibiotic resistance elements, and track the spread of scarlet fever-causing GAS strains," she said.

Dr Ben Zakour said the evolutionary forces driving the outbreaks were unknown, but bacterial causes, the immune status of people contracting scarlet fever, and environmental factors such as temperature and rainfall could all play a significant role. "Only a continued study of the patterns, causes and effects of health and diseases will determine the full impact these recent gene changes will have on the global GAS disease burden," she said.

The research, published in Scientific Reports, was conducted by Associate Professor Scott Beatson's microbial genomics group at UQ, with collaborators at the Wellcome Trust Sanger Institute, UK, and in China at the Chinese Center for Disease Control and Prevention, the Collaborative Innovation Center for

Diagnosis and Treatment of Infectious Diseases, The University of Hong Kong, and the Beijing Institute of Microbiology and Epidemiology.

The work was supported by the Wellcome Trust, the National Health and Medical Research Council of Australia, the Australian Research Council, and the Research Fund for the Control of Infectious Diseases Commissioned Grant of the Hong Kong Government.

http://www.eurekalert.org/pub_releases/2015-11/osuw-srb110415.php

Study rejects biologic age as limiting factor for stem cell transplants

Results from a phase 2, multicenter trial show 40 percent of patients can achieve cancer remission with reduced-intensity regimen for stem cell transplant

COLUMBUS, Ohio - More than 40 percent of older patients with acute myeloid leukemia (AML) can remain in long-term cancer remission through a modified, less aggressive approach to donor stem cell transplantation, according to the results of a phase 2 study led by oncologists at The Ohio State University Comprehensive Cancer Center -- Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC -- James).

AML is an aggressive blood cancer that is life threatening and is typically diagnosed in patients older than 60. The data represents new hope in a disease where the five-year survival rate is often below 10 percent, despite achieving initial remission.

Previous observational studies have suggested that allogeneic hematopoietic stem cell transplantation -- which involves infusing a patient with healthy stem cells from a donor -- can reduce cancer recurrence and, therefore, improve overall survival for AML patients.

Patients over 60, however, traditionally have been considered poor candidates and excluded from stem cell transplants due to other prohibitive health conditions or concerns about their ability to tolerate the intensive chemotherapy treatments necessary to eradicate leukemia cells before infusing the body with donor stem cells to rebuild healthy bone marrow.

Study Methods and Findings

Under the direction of OSUCCC -- James Director of Blood and Marrow Transplantation Steven Devine, MD, the current study sought to determine whether a modified conditioning regimen for stem cell transplantation could improve long-term cancer remission rates for patients with AML between the ages of 59 and 75.

The phase 2 cooperative group trial enrolled 114 patients with a median age of 65 at 21 U.S. hospitals between Nov. 2004 and Nov. 2011.

The trial was conducted with grant support through the National Cancer Institute's cooperative group trials network (Alliance for Clinical Trials In Oncology, formerly the Cancer And Leukemia Group B).

Treatment with bone marrow transplant involves collecting stem cells -- which are produced in the bone marrow -- either from the cancer patient (autologous) or a donor (allogeneic). Traditionally, these stem cells are then infused back into the patient after high-dose chemotherapy cancer treatment is completed to help restore bone marrow's ability to produce red and white blood cells that fight infection.

For this study, all patients received reduced-intensity chemotherapy (fludarabine followed by busulfan) prior to transplant -- which essentially cut treatment strength by half compared to the traditional high-dose chemotherapy regimens used in younger patients.

Patients were also given medications (tacrolimus and methotrexate) to help prevent graft-versus-host disease, a condition that can occur when the newly transplanted donor cells try to reject the patient's normal cells.

Researchers found that 42 percent of patients enrolled onto the study remained cancer free two years after stem cell transplantation. Previously published data suggested that not more than 20 percent of similar patients who underwent conventional chemotherapy regimens would remain cancer free after two years.

Devine and his colleagues reported their results in the Journal of Clinical Oncology online ahead of print Monday, Nov. 2, 2015. This is the first prospective study of this less-intense approach (known medically as 'reduced-intensity conditioning').

"This new data offers strong support against using biological age as a limiting factor for stem cell transplantation in AML patients who are otherwise well positioned to tolerate and achieve long-term remission with this approach," says Devine, corresponding author of the JCO study and principal investigator of national clinical trial.

"Close to half of the patients treated in this study achieved long-term cancer-free survival after two years. These outcomes are similar to what we would expect to see in younger patients and appear to be better results than those that can be achieved with conventional chemotherapy-based approaches typically used in AML patients over 60."

Adult acute myeloid leukemia is a type of cancer in which bone marrow makes abnormal myeloblasts (a type of immature white blood cell), red blood cells or platelets. Nearly 21,000 cases of AML are diagnosed annually, the majority of them in adults.

http://rsc.li/1MQ32C1

Biomarkers identify stroke victims with cognitive problems

Scientists in China have pinpointed three metabolites that indicate if a stroke victim has suffered cognitive damage.

Charlie Quigg

The finding not only builds understanding on the biochemical pathway behind strokes but could also help treatment plans to be prepared sooner, improving rehabilitation times for patients.

A stroke happens when blood flow to the brain is interrupted and brain cells starve of oxygen. Aftereffects include muscle weakness and altered senses.

In many cases, strokes also affect the way a patient thinks or processes information.

Quickly identifying the effects of a stroke helps doctors to tailor rehabilitation programs to the needs of a patient. Currently, structural neuroimaging and neuropsychological tests assess cognitive damage, but these take time and require the patient to be involved and compliant.

Now, a team led by Weizhong Wang and Xiaoying Bi from the Second Military Medical University in Shanghai has analysed metabolic changes following a stroke.

The researchers were particularly interested in identifying changes related to post-stroke cognitive impairment. Bi explains that these changes may be ‘caused by inflammation, neurotoxicity or oxidative stress’ because of the stroke.

The team used paired ultra-high performance liquid chromatography and Q-TOF mass spectrometry to study serum samples from a control group, a post-stroke cognitively impaired group and a post-stroke non-cognitively impaired group of patients.

Multivariate data analysis of the data set highlighted the different metabolic profiles of the groups and identified a wide range of metabolic changes.

To create a practical test, the team then used a regression model to pare down the metabolites to three that were simple to check for: glutamine – an amino acid; kynurenine – a metabolite of tryptophan; and lysoPC(18:2) – a lysophospholipid. These biomarkers can rapidly identify post-stroke cognitive impairment without actively involving the patient in the testing.

Peng Song, a specialist in neuro-analytical chemistry, from the Eastman Chemical Company in the US says the research signals the coming age of clinical metabolomics.

‘The finding paves the way for a better understanding of the molecular mechanisms and eventually, more effective treatment,’ he adds.

Min Liu et al, Mol. BioSyst., 2015, DOI: 10.1039/c5mb00470e

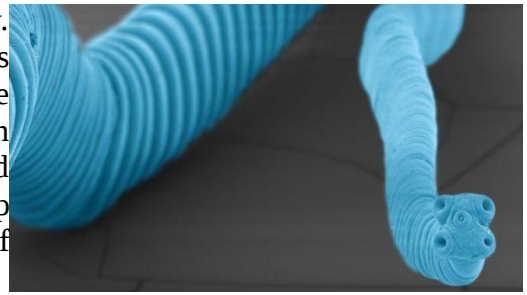
http://www.bbc.com/news/health-34721419

Man died with 'tapeworm tumours'

A man has died with tumours made of cancerous parasitic worm tissue growing in his organs, doctors report.

By James Gallagher Health editor, BBC News website

The patient had HIV and his weakened immune system allowed the worm-cancer to flourish. The unusual case was diagnosed through a collaboration between the US Centers for Disease Control and the UK's Natural History Museum. Doctors said the case, detailed in the New England Journal of Medicine, was "crazy" and unusual. Colombian doctors had tried to diagnose the 41-year-old man in 2013. He had what appeared to be normal tumours, some more than 4 cm across, in his lungs, liver and elsewhere in his body. But on closer inspection the cancerous cells were clearly not human - they were tiny at just a tenth of the size of a human cell. "It didn't really make sense," said Dr Atis Muehlenbachs, who picked up the "crazy" case at the US Centers of Disease Control.



The dwarf tapeworm **Peter Olson**

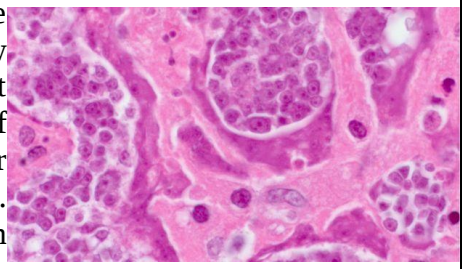
He ran through several theories including shrinking human cancer cells or even a newly discovered infection. Eventually, molecular testing identified high levels of tapeworm DNA in the tumours and the reaction was "complete disbelief" from Dr Muehlenbachs. He told the BBC News website: "This has been the most unusual case, it caused many sleepless nights. "It should have been obvious this was cancer or an infection and not being able to tell between the two for months is unusual." The patient was too sick to treat by the time doctors were able to identify the cause of his tumours. He died, in Medellin in Colombia, three days after the worm DNA was discovered.

Unique worm

The worm tissue in question came from dwarf tapeworm - *Hymenolepis nana* - a specialism of Dr Peter Olson from the Natural History Museum. "There is something very special about this species," he told the BBC, "It is able to carry out its whole lifecycle in one host and that is absolutely unique." Around 90% of the worm's body is given over to reproduction as it spews out thousands of eggs into the gut every day. Rather than the worm getting cancer, it is thought one of these eggs penetrated the lining of the intestines, mutated and ultimately became cancerous. "They were dividing and proliferating out of control and that is really what defines a cancer so they had a tape worm tumour," Dr Olson said.

'Extraordinary'

Up to 75 million people have an *H. nana* infection at any one time. Doctors believe that worm-cancer is rare, but know many cases could be going undiagnosed. The US Centers for Disease Control said hand washing and cooking raw vegetables was the best way to prevent infection. There have been some cases of cancers going from one person to another through organ transplant or in the womb. Another cancer, this time in dogs, has been spread from canine to canine for 11,000 years.



Tiny cancerous worm-tissue was growing in the patient **CDC**

Prof Mel Greaves, the director of the centre for evolution and cancer at The Institute of Cancer Research in London, said the latest case was "interesting and unique". He told the BBC News website: "What is extraordinary is that it is free cells of the parasite growing and in a cancer-like fashion rather than whole tapeworms. "Species from almost all invertebrate phyla can develop cancer and the potential seems inherent to animal cells, and particularly the stem cells of multicellular animals. "What has transpired in this case is that an exceptional combination of circumstances permitted this potential to be expressed in a very foreign host."

http://www.eurekalert.org/pub_releases/2015-11/acoa-cpe102715.php

Consider penicillin, even if you have had a prior reaction

Research indicates you can start taking penicillin again once you've tested negative

SAN ANTONIO, TX - Most people who think they're allergic to penicillin have been told so by a doctor after they've had a reaction to the drug. And the majority, even though they've never been allergy tested, never take penicillin again.

A study presented at the American College of Allergy, Asthma and Immunology (ACAAI) Annual Scientific Meeting, examined the records of 15 patients who, after being told they were penicillin-allergic, tested negative for penicillin allergy, and were then able to be treated with intravenous penicillin on multiple occasions.

"We found intravenous penicillins to be safe for repeated use in patients who had been told they were allergic," said allergist David Khan, MD, study author and ACAAI fellow. "Of the patients whose records we examined, there were no adverse drug reactions or evidence of recurrence of their penicillin allergy. There is often thought to be a higher risk in patients who get intravenous penicillin, but we did not find this to be the case. Previous reported reactions included rash, hives and swollen lips, but none of those reactions occurred after allergy testing, and treatment with multiple courses of intravenous penicillins."

About 10 percent of Americans carry a label of penicillin allergy, and others have an "allergic history" to other antibiotics. As a result, they are often prescribed more toxic, dangerous and expensive antibiotics that might not be necessary.

"Recent research has shown that patients who are labeled penicillin-allergic and take other antibiotics are more likely to have poor outcomes, such as development of colitis, longer hospital stays and greater numbers of antibiotic-resistant infections," said allergist Roland Solensky, MD, ACAAI member and meeting presenter. "There has been a push to be more proactive and evaluate patients with history of penicillin allergy even when they're well and not in need of an antibiotic. The vast majority turn out not to be allergic and can be treated with penicillin."

At the Annual Meeting, Dr. Solensky will present "Drug allergy: options beyond avoidance" where he will discuss options for patients who have drug allergies, as well as patients who have been told they have drug allergies, but do not.

"Anyone who has been told they are penicillin allergic, but who hasn't been tested by an allergist, should be tested," said Dr. Khan. "An allergist will work with you to find out if you're truly allergic to penicillin, and to determine what your options are for treatment if you are. If you're not, you'll be able to use medications that are safer, often more effective and less expensive."

Abstract Title: Risk of Re-sensitization to Penicillins After Recurrent Intravenous Administration in Skin Test Negative

Author: David Khan, MD, ACAAI fellow

http://www.medscape.com/viewarticle/852143

Three Heart Transplants for One Child While Others Get None?

How Many Hearts Should One Child Receive?

Neil Chesanow

In a recent Medscape video, bioethicist Art Caplan, PhD, of the Division of Medical Ethics at the New York University Langone Medical Center in New York, addressed one of the most difficult ethical and moral issues in medicine: Should a child whose heart transplant failed receive another heart, when the odds of success a second time are significantly less and many more children need organ donors than hearts are available?

Dr Caplan focused on the case of 8-year-old Aiyana Lucas, who received not one heart but three. "Her physicians at Seattle Children's Hospital fought very hard to get these hearts for her, and it is hard not to do anything but celebrate the fact that she is still here and she was able to be rescued," Dr Caplan said. "But there is a

tough moral issue when somebody, even a child, gets three heart transplants. The third and fourth heart transplant survival statistics are not good."

"From the point of view of the physicians taking care of Aiyana at Seattle Children's Hospital, they are going to fight to get every resource they can," Dr Caplan concedes. "There is no doubt that what they consider the right thing to do is to get hearts for their patient. If they could get five, six, or seven, I suspect that they would try to do it. But is that the right use of hearts? When Aiyana gets hers, somewhere there is a kid waiting who isn't going to get a heart, who is not going to get a first chance, perhaps with much better statistics, because we are trying to rescue a particular little girl who is in dire circumstances."

This isn't a question for a patient's doctors to grapple with, Dr Caplan asserts. "They are not going to abandon their patient; they are going to be good advocates for their patient. The only way that we are going to limit the number of hearts that this little girl or anybody can get is if the system has a rule that says, 'After X number, we are not sending any more hearts to you. We have to give other people a chance.' That is the right thing to do if we value efficacy, if we want to save the most lives using the scarce supply of hearts for kids that we have."

The video prompted dozens of thoughtful, poignant, often impassioned, and sometimes angry comments from doctors—including a number of edifying responses to those comments.

"Art raises a very challenging issue," a cardiologist wrote. "If early rejection is a major factor in nonsurvival of repetitive organ transfers, that must have a deterrent effect. Obviously, a not-yet-transplanted recipient must have a higher claim in choices, unless there are 'local' factors that limit eligibility. If ever there were an urgent need for total transparency in making such matching decisions, this may be it."

"Without a doubt, such a system must be instituted," a urologist agreed. "However, it will be hated. We already have a similar system at the VA. It is not well-liked."

"I agree that we need to consider resources when allocating any kind of medical care," a pediatrician opined. "What I object to is creating blanket rules regardless of the situation. What should happen is that when a need is discovered, the scenario and risk/benefit ratio should be entered into the needs analysis. There is already a needs analysis pool being used. It is the benefit analysis that needs to be added to the consideration. And we do obtain that information. What we don't need is some rule like 'three hearts and you're out.'"

"Rationing is never easy, but meeting the needs of as many children as possible needs to be given utmost priority," another pediatrician insisted. "However, you must allow each physician to advocate for their patient and have an unbiased body of experts make the final call. As a physician, it is not ethical for me to say 'You take it' to another patient if there is a remote possibility that this organ could save my patient."

"Just as prospective liver and lung transplant recipient patients are 'scored' using many eligibility factors before being deemed a candidate for a transplant, I believe that the risks of success of multiple cardiac transplants should also be taken into consideration as a 'negative score,'" a radiologist stated. "The first-time cardiac-transplant child waiting for a heart might then receive a higher eligibility score and move up in the queue. We must begin to address the ethical issues associated with the most limited of our precious human resources, and pediatric hearts must be one the most limited of these resources."

"I don't think physicians fail to understand the concept of limitations; I think they are uncomfortable telling the patient in front of them that that person is the one who will have to accept those limitations," an otolaryngologist wrote. "A national consensus would be useful, but only up to a point. People are more than ready to keep someone else's medical costs down, but they balk when it is their own care that is being denied."

"I worked for many years in pediatric liver and gastrointestinal transplantation," a surgeon commented. "I did that after working in the jungle in Africa for few months. I have seen both extremes of medical care, in terms of limited resources and waste of resources."

The surgeon continued, "Every doctor should spend some time in the jungle. When a premature baby or newborn baby comes to life with major life-threatening conditions, very often they cannot be saved. This is socially accepted, and few months later a new, healthy baby will come to life. In America, we are able to save a 600-g baby who lost his gut; wait months for a transplant or sepsis-induced liver failure, whichever comes first; and then give him a multivisceral transplant if he's still alive. However, this will destroy the lives of the two often very young parents, will cost the baby years of tremendous suffering, and will cost the community millions of dollars. Sometimes medicine needs to stop, and doctors should write fewer papers about the craziest interventions."

In response to the surgeon's comment, a radiologist wrote, "I agree. We play God every time we 'save' a 600-gram baby who would not have lived if not for the interventions we provide. Our technology has progressed beyond our ability to use it rationally. There needs to be a discussion of outcomes, not just survival. I have seen patients who would have died except for heroic medical interventions, only to be left with severe debilities or no cerebral function but who were considered a 'success' because they lived. Life at all costs is not acceptable, and quality of life needs to enter into decision-making."

"The limitations of medicine are no longer technical; they are financial," a family physician maintained. "We cannot afford to do what we know how to do for everyone, every time. If you agree with this proposition, the only conclusion is that we have to ration. The truth is that we already do, but in an arbitrary and irrational fashion. As unpalatable as it may be. We need to come to grips with this problem and learn to ration in a thoughtful and rational way."

http://www.eurekalert.org/pub_releases/2015-11/aaft-cp110215.php

Compound 'dissolves' protein clumps that cause cataracts

Compound reduces "cloudiness" associated with cataracts and could lead to a new therapeutic

Identification of a compound that reduces the "cloudiness" associated with cataracts could lead to a new therapeutic for this common, age-related eye disorder. Cataracts are the most frequent cause of blindness in the world and therapy is currently limited to surgery, which is not always available in developing countries.

Cataracts occur when crystallin proteins within the lens become damaged, causing them to misfold and aggregate into insoluble clumps. Two abundant lens proteins that play an important role in dissolving other proteins and are also known to contribute to age-related cataracts are αA-crystallin (cryAA) and αB-crystallin (cryAB).

Leah Makley et al. therefore sought to identify molecules that would bind and stabilize these crystallins. They noted a distinct difference between the melting point of normal cryAB proteins and a hereditary mutant form (R120G cryAB) that results in misfolding.

The team screened 2,450 compounds for a candidate that would normalize the melting transition point of these mutant proteins. They identified compound 29, which "fit" nicely between two subunits of the cryAB protein, effectively stabilizing it.

In a test tube, compound 29 was able to prevent the aggregation of R120G cryAB, as well as partially reverse aggregation that had already occurred. Importantly, this molecule partially restored the transparency of cataracts in mice, as well as in samples of human lenses studied ex vivo.

A Perspective by Roy Quinlan discusses these findings in more detail.

Article #20: "Pharmacological chaperone for ?-crystallin partially restores transparency in cataract models," by L.N. Makley; K.A. McMenimen; B.T. DeVree; B.M. Dunyak; T.J. McQuade; A.D. Thompson; R. Sunahara; J.E. Gestwicki at University of Michigan in Ann Arbor, MI; J.W. Goldman; B.N. McGlasson; U.P. Andley at Washington University School of Medicine in St. Louis, MO; P. Rajagopal; R.E. Klevit at University of Washington in Seattle, WA.

http://www.eurekalert.org/pub_releases/2015-11/dnal-rda110215.php

Gut bacteria can dramatically amplify cancer immunotherapy

Manipulating microbes maximizes tumor immunity in mice

By introducing a particular strain of bacteria into the digestive tracts of mice with melanoma, researchers at the University of Chicago were able to boost the ability of the animal's immune systems to attack tumor cells.

The gains were comparable to treatment with anti-cancer drugs known as checkpoint inhibitors, such as anti-PD-L1 antibodies.

The combination of oral doses of the bacteria and injections with anti-PD-L1 antibody nearly abolished tumor outgrowth, the researchers report online Thursday in the journal Science.

"Our results clearly demonstrate a significant, although unexpected, role for specific gut bacteria in enhancing the immune system's response to melanoma and possibly many other tumor types," said study director Thomas Gajewski, MD, PhD, professor of medicine and pathology at the University of Chicago.

"The field has recently recognized close connections between the gut microbiome and the immune system," he said. "This finding provides a novel way to exploit that connection, to improve immunotherapy by selectively modulating intestinal bacteria."

Checkpoint inhibitors such as ipilimumab, nivolumab and pembrolizumab have had a dramatic impact on treatment of several tumor types, including melanoma, lung cancer, head and neck cancers and others. But only a minority of patients--one-third or less--have a vigorous response. Cancer researchers have wondered why so few benefit.

Gajewski and colleagues found a similar pattern in the mice they use for cancer research. They noticed that mice purchased from Jackson Laboratory (JAX) tended to have a robust spontaneous immune response to small melanoma tumors implanted under their skin. Mice from Taconic Biosciences (TAC) showed only a weak immune response.

But when the researchers put the mice from both sources in cages together for three weeks, they found that co-housing "completely abolished the differences in tumor growth," Gajewski said. This made them suspect that by sharing exposure to various types of bacteria, the TAC mice had acquired microbes from JAX mice that somehow enhanced their immunity to tumors.

They confirmed their suspicion by collecting fecal matter from JAX mice and transferring it into the stomachs of TAC mice. It worked. Treated TAC mice were then able to mount a strong immune response and delay tumor growth.

The reverse process, transferring fecal bacteria from TAC to JAX mice had no effect.

Next, they compared the effects of bacterial transfer against a checkpoint inhibitor, anti-PD-L1 antibodies.

They found that introducing the bacteria was just as effective as treating them with anti-PD-L1 antibodies, resulting in significantly slower tumor growth. Combining the benefits associated with the bacteria with anti-PD-L1 treatment dramatically improved tumor control.

So they began searching for the specific bacteria that made the difference. They identified microbes from the digestive tracts of JAX and TAC mice by large-scale sequencing. Although there were significant differences in 254 taxonomic families of bacteria from the two sets of mice, three groups were prominent.

When they tested the effects of each group on the mice's immune systems, one group, the Bifidobacterium, stood out. Within two weeks of oral administration, TAC mice that received just Bifidobacterium species had a marked increase in the anti-tumor T cell responses.

Mice treated just with Bifidobacterium, rather than the full fecal transfer, displayed tumor control comparable to those who received the full mixture. The effect was long-lasting. TAC mice exposed to tumors as late as six weeks after the Bifidobacterium transfer were still able to mount a robust immune response.

Additional tests showed that the Bifidobacterium did not leave the intestine. They appeared to trigger the immune response by interacting with roaming dendritic cells.

These scavenger cells detect and process potential threats and present them to the T cells. The researchers suspect that Bifidobacterium colonize a compartment in the intestines. This enables them to interact with the cells that interact with dendritic cells, which activate tumor-killing T cells.

There may be other bacteria that also contribute to this process, the researchers note, either positively or negatively. They are investigating other bacteria that could influence other immune therapies, such at the CTLA-4 pathway, exploited by ipilimumab.

A second study--from the Institut Gustave Roussy in Paris, published in the same issue of Science--found that antibiotics could disrupt the antitumor effects of ipilimumab. Replenishing lost microbes in germ-free and antibiotic-treated mice restored the drug's anti-cancer effects.

The UChicago study was funded by a Team Science Award from the Melanoma Research Alliance and the National Institutes of Health. Additional authors include Ayelet Sivan, Leticia Corrales, Nathaniel Hubert, Jason Williams, Keston Aquino-Michaels, Zachary M. Earley, Franco W. Benyamin, Yuk Man Lei, Bana Jabri, Maria-Luisa Alegre, and Eugene B. Chang, all from the University of Chicago.

http://bit.ly/1MEPmDG

Gene editing saves girl dying from leukaemia in world first

Gene editing saves life of girl dying from leukaemia

For the first time ever, a person's life has been saved by gene editing.

One-year-old Layla was dying from leukaemia after all conventional treatments failed. "We didn't want to give up on our daughter, though, so we asked the doctors to try anything," her mother Lisa said in a statement released by Great Ormond Street Hospital in London, where Layla (pictured above) was treated.

And they did. Layla's doctors got permission to use an experimental form of gene therapy using genetically engineered immune cells from a donor. Within a month these cells had killed off all the cancerous cells in her bone marrow.

It is too soon to say she is cured, the team stressed at a press conference in London on 5 November. That will only become clear after a year or two. So far, though, she is doing well and there is no sign of the cancer returning. Other patients are already receiving the same treatment.

Experimental therapy

Layla was diagnosed with acute lymphoblastic leukaemia when she was just three months old, a disease in which cancerous stem cells in the bone marrow release vast numbers of immature immune cells into the blood. She was immediately taken to Great Ormond Street to start the standard treatment of chemotherapy followed by a bone marrow transplant to restore the immune system.

In older children, this treatment is usually successful, says Sujith Samarasinghe, a leukaemia specialist at the hospital and one of Layla's doctors. But for children as young as Layla, the cure rates are only 25 per cent.

Layla was one of the unlucky ones. Cancerous cells were still detectable after the chemotherapy. Despite this, it was decided to go ahead with a bone marrow transplant. "We hoped for a graft-versus-leukaemia reaction," says Paul Veys, head of bone marrow transplants at the hospital. This is where immune cells in the donor bone marrow attack the cancer – but this failed too.

Within two months, Layla had relapsed. "At this stage, it is usually hopeless," says Veys. Her parents Ashleigh and Lisa were told nothing more could be done. But they insisted the doctors did not give up. So the team emailed Waseem Qasim of University College London, who is developing a form of gene therapy to treat cancer.

Cell attack

The basic idea is to remove immune cells from a patient's body, genetically engineer them to attack cancerous cells and place them back in the body. Several human trials are already underway around world. Some trials involve adding a gene for a receptor called CAR19, which sits on the outside of the T-cells. This

programs the T-cells to seek out and kill any cells with a protein called CD19 on their surface – which is found on the cells that cause acute lymphoblastic leukaemia.

But engineering bespoke T-cells for every cancer patient is not cheap. And in Layla's case, it would not have worked because she didn't have enough T-cells left to modify. "She was too small and too sick," says Qasim.

Qasim's team, however, has been developing "off-the-shelf" treatments, in which T-cells from a healthy donor are modified so they could potentially be given to hundreds of patients. Normally if T-cells from another person were injected into a recipient who was not a perfect match, they would recognise all of the recipient's cells as foreign and attack them. To prevent this, Qasim's team used gene editing to disable a gene in the donor cells that makes a receptor that recognises other cells as foreign.

Molecular scissors

Conventional gene therapy can only be used to add genes to DNA. But with gene editing, specific DNA sequences can be cut with "molecular scissors", introducing mutations that disable a particular gene. Qasim's molecular scissors were of a kind known as TALEN proteins.

But there was still another problem to overcome. The recipient's immune system also recognises non-matched T-cells as foreign and will attack them. In leukaemia patients, this is not a problem because they are given drugs that destroy their immune system. Except, one of these drugs – an antibody – also destroys donor T-cells. So Qasim's team also disabled a second gene in the donor T-cells, which made them invisible to the antibody.

At the time that Qasim was contacted by Layla's doctors, his engineered T-cells, called UCART19 cells and developed in collaboration with New York biotech company Cellectis, had only ever been tested in mice. "It was scary to think the treatment had never been used in a human before," said Layla's father Ashleigh, "but there was no doubt we wanted to try the treatment. She was sick and in lots of pain, so we had to do something." And it worked within weeks.

This is only the second time that gene-edited cells have been used in people. The first ever trial involved modifying T-cells in people with HIV to make them more resistant to the virus, although these participants were not in immediate danger of dying.

Chop and change

The molecular scissors used to disable genes do sometimes make cuts in the wrong place, which carries a small risk of causing adverse effects such as turning cells cancerous.

But after three months, Layla was given a second bone marrow transplant to restore her immune system. These healthy immune cells recognised the UCART19 cells as foreign and destroyed them, so Layla no longer has any genetically modified cells in her body.

Layla will continue to have regular tests until her doctors are sure the cancer is gone. "It is too early to say she is cured," says Samarasinghe, but she is alive and well.

Cellectis plans to start full clinical trials early in 2016. Qasim says other patients in the UK are already being treated with these cells, although he would not reveal any details. The team will present the case study at the American Society of Hematology meeting in Florida in December.

We will have to wait for the results of those trials to be sure this was not a one-off, but if they are successful, it would be a huge step forward for treating leukaemia and other cancers, Qasim says. "It's incredibly encouraging," he says. "There are a whole bunch of other disorders we can now create fixes for."

http://nyti.ms/1MikxFD

No, Hot Dogs Do Not Contain Human Meat

The eye-catching headlines on the new findings started coming in waves. "Report: Human DNA Found in Hot Dogs" said USA Today, in a typical example.

By JONAH BROMWICH NOV. 5, 2015

This bizarre information came from a single document released on Oct. 17 by the consumer marketing arm of a company called Clear Labs, which had found traces of human DNA in 2 percent of the products sampled.

But don't worry: There's no evidence that hot-dog lovers are unwitting cannibals. It's more a matter of hygiene in food production. The tiniest particles of hair, nails and skin could show up in these tests.

Even so, an executive at the company interviewed last week was unapologetic about the attention-grabbing finding. "Its pretty unlikely that the human DNA piece is actually harmful to consumer health," said Mahni Ghorashi, a Clear Labs founder. "We consider it more of a hygienic issue that degrades the quality of the food." Snopes, the rumor-debunking site, was rather more harsh, labeling the information "unproven."

Consumers should brace themselves for more buzzworthy headlines as genome sequencing gets cheaper and Silicon Valley companies like Clear Labs, Beyond Meat and Soylent try to disrupt eating itself.

Chris Dixon, a partner at the venture capital firm Andreessen Horowitz, an investor in Soylent, said a broad cultural fixation on Silicon Valley is focusing attention on new food technology. "People are much more interested in food start-

ups now, partly because they are coming out of Silicon Valley, and they have the kind of Silicon Valley approach to things," he said.

Beyond Meat, for example, is pushing synthetic meat. Biz Stone, a Twitter co-founder and investor in the company, described the marketing approach: "Grow the brand as big as you can, like a fake it till you make it type of thing, and then back into it with a stellar product."

The Clear Labs story was an effort to bring marketing attention to the company's use of gene-sequencing technology, first pioneered by the Human Genome Project. Looking at regions of the genome called bar code regions, the company identifies traces of animal species in food samples, including those that are not supposed to be there. The Hot Dog Report did contain significant findings, notably that pork had been substituted for chicken and turkey in 3 percent of samples, and that 10 percent of vegetarian products contained real meat.

But it was the human DNA detail that took off on social media.

The focus on marketing by food start-ups should not be surprising. While the technology is getting faster and cheaper, start-ups still have to attract investors. The Clear Labs technology has been in development for over two years, costing about $8 million in venture funding to build the platform and database.

Mr. Ghorashi, of Clear Labs, said he expected the number of companies getting into the genome sequencing business to increase.

But while it put considerable effort in marketing the Hot Dog Report, Clear Labs refused to name the food brands that it claims were misleading customers.

"We've made a conscious choice not to be a whistle-blowing group, and we never will be," Mr. Ghorashi said. "We believe that alienating industry will ultimately hurt consumers more than help them."

That exposed the start-up to criticism. Dan Nosowitz, a journalist who covers the intersection of food and technology, recently questioned whether the company's findings should be available only to "the entities that produce and sell the food."

Mr. Nosowitz also urged skepticism about Silicon Valley food start-ups. They are prone to cherry-picking scientific evidence in order to come up with appealing messaging for their products, he said. "There's this mentality that if you can find a study that says something, it is irrefutably correct," he said in an interview, "when in fact it's chaos in the scientific world when it comes to nutrition."

Ethan Brown, the founder of Beyond Meat, expressed a view similar to that of Mr. Nosowitz but insisted that Silicon Valley's approach to technology was a good fit for the food industry.

"I think about our chicken like I think about a big Wang computer at the beginning of the computing days," he said. "It's good, it works, it has some really good qualities to it, but it's nowhere close to what's in our labs today."

Advocates of Beyond Meat's effort to synthesize meat from amino acids, carbohydrates and fats promote the company as eco-friendly, an alternative for those concerned about animal welfare, climate change and health.

But Mr. Brown says that none of that matters if the food does not pass consumers' taste test. He recalled something a friend said: "Innovation might be great for the iPhone but it's not necessarily something I want to put in my mouth."

http://www.eurekalert.org/pub_releases/2015-11/lu-m-t110615.php

Mucus -- the first line of defense

By licking a wound it heals faster -- this is not simply popular belief, but scientifically proven

Our saliva consists of water and mucus, among other things, and the mucus plays an important role. It stimulates white blood cells to build a good defense against invaders, according to a group of researchers at Lund University in Sweden together with colleagues from Copenhagen and Odense in Denmark.

"White blood cells are among other places located in the oral mucosa, and they represent the body's first line of defence against infectious agents. The mucus in the mouth causes the white blood cells to throw out a 'net' that traps bacteria", explains Ole Sørensen from the Division of Infection Medicine.

This trapping mechanism is in itself not new - it was first discovered about a decade ago. But the Lund research group now shows that the nets in the oral mucosa specifically, have special properties. These nets are much better at capturing and killing bacteria than the nets produced by white blood cells in other parts of the body.

"It appears to be precisely the mucus in the saliva that stimulates white blood cells to form these effective nets of DNA and proteins", says Ole Sørensen.

The researchers also found that patients with two diseases that both cause mouth ulcers lack saliva that manages to stimulate a successful net formation. One of the two diseases is aphthous stomatitis, a common ailment, which means that a person will often develop ulcers in the mouth and on the lips. In the best cases, the ulcers are minor and heal within a week, but they can also be major and more long-lasting.

The second disease is Behçet's disease, which is unusual in Scandinavia but more common in the eastern Mediterranean region and further east. This disease causes problems not only in the mouth but also on the genitals and in the eyes.

"We cannot determine that these diseases are caused by the mucus's inability to stimulate the white blood cells to produce efficient nets. There may also be another, underlying cause for the ulcers and the changes in the saliva", says Ole Sørensen. He hopes to be able to continue researching these connections.

As long as the root cause of the disease is unknown, there is no fully effective cure. People with aphthous stomatitis are usually recommended to use special mouthwashes and toothpastes, and patients with Behçet's disease receive anti-inflammatory drugs. The new knowledge about the mucus's formation of nets could possibly lead to new drugs in the future.

A novel mechanism for NETosis provides antimicrobial defense at the oral mucosa, Tirthankar Mohanty, Jonathan Sjögren, Fredrik Kahn, Anas H. A. Abu-Humaidan, Niels Fisker, Kristian Assing, Matthias Mörgelin, Anders A. Bengtsson, Niels Borregaard and Ole E. Sørensen: Blood online October 29, 2015

http://www.bloodjournal.org/content/126/18/2128

http://www.eurekalert.org/pub_releases/2015-11/ason-ckf102315.php

Cadaveric kidneys from infants and toddlers benefit adults in need of transplants

Adults with kidney failure can benefit from cadaveric kidney transplants from infants and toddlers when adult organs are unavailable

San Diego, CA - Adults with kidney failure can benefit from cadaveric kidney transplants from infants and toddlers when adult organs are unavailable, according to a study that will be presented at ASN Kidney Week 2015 Nov. 3-8 at the San Diego Convention Center in San Diego, CA.

While kidney transplantation is the best treatment for patients with kidney failure, the waiting list for a deceased donor kidney transplant continues to increase. In this era of extreme donor shortage, clinicians led by Jimena Blandon, MD (Cleveland Clinic Florida) present their experience with transplanting cadaveric kidneys from infants and toddlers into adult recipients.

Their retrospective study included 12 adults who received kidneys between 2014 and 2015 from deceased pediatric donors aged 0 to 5 years. All patients were followed on average for 6 months to 1 year. In the early post-transplant period, 9 recipients had transiently elevated urinary sugar levels and pH imbalances. There were no surgical complications, organ failure or rejection, blood vessel complications, or recurrence of kidney disease.

"We report excellent outcomes after adult kidney transplant from cadaveric donor ages 0 to 5 years of age. Younger age and low weight of the donors did not adversely affect our results," the authors concluded.

Study: "Transplantation of Cadaveric Kidneys from Infants and Toddlers into Adults in the Era of Extreme Donor Shortage" (Abstract FR-PO1005)

Disclosures: Nader Najafian receives research funding from BMS and is a scientific advisor for AstraZeneca, Oxford Immunotec, and Alexion.

http://www.eurekalert.org/pub_releases/2015-11/uow-pam110615.php

People attribute moral obligation and blame, regardless of ability

New research from the University of Waterloo debunks the age-old moral philosophy that if you are unable to do something, then you are not morally obligated to do it.

Professor John Turri and postdoctoral researcher Wesley Buckwalter of the Department of Philosophy at Waterloo investigated the link between being morally obligated to do something and having the ability to do it. Traditional philosophical wisdom says that "ought implies can." However, their recent study found that people routinely attribute moral obligations to people who cannot fulfill them.

"In one experiment, participants considered a case where two swimmers are drowning," explains Buckwalter. "Because the drowning swimmers are so far apart, the lifeguard on duty can save one or the other but not both of them. Despite acknowledging that the lifeguard is literally unable to save both swimmers, the overwhelming majority of participants judged that the lifeguard was still obligated to do so."

The research team conducted eight experiments to test the link between a range of moral requirements and abilities in ordinary moral evaluations. Participants were assigned to groups, asked to read a story that described different inabilities (short-term or long-term, physical or psychological), and then asked to answer questions about moral obligation or blame. The study also revealed important differences between the way people perceive physical and psychological inabilities.

"People are less willing to believe that an agent is unable to drive a car due to clinical depression than due to physical injury," said Professor Turri. "Moreover, people are more willing to blame agents suffering from psychological inabilities. This asymmetry may reflect the assumption that people can just get over mental inabilities, such as clinical depression, in ways that they cannot just get over, say, a broken leg."

These findings may also apply to issues such as the refugee crisis European nations are facing and the immigration reform at the forefront of U.S. politics.

"One important practical question is the extent to which these nations have the ability to help all those in need around the world," said Buckwalter. "But another question involves figuring out what these nations have a moral obligation to do. Our results show that, in most people's minds, the moral question is not settled simply by learning, for instance, that a nation cannot take in more refugees."

Professor Turri, Buckwalter, and their research colleagues are currently studying why people are more likely to blame or stigmatize those with mental inabilities.

Progress on this question could have important social benefits, such as improving the treatment and experience of mental health patients.

http://www.eurekalert.org/pub_releases/2015-11/mgh-ttp110615.php

Targeted treatment produces rapid shrinkage of recurrent, BRAF-mutant brain tumor

BRAF inhibition stops regrowth of debilitating craniopharyngioma, suggests new treatment options

A team led by Massachusetts General Hospital (MGH) investigators has reported the first successful use of a targeted therapy drug to treat a patient with a debilitating, recurrent brain tumor. In a paper published online in the Journal of the National Cancer Institute, the researchers report that treatment with the BRAF inhibitor dabrafinib led to shrinkage of a BRAF-mutant craniopharyngioma that had recurred even after four surgical procedures. More than a year after dabrafinib treatment, which was followed by surgery and radiation therapy, the patient's tumor has not recurred.

"This is the first time that a systemic therapy has shown efficacy against this type of tumor," says Priscilla Brastianos, MD, of the MGH Cancer Center, co-lead author of the JNCI report. "This has the potential of completely changing the management of papillary craniopharyngiomas, which can cause lifelong problems for patients - including visual defects, impaired intellectual function, and pituitary and other hormonal dysfunction."

Craniopharyngiomas are pituitary tumors that, while technically benign, can cause serious problems because of their location near critical structures, such as optic and other cranial nerves and the hypothalamus. Not only does the growing tumor compromise neurological and hormonal functions by impinging on these structures, but treatment by surgical removal or radiation therapy can produce the same symptoms by damaging adjacent tissues. In addition, since the tumor can adhere to nearby brain and vascular structures, complete removal is difficult, leading to often rapid recurrence.

The patient described in the JNCI paper came to the MGH Emergency Department with confusion, impaired vision, severe headaches and vomiting seven months after he had been surgically treated for a brain tumor in another country. A CT scan revealed a 4 cm cystic tumor - tumor enclosed in a fluid-filled sac - that was pressing against midbrain structures and blocking drainage of cerebrospinal fluid. While his symptoms improved after surgical removal of part of the tumor, they did not disappear; and six weeks later he returned to the MGH, this time in a nearly comatose condition.

MGH neurosurgeons again removed the tumor, which was confirmed to be a BRAF-mutant craniopharyngioma. But two weeks later, before planned radiation therapy could be carried out, his condition again deteriorated into a minimally responsive state, leading to a fourth emergency surgery. Seven weeks later he was back at the hospital with progressive vision loss, and an MRI showed that the tumor had once again recurred. Since the growth of this tumor was likely driven by the BRAF mutation, which is known to drive the growth of melanomas and other malignant tumors, the team decided to try treatment with dabrafinib, which is FDA approved for the treatment of BRAF-mutant melanomas.

After only four days of treatment, the patient's tumor was around 25 percent smaller; and by day 17 the tumor was half the pretreatment size, and the surrounding cyst was 70 percent smaller. On day 21, the treatment team added the MEK inhibitor trametinib, which is known to enhance the effects of BRAF inhibition, to the protocol; and by day 35 both the tumor and the cyst had lost more than 80 percent of their pretreatment size. Endoscopic surgery to remove accessible tumor was performed on day 38, and drug treatment was stopped a week later, soon followed by radiation treatment. At the time the paper was written, the patient had remained symptom-free for seven months and continues to do so more than a year after his last treatment.

In addition to finding evidence of the antitumor effects of dabrafinib in the removed tumor tissues, the investigators were surprised to find the BRAF mutation circulating in blood samples taken at several times during the course of the patient's treatment. "That result was absolutely novel," says William Curry, Jr., MD, of MGH Neurosurgery, a co-senior author of the JNCI paper. "Finding evidence of the BRAF mutation in the blood raises the hope of potentially diagnosing this mutation and perhaps shrinking these tumors with targeted therapy before surgery, which could make surgical removal safer and possible unnecessary for some patients." He also notes that, since craniopharyngiomas are less molecularly complex than malignant tumors, they may be less likely to develop resistance to BRAF inhibition, a problem that has plagued targeted therapy for several types of cancer.

Sandro Santagata, MD, PhD, of Brigham and Women's Hospital's Pathology Department, a co-senior author of the JNCI paper, adds,"It is quite remarkable how quickly we have been able to go from identifying the genetic driver of papillary craniopharyngiomas to testing the idea in a patient that needed help. It was only last year that, along with Dr. Brastianos and colleagues, we first described in Nature Genetics that nearly all papillary cranionpharyngiomas have mutations in BRAF. This is the same mutation that is found in many melanomas,

allowing us to use treatment strategies that have been so promising in melanoma patients."

To further investigate the impact of this treatment in a larger group of patients, Brastianos is conducting a National Cancer Institute-sponsored, multicenter trial of BRAF and MEK inhibitor treatment for papillary craniopharyngiomas. She is an instructor in Medicine, Curry is an associate professor of Neurosurgery, and Santagata is an assistant professor of Pathology at Harvard Medical School.

Ganesh Shankar, MD, PhD, MGH Neurosurgery, and Corey Gill, MGH Neurology are co-lead authors, and Daniel Cahill, MD, PhD, and Fred Barker II, MD, both MGH Neurosurgery, are co-senior authors of the JNCI paper. Additional co-authors are Naema Nayyar, MGH Cancer Center; Ryan Sullivan, MD, MGH Medicine; Dennie Frederick, MGH Surgery; Pamela Jones, MD, and Brian Nahed, MD, MGH Neurosurgery; Javier Romero, MD, MGH Radiology; David Louis, MD, and Gad Getz, PhD, MGH Pathology; Malak Abedalthagafi, MBBS, and Ian Dunn, MD, Brigham and Women's Hospital; David Panka, PhD, Beth Israel Deaconess Medical Center; and Amaro Taylor-Weiner, Broad Institute. The study was supported by National Institutes of Health grant 2K12 CA090354-11, and grants from the Brain Science Foundation, Susan G. Komen for the Cure, Terri Brodeur Breast Cancer Foundation, Conquer Cancer Foundation, and the American Brain Tumor Association.

http://nyti.ms/1HAzPU1

More Oil Companies Could Join Exxon Mobil as Focus of Climate Investigations

Attorney general's investigation of Exxon's record on climate change may well spur legal inquiries into other oil companies

By CLIFFORD KRAUSS NOV. 6, 2015

HOUSTON — The opening of an investigation of Exxon Mobil by the New York attorney general's office into the company's record on climate change may well spur legal inquiries into other oil companies, according to legal and climate experts, although successful prosecutions are far from assured.

Many oil companies have funded lobbying efforts and research on climate change, so prosecutors would most likely be able to search through vast amounts of material. The industry has also resisted pressure for years from environmental groups to warn investors of the risks that stricter limits on carbon emissions could have on their businesses, although that appears to be changing.

"Exxon Mobil is not alone," said Stephen Zamora, a professor at the University of

Energy experts said prosecutors may decide to investigate companies that chose to fund or join organizations that questioned climate science or policies designed to address the problem, such as the Global Climate Coalition and the American Legislative Exchange Council, to see if discrepancies exist between the companies' public and private statements.

Continue reading the main story

A Range of Opinions on Climate Change at Exxon Mobil

Statements made by Exxon Mobil – including executives and its own scientists – about climate change over the years.

British Petroleum (now BP), Shell Oil, Texaco (now part of Chevron) and Exxon, along with several manufacturing companies, were all members of the coalition, a group of companies and trade associations that started an advertising campaign in the 1990s opposing Washington's involvement in strong international efforts like the Kyoto Protocol initiative to reduce greenhouse gas emissions.

Energy experts said internal documents from member companies about climate change could contradict what the companies said as part of the coalition, which disbanded in 2002.

"There was a concerted effort by multiple American oil companies to obscure the emerging climate science consensus throughout the 1990s," said Paul Bledsoe, a former White House aide to President Bill Clinton on climate issues. "This group may be vulnerable to legal challenge."

British Petroleum and Shell Oil left the coalition early on, setting a pattern in which European oil companies took a very different course on climate and other environmental issues than most of their American competitors.

Shell announced this summer that it would not renew its membership in the American Legislative Exchange Council, or ALEC, a free-enterprise group that has opposed government mandates, subsidies and other efforts to force or encourage companies to develop and use more renewable energy sources.

Occidental Petroleum and several other companies have also left ALEC, but Chevron and Exxon Mobil still support the group.

Big American and European oil companies can point to efforts they have made to support renewable energy, perhaps clouding attempts by prosecutors to paint them as one-sided on the issue of climate change.

Chevron, for example, has been a pioneer in geothermal energy for decades. Exxon Mobil has a project underway to convert algae into a biofuel that can run vehicles and soak up carbon. BP is active in wind power. Several companies in the United States have begun working with the Environmental Defense Fund to limit emissions of methane.

"The oil and gas industry has probably been the biggest funder of research into decarbonization, maybe more even than the federal government," said Michael Webber, deputy director of the Energy Institute at the University of Texas.

But foreign oil and gas companies, including most recently Total of France and BHP Billiton of Australia, have been far more outspoken about the dangers of climate change than American ones.

Last month, 10 of the world's biggest oil companies, including BP, Royal Dutch Shell, Saudi Aramco, Repsol of Spain, Eni of Italy and Total, made a public declaration acknowledging that their industry must help address global climate change.

None of the big American companies joined the group, largely because they oppose carbon taxes and trading of carbon-emission permits — remedies that would raise the price of fossil fuels like oil and natural gas.

Last September, five major European, Asian and Latin American oil and gas companies signed on to a voluntary United Nations-backed program to monitor and disclose methane emissions, as well as invest in technologies to control greenhouse gases from their operations. The only American company to join was Southwestern Energy, a midsize Houston-based company that mostly invests in natural gas. "There are times to go off the reservation, and this may be one of them," said Steven L. Mueller, chief executive of Southwestern Energy, just after his company joined the effort.

Energy experts say it will be harder to make cases against the oil companies than it was against tobacco companies that deliberately hid research from their customers, since many oil company scientists, including those of Exxon Mobil, have presented papers on climate change publicly at conferences and contributed to the research of international groups concerned with the issue.

"Unless they directly lied in Congress, the legal case against them is kind of thin," said Hal Harvey, chief of Energy Innovation, an energy consultancy. But he added, the record shows that the companies "have walked away from being a credible spokesman on science."

http://www.bbc.com/news/health-34744903

No woman 'totally straight', study says

New study concluded that no woman is "totally straight" and that women's sexualities are more complex than men's

By Alex Therrien BBC News Online

Gay women tend to be exclusively sexually attracted to women, while straight women are more likely to be aroused by both sexes, a study says.

Researchers asked 345 women about their sexual preferences and compared these with their arousal levels when shown videos of attractive men and women. They found 28% of straight women were mostly aroused by their preferred sex, compared with 68% of gay women. The University of Essex study concluded that no woman is "totally straight".

Study findings 'amazing'

The new study, led by Dr Gerulf Rieger from the University of Essex and published in the Journal of Personality and Social Psychology, measured the arousal of women using eye tracking devices and direct measures of physiological sexual response. Previous studies had already suggested that straight women were aroused by both sexes when tested, but researchers had never looked at whether the same was true for gay women.

Dr Rieger said the study's conclusion that women who identified as being completely gay were much more aroused by their preferred sex was "amazing".

He said their sexual arousal patterns were much more similar to men, whose responses tend to very accurately mirror their stated sexual preferences.

Dr Rieger said: "In the past we thought it was true of all women that they were aroused by both sexes. The fact that it appears this is not the case is amazing."

'More complex'

Dr Rieger said it was not known why gay women were more often only aroused by their preferred sex, but he believes it may be to do with the amount of testosterone female babies receive in the womb.

It was possible, he said, that women who experienced testosterone early in pregnancy had sexual behaviours that were more similar to men, but this has not yet been proven. He said tests showed similar behaviours occurring in monkeys.

Dr Rieger said the wider conclusions of the study was that, while the majority of women identified as straight: "Our research shows that, when it comes to what turns them on they are usually bisexual or gay, but never totally straight".

However, he added the research did not necessarily mean women were repressing their true sexual preferences, but that their sexualities were simply more complex than men's. "When it comes to straight women and sexual arousal there is such a disconnect between what a woman tells me and what her body does. "It suggests that it's a different world for women when it comes to their sexualities."

http://www.eurekalert.org/pub_releases/2015-11/ason-dom102415.php

Donor organs may be discarded due to 'weekend effect' at hospitals

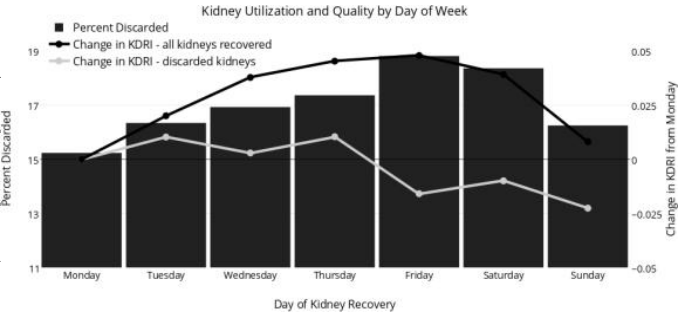
Deceased donor kidneys are increasingly being discarded, and efforts to boost their use for transplantation are needed.

San Diego, CA - A new study indicates that organs are more likely to be discarded on weekends than on weekdays. The findings, which will be presented at ASN Kidney Week 2015 November 3¬-8 at the San Diego Convention Center in San Diego, CA, indicate that efforts to save organs procured on weekends may help address the kidney shortage.

For their study, Sumit Mohan, MD (Columbia University) and his colleagues examined information from the Scientific Registry of Transplant Recipients,

identifying and comparing all deceased donor kidneys procured on Friday to Saturday with those that were procured on other days of the week.

The investigators found that kidneys that would normally be made available for transplantation were less likely to be procured from donors over the weekend (89.5% on the weekend vs. 90.2% during the week). Organs procured during the weekend were also 20% more likely to be discarded than kidneys procured on other days, and those that were discarded were of higher quality than those discarded during the rest of the week. Organs procured on the weekend were more likely to transplanted at large transplant centers.



Kidneys that would normally be made available for transplantation were less likely to be procured from donors over the weekend, and organs procured during the weekend were more likely to be discarded than kidneys procured on other days. **Mohan**

"The day of the week when a donor kidney becomes available appears to impact the likelihood of procurement and its subsequent utilization, if procured," said Dr. Mohan. "Deceased donor kidneys that would normally be transplanted over the weekend are less likely to be procured and if procured appear less likely to be transplanted even after adjusting for the quality of the kidney." He noted that weekends are typically associated with fewer available resources, which likely impacts kidney transplantation. Larger centers tend to have more resources available and the ability to continue to perform transplantation over the weekends more easily than smaller centers. "Recognition of the impact of factors beyond organ quality on the procurement and transplantation of deceased donor organs should influence future policy aimed at improving kidney transplantation rates in the United States," said Dr. Mohan.

Study: "Discard of deceased donor kidneys in the United States: The weekend effect" (Abstract SA-PO1013)

Disclosures: Sumit Mohan receives research funding from Pfizer, Gambro. Geoffrey K. Dube is a consultant for Alexion. Stephen O. Pastan is a consultant for Retrophin and a member of the Data Safety Monitoring Board for Dompe; owns a small percentage of the Fresenius College Park Dialysis unit in College Park, Georgia, in a joint venture with Fresenius Medical Care; receives research funding from Bristol Myers Squibb; and receives honoraria from Retrophin and Dompe. Rachel E. Patzer is a consultant for Parkland Center for Clinical Innovation; receives honoraria from Patient Centered Outcomes Research Institute; receives research funding from the National Institute of Health, the Satellite Healthcare Normon S. Coplon Grant, Bristol Myers Squibb, and the Carlos and Margeurite Mason Foundation. David J. Cohen is a consultant for Alexion - International aHUS Registry, and Merck - Data Safety Monitoring Board; receives research funding Novartis, Pfizer, Genentech; receives honoraria from BMS, Genzyme, Astelas, Novartis, Alexion; is a scientific advisor to Alexion - aHUS International Registry.

http://bit.ly/20Eyqre

Self-Medicating Monkeys Gobble Painkilling Bark

Sick red colobus monkeys in Uganda ate the very same plants that local people use to treat illnesses

By Jason G. Goldman | Oct 20, 2015

When a monkey has the sniffles or a headache, it doesn't have the luxury of popping a few painkillers from the medicine cabinet. So how does it deal with the common colds and coughs of the wildlife world?

University of Georgia ecologist Ria R. Ghai and her colleagues observed a troop of more than 100 red colobus monkeys in Uganda's Kibale National Park for four years to figure out whether the rain forest provides a Tylenol equivalent.

Monkeys infected with a whipworm parasite were found to spend more time resting and less time moving, grooming and having sex. The infected monkeys also ate twice as much tree bark as their healthy counterparts even though they kept the same feeding schedules. The findings were published in September in the journal Proceedings of the Royal Society B.

The fibrous snack could help literally sweep the intestinal intruder out of the simians' gastrointestinal tracts, but Ghai suspects a more convincing reason. Seven of the nine species of trees and shrubs preferred by sick monkeys have known pharmacological properties, such as antisepsis and analgesia. Thus, the monkeys could have been self-medicating, although she cannot rule out other possibilities. The sick individuals were, however, using the very same plants that local people use to treat illnesses, including infection by whipworm parasites. And that “just doesn't seem like a coincidence,” Ghai says.

Poison That Purifies

University of Helsinki researchers recently announced the first evidence of self-medication in ants. When the biologists exposed hundreds of Formica fusca ants to a dangerous fungus, many of the infected insects chose to consume a 4 to 6 percent hydrogen peroxide solution made available for the experiment. Healthy ants avoided the household chemical, which can quash infections in small doses but is otherwise deadly. The sick ants that partook were less likely to succumb to the grips of the fungus. In the wild, they could perhaps acquire the compound by eating plants that release it to fight aphid infestations.

http://bit.ly/1kD1X3K

For Most of Us, Obesity Is Unrelated to Junk Food

Don't start stuffing your face, though. It's not like burgers and pop are good for you.

Nathan Collins

Just over a year ago, Berkeley, California, became the first city in the nation to tax soft drinks. In theory, that was supposed to cut into America's obesity epidemic: Make the stuff more expensive, and people—especially kids—will drink less of it. But Berkeley's new regulations may be misguided: For most of us, new research suggests, obesity has little, if anything, to do with eating fast food and drinking soda pop.

"To lose weight, patients are commonly told to reduce or eliminate their intake of indulgent foods, such as fast food, soft drinks and candy," Cornell University Food and Brand Lab's David Just and Brian Wansink write in a paper forthcoming in Obesity Science & Practice. "Interestingly, for the majority of patients ... there was no relationship between their intake of these foods and their BMI [body mass index] in this sample."

The connection between junk food and obesity really only applies to those with BMIs of 44.9 and above.

It's easy to see why researchers would think otherwise. Past studies have linked fast food and obesity. "Fast-food consumption has strong positive associations with weight gain ... suggesting that fast food increases the risk of obesity," according to a 2005 study that tracked the health and eating habits of more than 3,000 young adults for 15 years. In fact, recent research has suggested other studies may have even underestimated the impact of fast food on obesity.

The problem, Just and Wansink argue, is that the link might be due only to the people at the extremes—in particular, very overweight people who eat at fast-food restaurants more often than others. Suppose, for example, that everyone with a BMI under 45 ate at burger joints twice a week, but people with BMIs over 45 did so three times a week. Even though BMI and fast food are unrelated for all but the most morbidly obese, researchers using standard methods would conclude otherwise. Unfortunately, the standard methods aren't sensitive to such details.

Just and Wansick tested their hypothesis with data from the National Household and Nutrition Examination Study, which recorded height, weight, and eating habits for nearly 5,000 people in 2007 and 2008. Just and Wansick's conclusion: "After excluding the clinically underweight and most morbidly obese, consumption of indulgent foods was not positively correlated with measures of BMI." The connection between junk food and obesity, they find, really only applies to those with BMIs of 44.9 and above, or roughly one in 40 Americans.

"We were hoping to see what the impact of policies that were narrowly focused on a single food (like soda) or a small group of foods (like fast foods) would be," Just writes in an email. It's not that junk food isn't bad for you, he explains, "just that they don't seem to be a differentiator between healthy weight and overweight on average."

From lawmakers' point of view, Just writes, "I think the takeaway is that the situation is not that simple. We need to be thinking much more broadly about overall diet and exercise."

http://www.eurekalert.org/pub_releases/2015-11/aha-tn1103015.php

The No. 1 killer is invisible to most women

Though CV disease is the No. 1 killer of women in the U.S., most women say they are not personally connected

Even though heart disease and stroke are the No. 1 killer of women in the U.S., most women say they don't have a personal connection to cardiovascular disease, according to research presented at the American Heart Association's Scientific Sessions 2015.

A 2014 nationally representative survey of 1,011 adult women found that those who know another woman with heart disease are 25 percent more likely to be concerned about it for themselves and 19 percent more likely to bring up heart health with their doctors. The survey was developed and conducted by the Women's Heart Alliance.

"Since women who report knowing another woman with heart disease are more apt to express concern and importantly -- bring up this issue with their doctor -- awareness of heart disease is crucial," said lead author C. Noel Bairey Merz, M.D., director of the Barbra Streisand Women's Heart Center and professor of medicine at Cedars-Sinai Medical Center in Los Angeles, California.

Yet, only 27 percent of women can name a woman in their lives with heart disease and only 11 percent can name a woman who has died from heart disease. Among those age 25 to 49, about 23 percent know a woman with heart disease, compared to 37 percent of women aged 50 to 60.

In addition, the survey found that healthcare providers more often focused on a woman's weight rather than other cardiovascular disease risk factors, compared to men who were more likely to be told their cholesterol or blood pressure is too high by their doctors.

"We are stalled on women's awareness of heart disease, partly because women say they put off going to the doctor until they've lost a few pounds. This is clearly a gendered issue," Bairey Merz said.

The survey underscores the disconnect most women experience between the widespread nature of women's heart disease and their personal perceptions.

One in three women die from heart disease and stroke in the U.S. every year. Although heart disease and stroke death rates among men have dropped steadily over the last 25 years, women's rates have fallen at a much slower rate.

Professional surveyors questioned a random sampling of women ages 25 to 60 across the country. The survey covered about 97 percent of U.S. households and took about 15 minutes. Women answered online questions and were provided computers and internet access if unavailable. Researchers factored out the effects of age, region, race, ethnicity, education and income.

A risk calculator developed jointly by the American Heart Association and the American College of Cardiology in 2013 helps identify women at risk of heart disease.

"Women should be screened for heart disease, including finding out their atherosclerotic cardiovascular disease (ASCVD) score - also called the "A-risk score," Bairey Merz said. "This figure uses your age, sex, race, blood pressure, cholesterol levels, blood pressure medication use, diabetes status and smoking status to get a 10-year cardiovascular disease risk and a lifetime risk score."

Her advice to women: "Talk to your doctor about heart disease. Every woman 40 and older needs to get their A-risk score. If you're under 40 you still need to know your blood pressure and cholesterol," Bairey Merz said.

Find your ASCVD score from your doctor, nurse, pharmacist, or by downloading the CV Risk Calculator app.

Co-authors are Paula Johnson, M.D., M.P.H.; Holly Andersen, M.D.; Mark Keida, Ph.D.; Emily Sprague; Mary Walsh, M.D.; Phyllis Greenberger, M.S.W.; Susan Campbell, M.P.H.; Irene Pollin, M.S.W., Ph.D.; Marjorie Jenkins, M.D.; Rita Redberg, M.D., M.Sc. and British Robinson, M.A.

The Women's Heart Alliance funded the study.

http://www.eurekalert.org/pub_releases/2015-11/tjnj-sep110515.php

Study examines prevalence of 'silent' heart attacks in population

Nearly 8% prevalence of myocardial scars, with nearly 80% unrecognized by ECG or clinical evaluation

In a multiethnic, middle-aged and older study population, the prevalence of myocardial scars (evidence of a heart attack) was nearly 8 percent, of which nearly 80 percent were unrecognized by electrocardiography or clinical evaluation, according to a study in the November 10 issue of JAMA.

This issue, a cardiovascular disease theme issue, coincides with the American Heart Association's Scientific Sessions 2015.

Ischemic heart disease is an important public health concern, but a considerable proportion of myocardial infarctions (MIs; heart attacks) are clinically unrecognized. Given the aging of the U.S. population, it is important to understand the prevalence, risk factors, and prognosis of unrecognized MI.

In patients who survive a heart attack, normal contractile (having the property of contracting) tissue is replaced by noncontractile fibrosis (formation of excess fibrous connective tissue in a reparative process) (scar).

Myocardial scarring leads to abnormal heart function and poor prognosis.

The prevalence of and factors associated with unrecognized MI and scar have not been previously defined using contemporary methods in a multiethnic U.S. population, according to information in the article.

David A. Bluemke, M.D., Ph.D., of the National Institute of Biomedical Imaging and Bioengineering, Bethesda, Md., and colleagues examined the prevalence of myocardial scar using cardiac magnetic resonance (CMR; considered a standard of reference for defining the presence of myocardial scar).

Participants were multiethnic, 45 through 84 years of age and free of clinical cardiovascular disease (CVD) at study entry in 2000-2002.

In the 10th year examination (2010-2012), 1,840 participants (average age, 68 years; 52 percent men) underwent CMR imaging with gadolinium to detect myocardial scar. Cardiovascular disease risk factors and coronary artery calcium (CAC) scores were measured at study entry and year 10.

The overall prevalence of myocardial scar by CMR was 7.9 percent (146 of 1,840).

The prevalence of previously unrecognized myocardial scar was 6.2 percent, whereas 1.7 percent had clinically recognized MI. Thus, 78 percent (114 of 146) of myocardial scars were unrecognized by clinical or electrocardiography (ECG) evaluation.

Men had a higher prevalence of myocardial scar than women (12.9 percent vs 2.5 percent).

Of individual risk factors, age, male sex, CAC score, body mass index, current smoking, and use of antihypertensive medications at study entry were associated with higher odds of myocardial scar.

"The clinical significance of unrecognized myocardial scar remains to be defined, although prior myocardial scar has been noted pathologically in more than 70 percent of patients with sudden cardiac death but without prior known coronary artery disease," the authors write.

"Further studies are needed to understand the clinical consequences of these undetected scars."

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http://www.eurekalert.org/pub_releases/2015-11/uoa-abt110415.php

Ancient brains turn paleontology on its head

A UA researcher has provided the strongest evidence yet that it's possible for brains to fossilize and, in fact, a set of 520-million-year-old arthropod brains have done just that

Science has long dictated that brains don't fossilize, so when Nicholas Strausfeld co-authored the first ever report of a fossilized brain in a 2012 edition of Nature, it was met with "a lot of flack."

"It was questioned by many paleontologists, who thought - and in fact some claimed in print - that maybe it was just an artifact or a one-off, implausible fossilization event," said Strausfeld, a Regents' professor in UA's Department of Neuroscience.

His latest paper in Current Biology addresses these doubts head-on, with definitive evidence that, indeed, brains do fossilize.

In the paper, Strausfeld and his collaborators, including Xiaoya Ma of Yunnan Key Laboratory for Palaeobiology at China's Yunnan University and Gregory Edgecombe of the Natural History Museum in London, analyze seven newly discovered fossils of the same species to find, in each, traces of what was undoubtedly a brain.

This image shows a Fuxianhuia protensa specimen from the Chenjiang fossil beds in southwest China. The ancient arthropod was 12 centimeters (just under 5 inches) in length. **Xiaoya Ma, London Museum of Natural History**

The species, Fuxianhuia protensa, is an extinct arthropod that roamed the seafloor about 520 million years ago. It would have looked something like a very simple shrimp. And each of the fossils - from the Chengjiang Shales, fossil-rich sites in Southwest China - revealed F. protensa's ancient brain looked a lot like a modern crustacean's, too.

Using scanning electron microscopy, the researchers found that the brains were preserved as flattened carbon films, which, in some fossils, were partially overlaid by tiny iron pyrite crystals. This led the research team to a convincing explanation as to how and why neural tissue fossilizes.

In another recent paper in Philosophical Transactions of the Royal Society B, Strausfeld's experiments uncovered what it likely was about ancient environmental conditions that allowed a brain to fossilize in the first place.

The only way to become fossilized is, first, to get rapidly buried. Hungry scavengers can't eat a carcass if it's buried, and as long as the water is anoxic enough - that is, lacking in oxygen - a buried creature's tissues evade consumption by bacteria as well. Strausfeld and his collaborators suspect F. protensa was buried by rapid, underwater mudslides, a scenario they experimentally recreated by burying sandworms and cockroaches in mud.

This is only step one. Step two, explained Strausfeld, is where most brains would fail: Withstanding the pressure from being rapidly buried under thick, heavy mud.

To have been able to do this, the F. protensa nervous system must have been remarkably dense. In fact, tissues of nervous systems, including brains, are densest in living arthropods. As a small, tightly packed cellular network of fats and proteins, the brain and central nervous system could pass step two, just as did the sandworm and cockroach brains in Strausfeld's lab.

"Dewatering is different from dehydration, and it happens more gradually," said Strausfeld, referring to the process by which pressure from the overlying mud squeezes water out of tissues. "During this process, the brain maintains its overall integrity leading to its gradual flattening and preservation. F. protensa's tissue density appears to have made all the difference."

Now that he and his collaborators have produced unassailable evidence that fossilized arthropod brains are more than just a one-off phenomenon, Strausfeld is working to elucidate the origin and evolution of brains over half a billion years in the past.

"People, especially scientists, make assumptions. The fun thing about science, actually, is to demolish them," said Strausfeld.

http://bit.ly/1kF4QkE

New Clues Point to Secret Chamber in King Tut Tomb

The investigation of King Tut's tomb to find secret chambers ended today with promising results, according to a statement from Egypt's antiquity ministry.

Nov 6, 2015 01:28 PM ET // by Rossella Lorenzi

A team from Cairo University's Faculty of Engineering and the Paris-based organization Heritage, Innovation and Preservation used infrared thermography to detect the temperature of the walls in the tomb. Preliminary analysis indicates the presence of an area different in its temperature than the other parts of the northern wall. "The experiment lasted for 24 hours," Egypt's Antiquities minister Mamdouh Eldamaty said in a statement.

In order to certify the results, Eldamaty said, a number of experiments will be carried out to determine more accurately the area showing the difference in temperature.

"The team was very impressed and full of emotion to spend the night in the tomb," Mehdi Tayoubi, founder of the Paris-based Heritage Innovation Preservation Institute, told Discovery News.

The non-invasive search follows a claim by Nicholas Reeves, a British Egyptologist at the University of Arizona, that high-resolution images of the tomb's walls show "distinct linear traces" pointing to the presence of two still unexplored chambers behind the western and northern walls of the tomb.

According to Reeves, one chamber contains the remains, and possibly the intact grave goods, of queen Nefertiti, the wife of the "heretic" monotheistic pharaoh Akhenaten, Tutankhamun's father.

He argued that a painting located behind King Tut's sarcophagus has been wrongly interpreted. Egyptologists have always believed the scene shows Ay (who largely directed King Tut's reign and succeeded him) performing the Opening of the Mouth ritual on the boy king.

Reeves believes the figure labelled Tutankhamun is actually Nefertiti. He noted that a line at the side of the figure's mouth, called "oromental groove," is a trademark in pictures of Nefertiti. On the other hand, the figure labelled Ay would be Tutankhamun, completing the death ritual for Nefertiti.

Reeves speculated that the tomb of King Tut was not ready when he died unexpectedly at 19 in 1323 B.C. after having ruled a short reign of nine to 10 years. Consequently, he was buried in a rush in what was originally Nefertiti's tomb, who had died 10 years earlier.

Reeves's claim about Nefertiti has stirred a debate among Egyptologists and mummy experts.

An international team of researchers led by mummy expert Frank Rühli, director of the Institute of Evolutionary Medicine at the University of Zurich, cautioned last month about the possibility of Nefertiti being the occupant of the secret crypt.

They argued Nefertiti might be the already found Younger Lady, a mummy found in 1898 by archaeologist Victor Loret in tomb KV35 in the Valley of the Kings.

Nefertiti is labelled in inscriptions to be Tutankhamun's mother; genetic analyses identified the "Younger Lady" as the mother of Tutankhamun.

Such evidence would automatically rule out Nefertiti, the researchers concluded.

If a mummy is found, it could belong to the elusive pharaoh Smenkhkare, or to queen Meritaton, the full or half sister of Tutankhamun, they added.

It is also possible that nothing at all will be found behind those walls, they said.

Investigations in King Tut's tomb are expected to continue.

According to Eldamaty, a longer time is needed — one week or more — using the thermography technique in order to confirm the results. However it is not known when infrared thermography will be used again in King Tut's tomb.

In the meantime, other methods might be used to help identify the area with a temperature difference.