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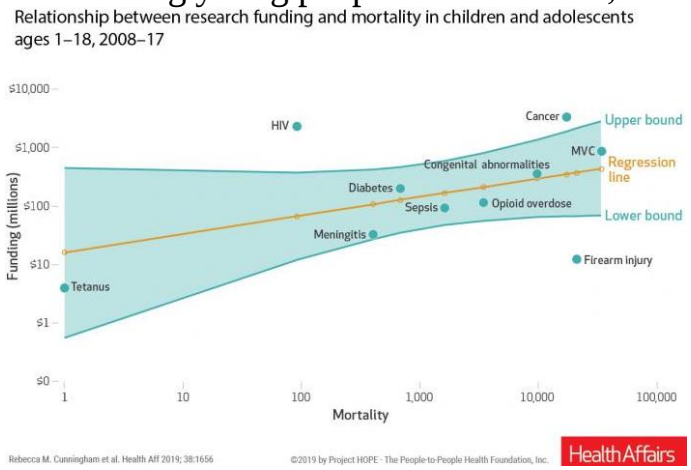
Research on US child firearm injuries lags far behind studies of other causes of death

Study spotlights mismatch between number of deaths in children age 1 to 18, and research to understand, prevent and treat the reasons for those deaths

ANN ARBOR, Mich. -- Firearm injuries kill 2,500 American children each year, and send another 12,000 to the emergency department. But a new study finds that the nation spends far less on studying what led to these injuries, and what might prevent and treat them, than it spends on other, less-common causes of death in children between the ages of 1 and 18 years.

In fact, on a per-death basis, funding for pediatric firearm research is 30 times lower than it would have to be to keep pace with research on other child health threats.

That mismatch between death toll and research funding may help explain why firearm deaths among young people have climbed, when deaths from other causes have dropped, according to the new study published in the October issue of Health Affairs by a team from the University of Michigan and Brown University.



US research funding for different causes of childhood death, mapped according to the dollars spent and the number of deaths from each cause over the period of 2008 to 2017. **Credit: Health Affairs**

The researchers analyzed records from a wide range of federal research funding sources, and catalogued grants given over a 10-year period to teams studying the major causes of death in children and teens. Using data on the causes of death of children and teens during this same time, they then compiled a dollars-per-death amount for each area of research.

Child-specific research on motor vehicle crashes - the top cause of death in U.S. young people - received an average of $88 million per year from 2008 to 2017. That comes out to about $26,000 in research funding for each one of the 33,577 young people killed in a vehicle crash in that decade.

Meanwhile, research on pediatric cancer - the third leading cause of death in this age group - received $335 million per year. That's $195,500 for each of the 17,111 child cancer deaths in the 10-year window.

During this same time, the federal government provided $1 million a year to fund research on firearm-related injuries - the second-leading cause of death among children and teens.

That works out to $597 per death for the 20,719 young people who died from intentional and accidental firearm injuries in the years of the study. In all, the researchers say, pediatric firearm research receives 3.3% of the $37 million per year it would need to keep pace with research on other causes of death among American children.

Fewer dollars, fewer discoveries

Less funding means less new knowledge being generated through studies and evaluations, the researchers explain. "This lack of knowledge does not result from the scientific questions or data being more difficult to research than they were for research on the molecular basis of cancer, polio prevention, or motor vehicle crash prevention. Instead, it is because federal agencies have not invested

in scientists seeking to discover answers to the key research questions about firearm injuries," they write.

"We know that when researchers study a health issue, and evaluate efforts to reduce its impact, the toll on individuals and society can drop. This is a stark demonstration of the lack of support for research that could help reduce the chances that children will be hurt or killed by firearms," says first author Rebecca Cunningham, M.D., interim vice president of research at U-M, emergency medicine physician at Michigan Medicine.

"Our goal with this study," says senior author Patrick Carter, M.D., M.P.H., "is to illuminate the vast opportunity we have as a nation to study firearm-related issues in young people, and apply new knowledge to the problem, if more funding were made available."

Cunningham and Carter's co-authors include Brown University/Rhode Island Hospital emergency physician Megan Ranney, M.D., M.P.H. Cunningham and Carter are two of the three co-directors, and Ranney a member, of the Firearm Safety Among Children and Teens Consortium, which in 2018 received a $5 million grant from the National Institute on Child Health and Human Development to support research and education. U-M president Mark Schlissel, M.D., Ph.D. recently announced a new firearm injury prevention initiative that will catalyze further research and education projects at U-M.

The authors of the new paper suggest that the U.S. should create a national institute focused on firearm-related research.

Rare causes of death, large dollars

In addition to disparities in funding for the most common causes of child death, the team also finds that research on relatively rare causes of childhood death received even more dollars proportional to their toll on children and teens.

Meningitis, which killed 400 young people in 10 years, was the subject of $33.1 million in funding per year in that time.

Researchers studying pediatric AIDS shared about $25 million in annual funding for each of the 91 AIDS-related deaths of a child or teen. And diabetes, which led to 697 deaths of children and teens in the study decade, received $20 million per year in research funding.

Lack of data limits other comparisons

The authors acknowledge that deaths are only one way to measure the impact of a disease or cause of injury on children, teens, their families and society. But data on the other impacts of firearm injuries has not been compiled, a fact that the FACTS Consortium's members laid out in a group of recent papers published in the *Journal of Behavioral Medicine*. They also laid out the most urgent firearm-related pediatric research questions that need answers in a recent piece in the journal *Pediatrics*.

The new study goes beyond past efforts to quantify the scope of research on different causes of death among all Americans. Cunningham and her colleagues, included only research grants from federal agencies that were specific to children and teens.

They included grants from a wide range of federal agencies, and an estimate of pediatric-related vehicle crash research funding from the National Highway Traffic Safety Administration. The study did not include private foundation or industry funding or other public funding not available in federal databases, such as state funding.

In all, 32 research grants (called awards in the paper) went to pediatric firearm research in the decade studied, compared with 5,168 grants for pediatric cancer research.

The research team also compiled a total number of research papers published with findings about each of the causes of pediatric death. Cancer had the most, with 50,235 papers in one decade. By contrast, pediatric firearm research accounted for just 540 research papers in that same decade, and pediatric vehicle crash research results were reported in 2,223 papers.

Reference: Health Affairs, *DOI10.1377/hlthaff.2019.00476*

http://bit.ly/2VAurPW

UVA discovers surprise contributor to multiple sclerosis

Cells that scientists have largely ignored when studying multiple sclerosis are actually key contributors to MS development

Cells that scientists have largely ignored when studying multiple sclerosis are actually key contributors to MS development, new research from the University of Virginia School of Medicine shows. The discovery suggests new avenues for devising treatments and is a vital step toward finding a cure.

Understanding Multiple Sclerosis

Scientists had assumed that these cells, known as oligodendrocyte progenitor cells, could only serve a favorable role in MS. These glial cells make up about 5 percent of the brain and spinal cord, and they play an important and beneficial role by making cells that produce myelin - insulation for nerve cells.

In MS, the body's immune system begins to attack the myelin, leading to a progressively disabling neurological condition that affects more than 2 million people worldwide. (MS is the most common neurological condition among the young, and is often diagnosed between ages 20 and 50.)

It has been thought that these progenitors do not efficiently give rise to myelin-producing cells in people with MS. Yet, UVA's Alban Gaultier, PhD, and his team made the surprising discovery that they are also actively participating in the immune system's harmful attacks on myelin.

"This cell type is modulating the inflammatory environment," said Anthony Fernández-Castañeda, the PhD student who is the first author of the scientific paper outlining the findings. "I was very surprised that these progenitor cells, thought to be a bystander during the inflammatory process, are active contributors to neuroinflammation."

Promoting Brain Repair

The good news: The new insights into the progenitor cells suggest that doctors could potentially manipulate the environment inside the brain to avoid neurodegeneration and promote brain repair.

In the lab, blocking the effects of the cells reduced inflammation and aided in myelin restoration.

"In MS, we have many ways to modulate the initial immune attacks, but we really have no way to promote brain repair," explained Gaultier, of UVA's Department of Neuroscience and its Center for Brain Immunology and Glia (BIG).

"To come up with a cure, we have to target both aspects of the pathology."

That will be no easy feat, considering the multiple roles these progenitor cells play.

They can't just be shut down, so scientists would have to develop a more sophisticated approach.

"It's going to take a lot more work to translate these findings to any form of therapy," Gaultier said.

"We are shining the light on this cell type that very few people have studied as part of the inflammatory response in the brain.

More consideration should be given to the varied roles the progenitor cells play when focusing on finding a cure for MS."

Findings Published

The researchers have published their findings in the scientific journal Acta Neuropathologica. The study's authors were Fernández-Castañeda, Megan S. Chappell, Dorian A Rosen, Scott M. Seki, Rebecca M. Beiter, David M. Johanson, Delaney Liskey, Emily Farber, Suna Onengut-Gumuscu, Christopher C. Overall, Jeffrey L. Dupree and Gaultier

The research was supported by the National Institutes of Health's National Institute of Neurological Disorders and Stroke, grants R01 NS083542 and R21 NS111204; the National Multiple Sclerosis Society, grant PP1978; the UVA Double Hoo Research Grant; and the Owens Family Foundation.

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Distributing essential medicines for free resulted in a 44% increase in adherence

Study also found some improved health outcomes with free distribution of essential medicines

TORONTO - A new study out of St. Michael's Hospital's MAP Centre for Urban Health Solutions found that distributing essential medicines at no charge to patients resulted in a 44 per cent increase in people taking their medications.

The study, published today in *JAMA Internal Medicine*, also found that participants experienced a reduction in systolic blood pressure and that free distribution of essential medicines led to a 160 per cent increase in the likelihood of participants being able to make ends meet.

The list of 128 essential medicines made available in the study was adapted from the WHO Model List of Essential Medicines and based on Canadian clinical practice guidelines, suggestions from clinicians and patients, prescribing volumes and evidence syntheses. The medicines in the study included treatments for acute conditions, such as antibiotics and pain relievers, as well as chronic conditions, such as antipsychotics and HIV-AIDS medications.

"It is sad that in a high-income country like Canada, millions of Canadians cannot afford their prescribed medications - including life-saving medicines such as insulin," said Dr. Nav Persaud, a clinician-scientist at the Li Ka Shing Knowledge Institute of St. Michael's and lead author of the study.

"We hope that our findings help inform public policy changes. This is no longer a question of whether free distribution of medicines can improve health outcomes. It is a question of whether governments will act."

A total of 786 patients across nine primary care sites in Ontario who reported cost-related non-adherence to medications participated in the study. They were assessed at 12 months into the three-year study. Participants in the intervention arm of the study were randomly allocated to receive free distributions of essential medicines, while others in the control arm of the study had only their usual access to medication.

Dr. Persaud said Canada is considered a suitable setting to measure the effects of free medicine distribution because health care services such as physician visits and hospitalizations are publicly funded while there are cost barriers to medications.

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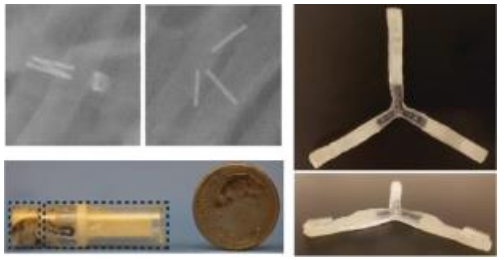
New capsule can orally deliver drugs that usually have to be injected

Coated pill carries microneedles that deliver insulin and other drugs to the lining of the small intestine

CAMBRIDGE, MA -- Many drugs, especially those made of proteins, cannot be taken orally because they are broken down in the gastrointestinal tract before they can take effect. One example is insulin, which patients with diabetes have to inject daily or even more frequently.

In hopes of coming up with an alternative to those injections, MIT engineers, working with scientists from Novo Nordisk, have designed a new drug capsule that can carry insulin or other protein drugs and protect them from the harsh environment of the gastrointestinal tract.

When the capsule reaches the small intestine, it breaks down to reveal dissolvable microneedles that attach to the intestinal wall and release drug for uptake into the bloodstream.



MIT

"We are really pleased with the latest results of the new oral delivery device our lab members have developed with our collaborators, and we look forward to hopefully seeing it help people with diabetes and others in the future," says Robert Langer, the David H. Koch Institute Professor at MIT and a member of the Koch Institute for Integrative Cancer Research.

In tests in pigs, the researchers showed that this capsule could load a comparable amount of insulin to that of an injection, enabling fast uptake into the bloodstream after the microneedles were released.

Langer and Giovanni Traverso, an assistant professor in MIT's Department of Mechanical Engineering and a gastroenterologist at Brigham and Women's Hospital, are the senior authors of the study, which appears today in *Nature Medicine*. The lead authors of the paper are recent MIT PhD recipient Alex Abramson and former MIT postdoc Ester Caffarel-Salvador.

Microneedle delivery

Langer and Traverso have previously developed several novel strategies for oral delivery of drugs that usually have to be injected. Those efforts include a pill coated with many tiny needles, as well as star-shaped structures that unfold and can remain in the stomach from days to weeks while releasing drugs.

"A lot of this work is motivated by the recognition that both patients and health care providers prefer the oral route of administration over the injectable one," Traverso says.

Earlier this year, they developed a blueberry-sized capsule containing a small needle made of compressed insulin. Upon reaching the stomach, the needle injects the drug into the stomach lining. In the new study, the researchers set out to develop a capsule that could inject its contents into the wall of the small intestine.

Most drugs are absorbed through the small intestine, Traverso says, in part because of its extremely large surface area --- 250 square meters, or about the size of a tennis court. Also, Traverso noted that pain receptors are lacking in this part of the body, potentially enabling pain-free micro-injections in the small intestine for delivery of drugs like insulin.

To allow their capsule to reach the small intestine and perform these micro-injections, the researchers coated it with a polymer that can survive the acidic environment of the stomach, which has a pH of 1.5 to 3.5. When the capsule reaches the small intestine, the higher pH (around 6) triggers it to break open, and three folded arms inside the capsule spring open.

Each arm contains patches of 1-millimeter-long microneedles that can carry insulin or other drugs. When the arms unfold open, the force of their release allows the tiny microneedles to just penetrate the topmost layer of the small intestine tissue. After insertion, the needles dissolve and release the drug.

"We performed numerous safety tests on animal and human tissue to ensure that the penetration event allowed for drug delivery without causing a full thickness perforation or any other serious adverse events," Abramson says.

To reduce the risk of blockage in the intestine, the researchers designed the arms so that they would break apart after the microneedle patches are applied.

Insulin demonstration

In tests in pigs, the researchers showed that the 30-millimeter-long capsules could deliver doses of insulin effectively and generate an immediate blood-glucose-lowering response. They also showed that no blockages formed in the intestine and the arms were excreted safely after applying the microneedle patches.

"We designed the arms such that they maintained sufficient strength to deliver the insulin microneedles to the small intestine wall, while still dissolving within several hours to prevent obstruction of the gastrointestinal tract," Caffarel-Salvador says.

Although the researchers used insulin to demonstrate the new system, they believe it could also be used to deliver other protein drugs such as hormones, enzymes, or antibodies, as well as RNA-based drugs.

"We can deliver insulin, but we see applications for many other therapeutics and possibly vaccines," Traverso says. "We're working very closely with our collaborators to identify the next steps and applications where we can have the greatest impact."

The research was funded by Novo Nordisk and the National Institutes of Health. Other authors of the paper include Vance Soares, Daniel Minahan, Ryan Yu Tian, Xiaoya Lu, David Dellal, Yuan Gao, Soyoung Kim, Jacob Wainer, Joy Collins, Siddartha Tamang, Alison Hayward, Tadayuki Yoshitake, Hsiang-Chieh Lee, James Fujimoto, Johannes Fels, Morten Revsgaard Frederiksen, Ulrik Rahbek, and Niclas Roxhed.

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Large, long-term study suggests link between eating mushrooms and a lower risk of prostate cancer

Results from the first long-term cohort study of more than 36,000 Japanese men over decades suggest an association between eating mushrooms and a lower risk of prostate cancer.

Their findings were published on September 5, 2019 in the International Journal of Cancer.

Prostate cancer begins when cells in the prostate gland -- a small walnut-shaped gland found only in men, which produces the fluid that forms part of the semen -- start to grow out of control. It is one of the most common forms of cancer affecting men, with over 1.2 million new cases diagnosed worldwide in 2018, the risk increasing with age.

A new study suggests a potential link between including mushrooms in the diet and a lower risk of prostate cancer. **Mushroom Council**

Mushrooms are widely in used in Asia, both for their nutritional value and medicinal properties.

"Test-tube studies and studies conducted on living organisms have shown that mushrooms have the potential to prevent prostate cancer," said Shu Zhang, an assistant professor of epidemiology in the Department of Health Informatics and Public Health at Tohoku University School of Public Health, Graduate School of Medicine in Japan, and lead author of the study.

"However, the relationship between mushroom consumption and incident prostate cancer in humans has never been investigated before."

"To the best of our knowledge, this is the first cohort study indicating the prostate cancer-preventive potential of mushrooms at a population level," said Zhang. "Although our study suggests regular consumption of mushrooms may reduce the risk of prostate cancer, we also want to emphasize that eating a healthy and balanced diet is much more important than filling your shopping basket with mushrooms." said Zhang.

For this study, the researchers monitored two cohorts consisting of a total of 36,499 men between the ages of 40 and 79 years in Miyagi and Ohsaki, Japan, from 1990 and 1994 respectively. The follow-up duration for the Miyagi cohort extended from June 1, 1990 to December 31, 2014 (24.5 years), while the follow-up duration for the Ohsaki cohort extended from January 1, 1995 to March 31, 2008 (13.25 years). The men were asked to complete a questionnaire related to their lifestyle choices, such as mushroom and other food consumption, physical activity, smoking and drinking habits, as well as provide information on their education, and family and medical history.

Long-term follow-up of the participants indicated that consuming mushrooms on a regular basis reduces the risk of prostate cancer in men, and was especially significant in men aged 50 and older and in men whose diet consisted largely of meat and dairy products, with limited consumption of fruit and vegetables. Statistical

analysis of the data (using the Cox proportional hazards model) indicated that regular mushroom consumption was related to a lower risk of prostate cancer regardless of how much fruit and vegetables, or meat and dairy products were consumed. Of the participants, 3.3% developed prostate cancer during the follow-up period. Participants who consumed mushrooms once or twice a week had an 8% lower risk of developing prostate cancer, compared to those who ate mushrooms less than once per week, while those who consumed mushrooms three or more times per week had a 17% lower risk than those who ate mushrooms less than once a week.

According to Zhang, "mushrooms are a good source of vitamins, minerals and antioxidants, especially L-ergothioneine" -- which is believed to mitigate against oxidative stress, a cellular imbalance resulting from poor diet and lifestyle choices and exposure to environmental toxins that can lead to chronic inflammation that is responsible for chronic diseases such as cancer.

"The results of our study suggest mushrooms may have a positive health effect on humans," said Zhang. "Based on these findings, further studies that provide more information on dietary intake of mushrooms in other populations and settings are required to confirm this relationship."

"Considering the average American consumes less than 5 grams of mushrooms per day, which is lower than that consumed by the participants in this study (7.6 g/day) one would expect that even a small increase in mushroom consumption to offer potential health benefits," said Zhang.

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Cell death blocker prevents healthy cells from dying

Scientists in Australia have developed a world-first compound that can keep cells alive and functioning in a perfectly healthy state when they otherwise would have died.

by Walter and Eliza Hall Institute

The ability to swiftly intervene and prevent cell death, or apoptosis, could be game-changing for medical emergencies and procedures, such as minimising cellular damage after heart attacks, or preserving organs for transplants.

The preclinical findings, published in the journal *Nature Chemical Biology*, follow 11 years of collaborative research at the Walter and Eliza Hall Institute of Medical Research—a world leader in cell death studies. The study was led by Professor David Huang, Professor Guillaume Lessene and Professor Benjamin Kile, who is now at Monash University.

Professor Lessene, head of the Institute's New Medicines and Advanced Technologies theme, said the new 'cell death blocker' was exceptional for its ability to keep cells alive and healthy in the laboratory.

"Never before have we seen such promising ability to intervene in the earliest stages of apoptosis before irreversible damage occurs," Professor Lessene said.

Professor Huang, a laboratory head in the Institute's Blood Cells and Blood Cancers division, said the ability to stop unwanted cell death could be invaluable for the future of medical care.

"Acute injury can cause cells to die rapidly leading to the loss and weakening of tissues and muscles. In such circumstances, being able to prevent uncontrolled cell death could improve a patient's recovery, or even their chances of survival," Professor Huang said.

Apoptosis is a form of tightly regulated cell death essential for health and development. This process is controlled by the 'BCL-2 family' of proteins. Within this family, some proteins promote cell survival, while others drive cell death. Proteins called BAK and BAX are involved in a critical step of cell death known as the 'point of no return'. Cells are committed to die once either BAK or BAX is activated.

Professor Kile, Head of Anatomy and Developmental Biology at the Monash Biomedicine Discovery Institute, said the compound successfully disabled BAK. "In laboratory models we found we could override apoptosis and keep cells functioning," he said. "We have shown it is possible to halt the biochemical cascade that triggers cell death, right at the point where it begins".

The proof-of-concept drug was developed through extensive medicinal chemistry following a high throughput screening campaign of a quarter of a million potential small drug molecules.

The laboratories involved have since formed the foundation of the Walter and Eliza Hall Institute's National Drug Discovery Centre, a world-class facility that has opened for scientists across Australia to pursue their drug discovery journeys without having to head overseas.

The Institute's expertise in cell death research spans more than 30 years, beginning with the landmark discovery in the late 1980s that the protein BCL-2 could enable prolonged cancer cell survival. This critical discovery helped to inform the development of an anti-cancer treatment for patients with leukaemia.

The new research shines light on 'the other side of the same coin'; offering hope that one day drugs that successfully intervene to block apoptosis could be used to treat conditions such as cardiovascular diseases and degenerative disorders.

The researchers are now looking to apply the knowledge to developing cell death blockers that are effective and safe in humans. Professor Huang said the next steps would also involve applying the knowledge we have gained to more advanced models of disease. "There could be applications for keeping cells alive to prevent degenerative diseases," he said.

More information: *A small molecule interacts with VDAC2 to block mouse BAK-driven apoptosis, Nature Chemical Biology (2019). DOI: 10.1038/s41589-019-0365-8 , https://nature.com/articles/s41589-019-0365-8*

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Unlocking the secrets of gallstones

Mechanism for the formation of gallstones has been discovered

We know all too well from fairy tales that stones in your stomach generally aren't good for your health. However, while the stones in these stories are placed in the wolf's belly, the human body can cunningly produce stones by itself. How stones are formed in the body was previously unknown, despite the fact that gallstones are among the ten most common reasons for a stay in hospital. The secret behind gallstones has now been revealed by a team of researchers at the Department of Medicine 1 and 3 at Universitätsklinikum Erlangen at FAU. The researchers' findings have recently been published in the journal Immunity.

Gallstones and the problems they cause are very common. Around 25 million Americans as well as 6 million people in Germany have gallstones that can not only cause extremely painful colic but also life-threatening infections in the abdomen. Patients who have gallstones very often need surgery to remove them. Surprisingly, very little was known until now about how these stones form and what they comprise of. Whilst scientists have known that crystals are involved, and in the case of gallstones, these are usually crystals of cholesterol, little or no research had been conducted up to now about how gallstones are formed from microscopic crystals and the mechanism behind this process has now been discovered.

During their research, Dr. Luis Munoz, Sebastian Böltz and Prof. Dr. Martin Herrmann from the Department of Medicine 3, who collaborate in Collaborative Research Centre 1181 and were supported by a team led by Dr. Moritz Leppkes and Prof. Dr. Markus F. Neurath at the Department of Medicine 1 at FAU, had to use an unconventional approach that took them to museums, abattoirs and operating theatres. They investigated human gallstones from the collection kept at the museum at the Charité

hospital in Berlin, bile from pigs from an abattoir and bile and gallstones from patients who underwent surgery to the abdomen. During the detailed investigation of these materials using modern methods, the team made a very surprising discovery. All gallstones are covered with the traces of a special type of white blood cell called neutrophil granulocytes. These cells are the body's first form of defence and they attack bacteria and other pathogens and also identify crystals as a threat. While attempting to ingest the crystals, these cells die and cover the crystals with their genetic material like a net. These nets, or neutrophil extracellular traps (NET), wind themselves around the crystals, clump them together and thus form stones that can take on surprising proportions.

'We observed that the nets, when released in the already sticky bile, clumped together calcium and cholesterol crystals to form gallstones. The production of gallstones can be greatly reduced or even stopped if the formation of these nets is inhibited using drugs,' says Dr. Munoz. This discovery has opened up previously unknown options for the treatment of gallstones. A simple pharmacological approach could be especially useful, for example, the use of Metoprolol, which is a so-called beta blocker that has been used successfully for many years for the treatment of high blood pressure. Metoprolol prevents neutrophil granulocytes from entering tissue from the blood supply, thus reducing the capacity for forming nets and therefore gallstones. In addition, specific inhibitors for preventing the formation of nets from neutrophil granulocytes, so-called PAD inhibitors, are already known that can inhibit the formation of gallstones produced in experiments, thus proving the significance of the immune system for the formation of these structures. The FAU research team also emphasises that this process is significant not only for gallstones, but also for other types of stones in the body such as kidney stones or salivary stones.

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Not Brain Dead: Patient Trapped in Vegetative State by Unethical Doctors

A man was kept in a vegetative state to save a hospital's reputation. What does that mean?

By Nicoletta Lanese - Staff Writer

A New Jersey hospital kept a patient alive in a vegetative state for nearly a year — not because the patient or his family requested it, but because the medical staff wanted to maintain the survival rate statistics used to evaluate their heart-transplant program, according to an investigative report by ProPublica.

As Caroline Chen reported, in recordings of his meetings with medical staff, the director of the hospital's heart and lung transplant programs said, "I'm not sure that this is ethical, moral or right," but it's "for the global good of the future transplant recipients."

What ProPublica uncovered was an incredible breach of medical ethics — and not just because his family was deprived of the opportunity to decide what was the best care option for him. To fully appreciate why, you only need to understand what being in a "vegetative state" really means. A vegetative state differs both from a coma and brain death. Being in a persistent vegetative state for over a year means that a person is unlikely to recover, but it does not mean that a person cannot feel pain or discomfort. In this case, the hospital staff prioritized their own prerogatives over their patient's quality of life.

When a patient enters a vegetative state

Sixty-one-year-old Darrel Young underwent heart transplant surgery on Sept. 21, 2018, at Newark Beth Israel Medical Center. Young never awoke from surgery, instead falling into a vegetative state. If he had died, the hospital's heart transplant program survival rate would have dropped to 84.2% — which would have triggered scrutiny by the federal government.

In a recording, transplant program director Dr. Mark Zucker said the team would "need to keep [Young] alive till June 30 at a minimum." It was then that a federally funded organization that tracks transplant survival rates would file its next report. "If he's not dead in this report, even if he's dead in the next report, it becomes an issue that moves out six more months," Zucker said in a recording.

So Young was kept alive in a vegetative state. But what exactly does that mean? The term "vegetative state" sounds a lot like "coma" or "brain-dead," but there are actually clear distinctions between each of these conditions.

Not brain-dead

The term "vegetative state" conjures images of patients lying still in hospital beds , unresponsive, their heart-rate monitor bleeping quietly in the background. In reality, people in a vegetative state may move, groan, and open their eyes, according to Johns Hopkins Medicine. Although their consciousness is diminished, a vegetative patient may perform involuntary muscle movements and react to loud sounds or feelings of pain. They may also exhibit wake-sleep cycles, meaning they continue to wake up in the morning, then fall asleep at night as they did when they were healthy.

At first glance, a patient in a persistent vegetative state resembles one in a coma, but comatose patients are far less responsive.

Both vegetative and comatose patients retain some brain stem function, meaning that they maintain some ability to breathe on their own, and exhibit other reflexes, like pupil dilation in response to bright lights, according to the Finger Lakes Donor Recovery Network. However, comatose patients do not open their eyes, nor do they speak. Their condition may resolve in a few days or weeks, or the patient may progress to a vegetative state, according to Johns Hopkins Medicine.

When patients fall into a profoundly deep coma, the electrical activity in their brains may even flatline, but research suggests that even these patients can eventually come back online, Live Science previously reported.

Brain-death is a different story.

When brain death occurs, the organ loses all functionality, including that of the brain stem, according to the Cleveland Clinic. These patients may sweat or perform spontaneous limb movements, but they are unconscious, unresponsive, and cannot breathe properly without the support of a respirator.

A test known as the "apnea test" determines whether the patient displays respiratory responses supported by the brain stem, according to ClinicalTrials.gov.

The test involves saturating a patient's blood with oxygen then removing them from their ventilator to see if their respiratory response kicks in. Specific levels of carbon dioxide in a person's arterial blood and physical signs of breathing indicate that they are not brain dead.

If the patient shows no respiratory response at this point, they can be declared both clinically and legally dead, according to the legal information site FindLaw.

Staying alive

From the depths of his vegetative state, Darrel Young would occasionally open his eyes, according to ProPublica, but his medical records noted that he "follow[ed] no commands. He look[ed] very encephalopathic," meaning his brain had clearly been damaged — in fact, the organ suffered injury during Young's transplant surgery.

Doctors have trouble predicting which people will recover after a brain injury puts someone into a vegetative state, though monitoring for distinct patterns of brain activity may help doctors predict which patients are most likely to pull through, Live Science

reported. A 2017 study also suggested that nerve stimulation may help revive vegetative patients, even in people who were in that state as long as 15 years.

Generally, patients who enter a vegetative state for more than four weeks are considered unlikely to recover, and their chances only worsen after a full year in limbo, according to Johns Hopkins. Though doctors at Newark Beth Israel told Young's family he may make a "full recovery," in truth, they expected no such outcome, ProPublica reported. In the meantime, they kept Young alive.

Patients can be sustained in a vegetative state as long as their healthcare providers give standard supportive care, according to the medical reference site Merck Manual.

This includes providing adequate nutrition and water, normally through a feeding tube; administering physical therapy to keep the muscles from seizing up; and working to prevent the development of disease or infection made more likely by the patient being immobilized (such as bedsores).

Young was treated for pneumonia, strokes, seizures and a fungal infection while in his vegetative state, according to the investigative report.

He was also placed on a ventilator overnight to support his breathing, and nurses pumped mucus from a hole in his throat several times a day.

Young made it to the one-year anniversary of his operation, ProPublica reported, and thus Newark Beth Israel met their transplant survivor quota.

The patient's family was informed that Young could now be transferred to a long-term care facility, and his sister asked why he was suddenly being moved after a year of stagnation. She never received a clear answer.

You can read the full, shocking story at ProPublica.

http://bit.ly/2nDnnFq

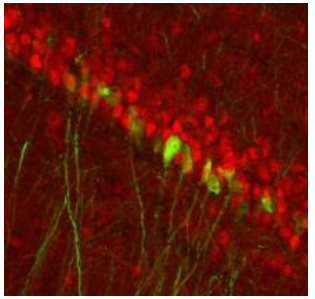
Scientists find gender-distinct circuit for depression

A single circuit in mice that activates during stress and is controlled by testosterone

EAST LANSING, Mich. - Depression affects women nearly twice as much as men, but unraveling the brain's blueprint that regulates this behavior, let alone identifying specific molecular differences between sexes, has proven difficult.

Michigan State University researchers, however, have found and flipped a switch in the brain, revealing a single circuit in mice that activates during stress and is controlled by testosterone.

The results, published in Biological Psychiatry, focus on the activity between neurons in the ventral hippocampus, which become active under stress and emotion, and their activation of nucleus accumbens neurons, critical players in reward and motivation.



MSU researchers have found a gender-distinct circuit for depression that activates during stress and is controlled by testosterone. **MSU**

"What makes these findings stand out is not only identifying this new circuit," said A.J. Robison, MSU physiologist and lead author of the study, "but also observing and confirming how it drives different behaviors in males and females."

Oddly enough, many circuit-specific animal model studies involving depression-related behaviors don't include female subjects. This gap exists despite sex differences in several depression-related brain regions, including the hippocampus, Robison added.

To help close this void, Robison and a team of MSU scientists focused on this hippocampus-accumbens circuit and saw that the activity in male brains during stress was significantly lower than in

females, and this required testosterone. When they removed testosterone, however, the male mice began expressing depression-like behaviors.

Conversely, the team observed increased circuit activity in female brains, but when testosterone was introduced, the neurons quieted, and the female mice became resistant to the depression-like behaviors.

"Even with our best antidepressants, such as Prozac, we don't know exactly how they work," Robison said. "This is the first time we've found a circuit that drives this sexually different behavior; other scientists can now explore how this could translate to identifying new therapeutic targets in humans."

Robison's group used chemogenetic tools to manipulate specific circuit activity in the mouse brain in this study. Such tools may inform the development of "genetic medicine" for the treatment of human diseases in the future.

Additional MSU scientists who contributed to this research include: Elizabeth Williams, Claire Manning, Andrew Eagle, Ashlyn Swift-Gallant (now at Memorial University of Newfoundland), Natalia Duque-Wilckens, Sadhana Chinnusamy, Adam Moeser, Cynthia Jordan and Gina Leinninger.

This research was funded in part by the National Institutes of Mental Health, the National Institutes of Neurological Disease and Stroke, the National Institutes of Drug Abuse and the Avielle Foundation. ***Original Paper Online:***
https://www.biologicalpsychiatryjournal.com/article/S0006-3223(19)31618-X/pdf

http://bit.ly/2OHLcau

Dietary supplement from tomatoes discovered to boost sperm quality

New discovery could transform outlook for men with fertility problems

Sperm quality can be improved with a simple diet supplement containing a compound found in cooked tomatoes, according to new research by the University of Sheffield.

The discovery could transform the outlook for men with fertility problems and lead to better ways to reduce the damaging impact of modern living on reproductive health. Of all infertility cases, approximately 40 to 50 per cent are due to "male factor" infertility.

The first ever double-blind randomised controlled trial to assess the impact of giving men a dietary compound called LactoLycopene, was led by Allan Pacey, Professor of Andrology Reproduction and Head of the University of Sheffield's Department of Oncology and Metabolism, and Dr Liz Williams, a leading specialist in Human Nutrition at the University of Sheffield. The team discovered it is possible to increase the proportion of healthy shaped sperm (sperm morphology) and boost 'fast swimming' sperm by around 40 per cent.

Lycopene can be found in some fruits and vegetables, but the main source in the diet is from tomatoes. Lycopene is a pigment that gives tomatoes their red colour, but dietary Lycopene is poorly absorbed by the human body, so the compound used for the trial was a commercially available formulation called LactoLycopene; designed by FutureYou Cambridge to improve bioavailability.

The 12-week trial designed by Dr Williams involved 60 healthy volunteers aged 19 to 30. Half took LactoLycopene supplements and the other half took identical placebo (dummy pills) every day for 12 weeks. Neither the researchers nor the volunteers knew who was receiving the LactoLycopene treatment and who was receiving the placebo. Sperm and blood samples were collected at the beginning and end of the trial.

"We didn't really expect that at the end of the study there would be any difference in the sperm from men who took the tablet versus those who took the placebo. When we decoded the results, I nearly fell off my chair," said Professor Pacey, a world expert in male reproduction.

"The improvement in morphology - the size and shape of the sperm, was dramatic. We used a computer system to make these measurements, which takes a lot of the human error out of the

results. Also, the person using the computer didn't know who had taken LactoLycopene and who had taken the dummy pills either.

"This was the first properly designed and controlled study of the effect of LactoLycopene on semen quality, and it has spurred us to want to do more work with this molecule."

"We were surprised by the improvement in sperm quality shown by the results," said Dr Williams.

"This was a small study and we do need to repeat the work in bigger trials, but the results are very encouraging. The next step is to repeat the exercise in men with fertility problems and see if LactoLycopene can increase sperm quality for those men and whether it helps couples conceive and avoid invasive fertility treatments."

Her team, which included three other researchers Madeleine Park, Aisling Robinson and Sophie Pitt, is hoping to embark on the new study as soon as possible.

Professor Pacey said the work so far has not investigated the mechanism for Lycopene's beneficial action but it is a known powerful antioxidant, so is potentially inhibiting the damage caused by oxidation of sperm which is a known cause of male fertility problems. He believes this antioxidant effect is key in producing the improvements in sperm quality seen in the trial, and is hoping to investigate this more. The results have been published in the European Journal of Nutrition.

http://bit.ly/2OJFu7M

Vaginal-fluid transplants treat incurable condition in pilot study

Transplanted vaginal fluids fully restored healthy microbiomes in 4 of 5 women.

Beth Mole

Vaginal-fluid transplants appeared to successfully treat devastating vaginal conditions that had failed all other treatments options, according to a small pilot study published this week in Nature Medicine. The study comes amid a gush of enthusiasm for the transplants, often dubbed vaginal microbiota transplants (VMTs). Though researchers are only now getting down to investigating their potential, many are optimistic that the microbe-toting fluid swaps will prove broadly successful at treating swaths of conditions in more rigorous trials.

In a recent conceptual study on screening potential fluid donors, Johns Hopkins researchers suggested that the transplants could "revolutionize the way we view and treat conditions affecting the female reproductive tract."

With the mood set, a team of Israeli researchers had been working on a first exploratory trial since 2014. The trial included five women (aged 27 to 47), who all suffered from intractable cases of bacterial vaginosis (BV) but were otherwise healthy. BV is a condition marked by alterations to the microbial communities that typically reside in the vagina, which can lead to a range of problems—from malodorous vaginal discharge to increased risks of upper-genital-tract infections and pregnancy complications, as well as greater susceptibility to sexually transmitted infections.

The women had experienced at least four bouts of symptoms from their condition in the previous year and endured repeated antibiotic regimens to try to kick the condition without success. They all reported that their BV had significant effects on their lives, including harming their relationships and self-esteem.

Microbial migration

Those BV patients were treated with microbe-laden vaginal fluids collected from three rigorously screened donors. The three volunteers (aged 35 to 48) submitted extensive medical records, had no history of BV, tested negative for sexually transmitted infections and other conditions, and reported no use of various medications. All reported abstaining from sexual activity for at least a week prior

to donating—two reported they had been sexually inactive for eight or more years, and one was in a 25-year monogamous relationship.

Analysis of their vaginal fluids suggested healthy vaginal microbial communities, which are typically dominated by *Lactobacillus*. In general, vaginal microbiomes are considered less complex and variable than those found in the intestines, despite also playing critical roles in health. All of the transplant recipients were primed for the donor fluids with an intravaginal antibiotic regimen. The fluids were then transplanted within 60 minutes of collection.

Two of the recipients showed long-term BV remission after just one transplant. They reported improvement in symptoms within one week of the procedure and stayed in remission for their follow-up periods, which lasted up to 11.5 months. Two others ended up undergoing three transplants before achieving complete remission through their follow-up periods, which lasted up to 21 months. Genetic analyses suggested that the recipients' vaginal microbiomes had shifted to look more like the donor communities.

The last recipient only achieved a partial resolution of BV, but her case was complicated by a throat infection that required her to take oral antibiotics after her first transplant. After that treatment, her BV symptoms returned. She underwent another transplant, which improved her symptoms and clinical signs of BV. But, at 6.5 months of follow-up, her vaginal microbial communities looked like a mix of her original community and the donor community.

"Collectively," the authors conclude, "we report the feasibility of using VMT as a long-term treatment for recurrent, antibiotics-nonresponsive, and intractable BV."

Now, with safety and benefits documented, "the efficacy of VMT as a treatment in intractable BV needs to be determined in randomized, placebo-controlled trials." Currently, there are at least two such trials in the works.

Nature Medicine, 2019. DOI: 10.1038/s41591-019-0600-6 (About DOIs).

http://bit.ly/32d6al9

Hip pain? Turn on your inner salamander

These clever little critters could teach us how to regrow cartilage.

Paul Biegler reports.

Repairing the worn-out cartilage in your dicky knee or even growing a whole new leg could one day be as simple as switching on your "inner salamander", according to new research published in *Science Advances*.

The salamander has the ability to regrow entire limbs following a trauma. **picture alliance**

The salamander – one incarnation of which is the bizarre-looking axolotl or Mexican walking fish – has the enviable ability to regrow entire limbs and even bits of major organs after an unfortunate accident.

It's a trick that would be very handy for people who have worn out the cartilage lining their hip or knee. Wear and tear can lead to bone scraping on bone and painful osteoarthritis, a leading reason for joint replacement surgery.

It has been thought that cartilage has a limited capacity to repair itself. But the new research, led by rheumatologist Virginia Kraus from the Duke University School of Medicine in North Carolina, US, finds that humans have an axolotl-style "switch" that could turn on cartilage growth.

To get their study rolling the team procured cartilage from the hips, knees and ankles of 18 people who had joint surgery for osteoarthritis or trauma.

Then they set about grading the biological age of the cartilage using a "molecular clock" that measures changes in two protein building blocks, asparagine and glutamine.

With a technique called mass spectrometry, the researchers could tell which cartilage samples had a higher turnover of protein, and so were regenerating more quickly. These specimens qualified as a "younger" example of the genre.

So, where do the cartilaginous youth like to hang out? Not surprisingly, perhaps, as "far out" as possible.

The molecular clock showed that ankle cartilage was noticeably younger than knee cartilage, which was younger again than the gristly stuff lining the hip.

Now that age gradient, from old hips down to young ankles, bears a curious likeness to the greater ability of some species, salamanders included, to regrow the bits further out on their limbs or tails.

The resemblance, the researchers have found, is no accident.

Humans share a regulator in the form of something called microRNA with salamanders; it controls formation of the limb bud or "blastema" in those slimy suckers and it also has a hand in making cartilage in people. MicroRNA, the team found, becomes more active as the joints descend, from hip down to ankle.

"We were excited to learn that the regulators of regeneration in the salamander limb appear to also be the controllers of joint tissue repair in the human limb," says the paper's first author Ming-Feng Hsueh, also from Duke.

"We call it our 'inner salamander' capacity," he says.

MicroRNA is also increased in the cartilage of joints affected with osteoarthritis, suggesting it is involved in repair of those joints. Which Kraus thinks could open the door to a whole new class of therapeutics. "We believe we could boost these regulators to fully regenerate degenerated cartilage of an arthritic joint," she says.

"If we can figure out what regulators we are missing compared with salamanders, we might even be able to add the missing components back and develop a way someday to regenerate part or all of an injured human limb."

http://bit.ly/2VCP0uR

Girl Diagnosed with Fatal Brain Disease Gets a Tailor-Made Drug within a Year

In a striking example of personalized medicine, doctors developed a tailor-made genetic treatment for the patient in just a year.

By Rachael Rettner - Senior Writer

When Mila Makovec was diagnosed with a rare neurological condition at age 6, her prognosis was grim. The condition, known as Batten disease, is fatal, with death usually occurring in late childhood or the early teen years. There is no cure, and at the time of Mila's diagnosis, in 2016, there was no specific treatment for her condition.

Mila Makovec at age 2, before she was diagnosed with a rare and fatal brain disease. **(Image: © Cliff Grassmick/Digital First Media/Boulder Daily Camera via Getty Images)**

But that soon changed. In a striking example of personalized medicine, doctors were able to develop a tailor-made genetic treatment for Mila and to initiate the therapy, all within a year of first seeing the patient, according to a new report of her case, published today (Oct. 9) in The New England Journal of Medicine. That's much shorter than the years or even decades it typically takes to develop new drugs.

What's more, the therapy appears safe, and Mila is showing signs of improvement; in particular, she is having shorter and fewer seizures than before, the report said. However, it's unclear exactly how much the treatment will help Mila in the long run or whether it will prolong her life.

Still, the report's authors, from Boston Children's Hospital, said that her case can serve as a "template" for the rapid development of tailored genetic treatments. "This report shows a path to

personalized treatments for patients with orphan diseases," the authors said, using a term for diseases that affect fewer than 200,000 people in the nation.

The study was funded in part by Mila's Miracle Foundation, a charity started by Mila's family to find a cure for Batten disease and other devastating neurological diseases.

Devastating diagnosis

As an infant and young toddler, Mila appeared healthy, learning to walk at age 1 and "talking up a storm" by 18 months, her mother, Julia Vitarello, wrote on the Mila's Miracle Foundation website. But as she grew older, her parents noticed some concerning signs. At age 3, her right foot started to turn inward and she would get stuck on words when talking. At age 4, she started pulling books closer to her face when looking at them, and at age 5, she began stumbling and falling backward.

Shortly before she turned 6, she was hospitalized for a rapid progression of symptoms, including vision loss, frequent falls, slurred speech and difficulting swallowing. Tests showed that her brain volume was shrinking, and she was having seizures, the report said.

Further lab and genetic testing finally led to her diagnosis: She had Batten disease, a rare and fatal genetic disorder of the nervous system that can take several forms depending on the specific genetic mutation involved. But all forms of the disease appear to affect structures inside cells known as lysosomes, which function as the cell's "trash can" or "recycle bin," breaking down waste products to be discarded or recycled, according to the National Institutes of Health. Without properly working lysosomes, junk material builds up, leading to cell death, including the death of brain and eye cells.

A detailed analysis of Mila's genome revealed that she had a unique mutation in a gene called CLN7, which is known to be associated with Batten disease. The authors found that a chunk of extra DNA had inserted itself into the CLN7 gene. This meant that when the cell tried to read the gene's instructions to make a protein for the lysosome, the instructions were getting prematurely cut off, preventing the cell from making the full protein.

Doctors realized that a type of genetic treatment that uses molecules called antisense oligonucleotides might work for Mila's case. These are short, synthetic molecules of genetic material (known as nucleic acids) that bind to the patient's faulty genetic instructions, essentially masking the error so the full protein can be produced, according to Boston Children's Hospital.

Doctors named the drug they created "milasen" after Mila. It resembles a recently approved drug for spinal muscular atrophy called nusinersen (brand name Spinraza).

Studies of samples of Mila's cells suggested that milasen could help rescue the lysosome function, and studies in animals suggested there would be no harmful side effects, the report said.

After the doctors received approval from the Food and Drug Administration for a one-person trial of milasen, Mila started treatment in January 2017. The drug was given as an injection into her spinal cord.

Results from the first year of her treatment suggested an improvement in seizures. Before the study, Mila experienced about 15 to 30 seizures per day, each lasting up to 2 minutes, as measured by reports from her parents. But over the course of her treatment, that frequency dropped to between zero and 20 seizures per day, and the duration decreased to less than 1 minute, the authors said.

Measures of Mila's brain waves also showed a decline of greater than 50% in the frequency and duration of the seizures. The treatment didn't cause any harmful side effects.

Personalized medicine

Mila's treatment "offers great hope," Vitarello wrote on the foundation website. "While we remain cautiously optimistic, we feel so fortunate that Mila was given a second chance."

Still, before Mila began the therapy, she lost the ability to see, speak and walk without assistance, and the treatment has not reversed these effects, Science Magazine reported.

Although friends have asked if Mila is now cured and will be able to have a normal life, "it's not that simple," Vitarello said. "Batten disease affects every part of the brain and body. It's unbelievably complicated and still very un-understood."

The authors noted that milasen is still an experimental drug, adding that it is not suited to treat other people with Batten disease, because it is specifically tailored to Mila's unique mutation.

Still, Mila's case suggests that antisense oligonucleotides "may deserve consideration as a platform for the rapid delivery of individualized treatments," the authors said. They noted that antisense oligonucleotides are customizable and have a relatively simple manufacturing process. However, the rapid approach used in Mila's case should be considered only in the context of very serious or life-threatening circumstances, the authors said.

https://bbc.in/2VC8qZv

Long-term Lyme disease 'actually chronic fatigue syndrome'

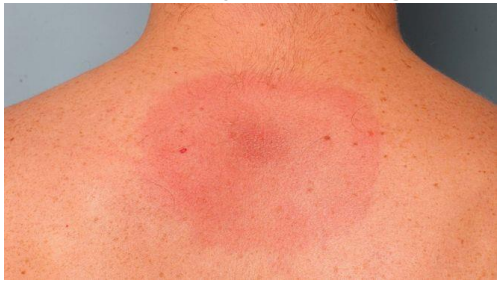
The majority of people who believe they have a chronic form of Lyme disease are more likely to have chronic fatigue syndrome, experts suggest.

There are around 3,000 cases of Lyme disease, caused by tick bites, in the UK each year. Most of those who take antibiotics make a full recovery within months.

But infectious disease doctors are warning that long-term Lyme disease cases are often misdiagnosed through expensive and unvalidated tests abroad.

Dr Sarah Logan, from London's Hospital for Tropical Diseases, said: "Most people who now think they may have had Lyme disease, in fact have a syndrome that is more in keeping with chronic fatigue syndrome."

Speaking at a Science Media Centre briefing, she added: "And because there is increased awareness about it, they are testing for Lyme disease and then they are going on to various different Lyme disease forums on the internet and being told, 'Well actually the UK tests are rubbish, but you need to send it off to Germany.'



The characteristic Lyme disease "bullseye" rash **Science Photo Library**

"Then they are coming back with a test that is positive and saying, 'You doctors are all wrong and I don't have chronic fatigue syndrome, I have chronic Lyme disease.' "I think that most people who think they have got Lyme disease in the UK, probably don't."

'Alternative' diagnosis

She cited two cases she had seen where patients, believing they had chronic Lyme disease, had been taking intravenous antibiotics - one developed a Clostridium difficile infection as a result of being on the medication for more than six months. The second patient also developed a serious infection.

Dr Logan said it could be that chronic fatigue syndrome was a difficult diagnosis for doctors to give, because it could be hard for patients to get treatment and support, and because of persisting negative views of the condition.

"I think there is a bit about patients not wanting to hear it because of all those stigma reasons, and there is a little bit about GPs hoping - probably not unreasonably - and saying, 'Let's look for an alternative diagnosis because then that is something we can treat.'"

When a Lyme disease test comes back negative, patients may decide to seek testing elsewhere, she said, adding that some patients were paying up to £600 for a consultation and test that has not been validated.

Dr Matthew Dryden, a consultant microbiologist at Hampshire Hospitals NHS Foundation Trust, said he was also concerned about the issue of "chronic" Lyme disease.

"These are reported as true cases of Lyme when almost certainly they're not. The symptoms are very real but most medical tests tend to be normal which confuses both doctors and patients."

He said the focus should be improving the management and care offered to patients with chronic fatigue. "It really needs improved research and improved management services for these patients."

What is Lyme disease?

- ***Lyme disease is caused by bacteria carried by some species of ticks - around 13% in the UK are believed to be infected***
- ***It cannot be passed from person to person***
- ***Symptoms - including the bullseye rash, fatigue and fever - usually develop around three weeks after a bite***
- ***The majority of those who take the full three-week course of antibiotics make a full recovery***
- ***The New Forest and the Scottish Highlands are known Lyme disease hotspots - but people should take care wherever there is long grass***
- ***The NHS test, which is highly accurate, looks at antibodies the body produces, which can take some weeks to reach detectable levels***

https://go.nature.com/2Mc3BdN

How treacherous brain cells aid cancer's invasion

The neural cells called astrocytes feed the brain's own fat to metastatic cancer cells.

Malignant cells from various tumours invade the brain with help from an unlikely source: star-shaped cells that are themselves part of the brain.

Metastasis — the spread of cancer cells from their original site in the body to distant organs — causes 80% of cancer deaths. But few therapies target metastatic brain cancer, which can be seeded by cells from melanomas, breast tumours and other cancers.

Qing Chen at the Wistar Institute in Philadelphia, Pennsylvania, and her colleagues found that brain cells called astrocytes encourage the multiplication of cancer cells that have infiltrated the brain. The researchers demonstrated that astrocytes shunt the brain's fatty acids to the invading cancer cells. The fat binds to a protein, PPAR-γ, within metastatic cells and triggers a molecular pathway that results in cell proliferation.

The researchers injected cancer-ridden mice with a compound that blocks PPAR-γ. After the injections, the animals' brain tumors stopped growing — suggesting that PPAR-γ-blocking compounds could help to control brain metastasis. The role of PPAR-γ possibly depends on cancer type; as a result, therapies that target it might help some people with cancer more than others.

Cancer Discov. (2019)

https://bbc.in/2VCbMmv

Israel cave bones: Early humans 'conserved food to eat later'

Scientists in Israel say they have found evidence that early humans deliberately stored bones from animals to eat the fatty marrow later.

It is the earliest evidence that humans living between 200,000 and 420,000 years ago had the foresight to anticipate future needs, they say. Early humans had not previously been thought capable of such dietary planning.

Researchers analysed bone specimens at Qesem cave near Tel Aviv. They identified cut marks on most of the bone surfaces - consistent with preservation and delayed consumption.

The researchers suggest the marks came about because the early humans had to make greater effort to remove skin which had dried on bones which had been kept longer. The cut marks were found on 78% of the more than 80,000 animal bone specimens analysed.

"Bone marrow constitutes a significant source of nutrition and as such was long featured in the prehistoric diet," said Ran Barkai from Tel Aviv University in Israel. "Until now, evidence has pointed to immediate consumption of marrow following the procurement and removal of soft tissues."

Marrow inside a bone after six weeks of storage **PA Media**

Early humans in the area frequently hunted fallow deer. They brought the limbs and skulls of their prey to the cave while the rest of the carcass had the meat and fat removed where it had been killed, Professor Jordi Rosell of Spain's Universitat Rovira i Virgili said.

"We found that the deer leg bones, specifically the metapodials, exhibited unique chopping marks on the shafts, which are not characteristic of the marks left from stripping fresh skin to fracture the bone and extract the marrow," he said.

The researchers simulated conditions in the cave to determine that bone marrow would have remained nutritious for up to nine weeks after the animal had been killed.

http://bit.ly/2B8l7Jw

Food comas and long-term memories -- New research points to an appetizing connection

Connection between food comas--resting after eating--and the formation of long-term memories

There may be a connection between food comas--resting after eating--and the formation of long-term memories, a team of neuroscientists concludes based on its study on brain activity in sea slugs. The research appears the Nature Research journal Scientific Reports.

"The sensation of a 'food coma' after a hearty meal is well known to anyone who has ever experienced a Thanksgiving dinner," says Thomas Carew, a professor in New York University's Center for Neural Science and the paper's senior author. "In fact, most animals tend to slow down and rest after a large intake of calories, suggesting that there is a biological function to this reaction.

"Our new study proposes that such 'rest-and-digest' responses to feeding may have been shaped by evolution to promote the formation of long-term memories."

The team, which included Nikolay Kukushkin, a postdoctoral fellow in the Carew lab, and Sidney Williams, an NYU undergraduate in Global Liberal Studies at the time of the research, studied Aplysia californica, the California sea slug. Aplysia is a model organism that is powerful for this type of research because its neurons are 10 to 50 times larger than those of higher organisms, such as vertebrates, and it possesses a relatively small network of neurons--characteristics that readily allow for the examination of linkages between neurological and other activity.

In their analysis, the scientists also considered existing scholarship on food intake and the brain.

"In humans, food intake promotes the release of the hormone insulin, which prompts the cells of the body to absorb nutrients from the bloodstream and turn them into fat for long-term storage," explains Kukushkin. "However, insulin is thought to have little effect on the brain. By contrast, a related hormone, insulin-like growth factor II, has been shown to be critical for proper brain function, including long-term memory formation. However, its release does not depend on calorie intake.

"Therefore, insulin-like molecules in humans are segregated into at least two distinct functional modules. A metabolic module, represented by insulin, controls feeding and energy balance, while a neurotropic module, centered on insulin-like growth factor II, controls memory formation."

In studying Aplysia, the scientists found that in this species the two distinct modules of insulin-like molecules are, in contrast to humans, unified into a single system that performs both metabolic and neurotropic functions. Moreover, they discovered that a single insulin-like molecule produced in the Aplysia nervous system simultaneously strengthens the contacts between neurons, a mechanism thought to underlie long-term memory, and promotes the absorption of nutrients into the mollusk's tissues.

The research also involved monitoring the slugs' behavioral response to food intake--in this case, their regular diet of seaweed.

Here, when animals were allowed to eat their fill, their movement activity was reduced, and this effect was blocked by preventing insulin-like receptors from working.

"Thus, Aplysia's 'food coma' is controlled by their insulin-like system, which acts by redistributing the animal's energy away from active behavior and towards storage of both nutrients and memory," observes Carew. "These results will help understand the mechanisms by which insulin and similar molecules elicit both their diet-related and memory-enhancing properties in humans and other animals."

The researchers note that Aplysia and humans share the general features of the hormone that forms their insulin systems, which evolved in both species to control nutrition, memory, and behavior. However, in Aplysia, these functions have remained unified, while in the human lineage they became partially independent.

"It remains to be established whether the human 'food coma' is a vestige of our evolutionary past, or still an important part of memory formation," Kukushkin acknowledges. "However, it's been widely established that in an array of animals, including humans, sleep is well known to be required for proper storage of long-term memories acquired during wakefulness."

"Perhaps the drowsiness experienced after a meal is a similar way to preserve a memory about that meal, so as to come back to it in the future," posits Carew. "Whether seaweed or Thanksgiving turkey, a good dinner is always worth revisiting."

DOI: 10.1038/s41598-019-50923-5

http://bit.ly/328LmeJ

It's Possible to Inherit More DNA From One Parent Than the Other

23andMe's 4-million-person database reveals how many people are living with undetected chromosomal anomalies.

Sarah Zhang

Before Natalie Nakles was born, before the egg from which she was conceived was even fully mature, something went slightly awry. The egg that would help form her ended up with two copies of chromosome 16. So today, 24-year-old Nakles does not, as most people do, have one set of chromosomes from each parent. She has two copies of chromosome 16 from her mother and none from her father.

This phenomenon, called uniparental disomy, can happen in any of the 23 pairs of chromosomes. In the scientific literature, it has been linked to spontaneous abortions—and if the fetus survives, skeletal abnormalities, seizures, intellectual disability, and childhood cancers. Nakles has Asperger's syndrome, but she is otherwise healthy. She has no serious health issues. She only found out about her uniparental disomy after sending in her saliva to 23andMe.

Now a new study of DNA from 4.4 million 23andMe customers—as well as 430,000 people in the U.K. Biobank—suggests many other healthy people, like Nakles, are living with uniparental

disomy. The study identified 675 such people and found no significant associations with deleterious traits. Uniparental disomy is both more common and less detrimental than the scientific literature suggested.

"I was really excited to see this paper," says Wendy Robinson, a medical geneticist at the University of British Columbia who was not involved in the study. She had suspected that uniparental disomy occurs in healthy people more often than reported. But until recently, healthy people were not taking DNA tests by the millions. A doctor might see a few patients with an unusual disorder, order DNA tests to discover uniparental disomy, and then publish a paper. It's like only searching for flowerpots under streetlights and concluding that every flowerpot must be under a streetlight.

The people in 23andMe and U.K. Biobank, on the other hand, skew healthy, and it turns out that even healthy people can have what might seem to be big genetic anomalies. "I like to say it's normal to be abnormal," Robinson says. She adds that uniparental disomy sometimes comes up in prenatal tests, and the results can make parents anxious because the existing scientific research is essentially a catalog of everything that can go wrong. This study might add some reassurance. "Just because you have that doesn't automatically mean there's going to be anything wrong with your child," she says.

Uniparental disomy is the result of an error during meiosis, the process that forms eggs and sperm. Scientists have proposed different mechanisms, but the most common scenario probably goes like this: The error in meiosis gives the egg or sperm an extra copy of one chromosome, so the resulting embryo ends up with three copies on it. Sometimes, these embryos are spontaneously aborted, but other times, they are able to go through "trisomy rescue," in which some cells lose that extra third chromosome and eventually outcompete the non-normal cells. The resulting child ends up with the right number of chromosomes, but not necessarily one from each parent.

This is all much more complicated than the standard story of sperm meets egg, yet the result is still a healthy child. "It goes against so many of the rules of biology you've memorized in school," says Priyanka Nakka, a postdoctoral fellow at Boston Children's Hospital and former 23andMe intern who co-wrote the study. Scientists have theorized and later discovered other ways that conception can go very much awry yet still result in healthy children, such as sesquizygotic twins.

When uniparental disomy does lead to health problems, it is for one of two reasons. First, a child might inherit two copies of a rare, recessive mutation from one parent. Second, some genes are normally turned off or on depending on which parent they're inherited from in a phenomenon called "genomic imprinting." That means inheriting two copies from the same parent can cause various health issues. For example, two maternal copies of chromosome 15 leads to Prader-Willi syndrome; two paternal copies leads to Angelman syndrome. They are distinct genetic disorders with very distinct symptoms.

Genomic imprinting does not appear to be spread evenly across all chromosomes though, and uniparental disomy is more serious when on some chromosomes than others. Nakka and her co-authors found that most of the existing papers on uniparental disomy focused on disorders related to chromosomes 6, 7, 11, 14, and 15. But uniparental disomy among relatively healthy people in 23andMe and U.K. Biobank tended to be more common on chromosomes 1, 4, 16, 21, 22, and X.

As at-home DNA tests have become more common, customers have been discovering uniparental disomies on their own. One prominent genetic genealogist, CeCe Moore, told me she had seen about a dozen cases from people who had approached her about

their unusual DNA test results. 23andMe doesn't flag uniparental disomy to customers—and the company says it doesn't plan to—but it's possible to deduce from closely scrutinizing the results.

Nakles figured it out after she and her mom both took 23andMe tests, and she noticed they shared more of chromosome 16 than usual. She got her dad to take a test, too, and it confirmed they shared no segments of chromosome 16 at all. Nakles is a medical student, and she quickly pieced together how she came to be in cellular detail. When we talked, she traced for me the initial error in meiosis and the trisomy rescue that "fixed" it. She marveled at how easily she could have not been born at all.

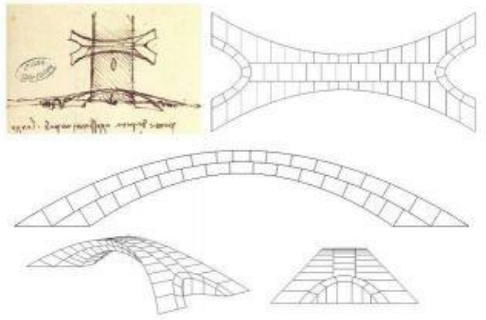
http://bit.ly/33v8KDv

Da Vinci's Forgotten Design for the Longest Bridge in the World Proves What a Genius He Was

It would have been held together by compression only.

By Yasemin Saplakoglu - Staff Writer 3 days ago History

Leonardo da Vinci was truly a Renaissance man, impressing both his contemporaries and modern observers with his intricate designs that spanned many disciplines. But although he's best known for iconic works such as "Mona Lisa" and "Last Supper," in the early 16th century, da Vinci designed a lesser-known structure: a bridge for the Ottoman Empire that would have been the longest bridge of its time. Had it been built, the bridge would have been incredibly sturdy, according to a new study.



Leonardo Da Vinci's original drawing of the bridge included a sailboat passing underneath it. Next to the original drawing, are models created by graduate students Karly Bast and Michelle Xie at MIT that they later 3D-printed. **(Image: © Karly Bast and Michelle Xie)**

In 1502, Ottomon ruler Sultan Bayezid II requested proposals for the design of a bridge that would connect Constantinople, what's today Istanbul, to the neighboring area known as Galata. Da Vinci was among those who sent a letter to the sultan describing a bridge idea. Though da Vinci was already a well-known artist and inventor, he didn't get the job, according to a statement from MIT. Now, a group of researchers at MIT has analyzed da Vinci's design and tested how robust his bridge would have been if it were built.

The group built a replica of the bridge, after taking into consideration the materials and construction equipment available 500 years ago and the geological conditions of the Golden Horn, a freshwater estuary in the Bosphorus Sea over which the bridge would've been built.

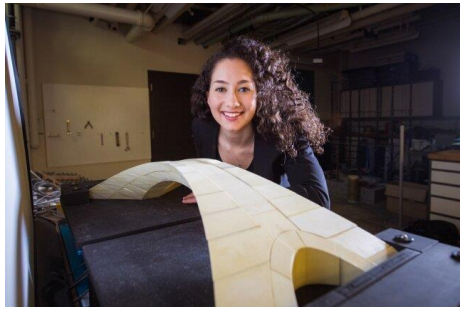
In his descriptions, da Vinci didn't indicate the materials or equipment needed to construct the bridge, but the only material available at the time, that wouldn't have collapsed under large loads on such a long bridge, would have been stone, Karly Bast, a recent graduate student at MIT who worked on the project, and her team found. The researchers also hypothesized that such a bridge would have stood on its own without any paste or material to hold the stone together.

To test the sturdiness of the bridge, the team 3D printed 126 blocks to represent the thousands of stone blocks the original bridge would have required. Their model was 500 times smaller than da Vinci's bridge design, which would have extended about 919 feet (280 meters).

Though the da Vinci bridge would have been nearly four times shorter than the modern George Washington Bridge and 4.5 times shorter than the Golden Gate Bridge, it would have been the longest of its time, according to the statement. "It's incredibly ambitious," Bast said in the statement. "It was about 10 times longer than typical bridges of that time."

What's more, most bridge supports at the time were designed as a semicircular arch and would have required 10 or more piers to support that length of bridge, according to the statement. But da Vinci's design was a single arch, flattened at the top, that would have been tall enough to allow sailboats to pass underneath.

The researchers put together the 3D-printed blocks using a scaffold, but once they put the "keystone" at the top of the arch, they removed the scaffold, and the bridge kept standing. "It's the power of geometry"; the bridge held together by compression only, she said.



Graduate student Karly Bast sitting next to the model of da Vinci's bridge her and her team built. **(Image credit: Gretchen Ertl)**

Da Vinci's design and the MIT scientists' model also included structures called abutments that extended outward on both sides of the ends of the bridge to stabilize it against side-to-side movements, likely because da Vinci knew the region was prone to earthquakes. Bast and her team built the bridge on two moving platforms. They stimulated what would happen when one platform moved away from the other, as can happen over time when heavy structures are built on weak soil. The bridge was resilient against the movement, though it deformed slightly after being stretched a lot.

"Was this sketch just freehanded, something he did in 50 seconds, or is it something he really sat down and thought deeply about? It's difficult to know," Bast said. But this testing of da Vinci's design suggests that he spent some time carefully thinking about it, she added.

The group presented the results at the International Association for Shell and Spatial Structures conference in Barcelona, Spain, this week. Their research has yet to be published in a peer-reviewed journal.

http://bit.ly/33sz0hF

Drug reverses signs of liver disease in people living with HIV

Tesamorelin prevented progression to liver fibrosis in NIH study

Researchers at the National Institutes of Health and their colleagues at Massachusetts General Hospital (MGH) in Boston report that the injectable hormone tesamorelin reduces liver fat and prevents liver fibrosis (scarring) in people living with HIV. The study was conducted by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Cancer Institute, both parts of NIH. The findings were published online today in *The Lancet HIV*.

"Many people living with HIV have overcome significant obstacles to live longer, healthier lives, though many still experience liver disease," said NIAID Director Anthony S. Fauci, M.D. "It is encouraging that tesamorelin, a drug already approved to treat other complications of HIV, may be effective in addressing non-alcoholic fatty liver disease."

Non-alcoholic fatty liver disease, or NAFLD, frequently occurs alongside HIV, affecting as many as 25% of people living with HIV in the developed world. However, no effective treatments currently exist to treat the condition, which is a risk factor for progressive liver disease and liver cancer. Investigators led by Colleen M. Hadigan, M.D., senior research physician in NIAID's Laboratory of Immunoregulation, and Steven K. Grinspoon, M.D., Chief of the Metabolism Unit at MGH, tested whether tesamorelin could decrease liver fat in men and women living with both HIV and NAFLD. Among the participants enrolled, 43% had at least mild fibrosis, and 33% met the diagnostic criteria for a more severe subset of NAFLD called nonalcoholic steatohepatitis (NASH). Thirty-one participants were randomized to receive daily 2-mg

injections of tesamorelin, and 30 were randomized to receive identical-looking injections containing a placebo. Researchers provided nutritional counseling to all participants, as well as training in self-administering the daily injections. Researchers then compared measures of liver health in both groups at baseline and 12 months.

After one year, participants receiving tesamorelin had better liver health than those receiving placebo, as defined by reduction in hepatic fat fraction (HFF)--the ratio of fat to other tissue in the liver. The healthy range for HFF is less than 5%. Thirty-five percent of study participants receiving tesamorelin achieved a normal HFF, while only 4% of those on placebo reached that range with nutritional advice alone. Overall, tesamorelin was well-tolerated and reduced participants' HFF by an absolute difference of 4.1% (corresponding to a 37% relative reduction from the beginning of the study). While nine participants receiving placebo experienced onset or worsening of fibrosis, only two participants in the tesamorelin group experienced the same. Additionally, levels of several blood markers associated with inflammation and liver damage--including the enzyme alanine aminotransferase (ALT)--decreased more among those taking tesamorelin compared to those on a placebo, particularly among those with increased levels at the beginning of the study.

Given these positive results, investigators suggest expanding the indication for tesamorelin to include people living with HIV who have been diagnosed with NAFLD. They also recommend additional research to determine if tesamorelin could contribute to long-term protection against serious liver disease in people without HIV.

"Our hope is that this intervention may help people living with HIV, as well as benefit HIV-negative people with liver abnormalities," said Dr. Hadigan. "Further research may inform us of the potential long-term benefits of this approach and develop formulations that can benefit everyone with liver disease, regardless of HIV status."

Egrifta (tesamorelin) was approved in 2010 by the U.S. Food and Drug Administration to reduce excess abdominal fat in HIV patients with lipodystrophy--a complication characterized by an abnormal distribution of body fat initially associated with older classes of HIV medications. The most commonly reported side effects in previous clinical trials evaluating Egrifta included joint pain (arthralgia), skin redness and rash at the injection site (erythema and pruritis), stomach pain, swelling, and muscle pain (myalgia). Worsening blood sugar control occurred more often in trial participants treated with Egrifta than with placebo.

"Because tesamorelin proved effective in treating abnormal fat build-up in the abdomens of people in the context of HIV and related medication use, we hypothesized that the drug might also reduce fat that accrues in the liver and causes damage in a similar population," said Dr. Grinspoon.

While liver disease is often associated with heavy alcohol use, NAFLD occurs when excess fat builds up in the liver without alcohol as a contributing factor. This condition may progress to liver damage, cirrhosis or cancer that could be life-threatening and necessitate liver transplantation.

Previous studies have found that vitamin E supplements, weight loss and other lifestyle changes can improve outcomes among HIV-negative people with NASH. However, treatment options for NASH and NAFLD are often not tested in people with HIV and none are available for this group. Obesity and type 2 diabetes raise the risk of developing NAFLD regardless of HIV status, and people with HIV are at increased risk of NAFLD because some HIV medications and HIV itself are associated with gaining abdominal fat and may contribute to liver fat build-up.

This research was supported through NIAID grant U01 AI115711. For more information about this trial, please visit ClinicalTrials.gov under study identifier NCT02196831.

Reference: *T Stanley et al. Effects of tesamorelin on nonalcoholic fatty liver disease in HIV: a randomized, double-blind, multicenter trial. The Lancet HIV DOI: 10.1016/PII (2019).*

http://bit.ly/32fkaLd

Under time pressure, people tell us what we want to hear

When asked to answer questions quickly and impulsively, people tend to respond with a socially desirable answer rather than an honest one, a set of experiments shows.

The findings, published in Psychological Science, a journal of the Association for Psychological Science, raise questions about a time-honored experimental technique, said John Protzko, a University of California, Santa Barbara (UCSB) cognitive scientist who co-led the study with colleague Claire Zedelius.

"The method of 'answer quickly and without thinking', a long staple in psychological research, may be doing many things, but one thing it does is make people lie to you and tell you what they think you want to hear," Protzko said. "This may mean we have to revisit the interpretation of a lot of research findings that use the 'answer quickly' technique.

"The idea has always been that we have a divided mind -- an intuitive, animalistic type and a more rational type," he continued. "And the more rational type is assumed to always be constraining the lower order mind. If you ask people to answer quickly and without thinking, it's supposed to give you sort of a secret access to that lower order mind."

To test this assumption, Protzko, Zedelius and their UCSB colleague Jonathan Schooler devised a test of 10 simple yes-or-no questions, such as "I sometimes feel resentful when I don't get my way," and "No matter who I'm talking to, I'm always a good listener." Through a survey, respondents were asked to take fewer than 11 seconds, or alternatively, more than 11 seconds to answer each question.They found that the fast-answering group was more likely to give socially-desireable answers, while the slow answerers and the ones who were not given any time constraints (fast or slow) were less likely to do so, Protzko said.

In a subsequent experiment, the researchers set out to learn whether people tend to give socially acceptable responses under time pressure because they view themselves as genuinely virtuous -- a phenomenon referred to as the good-true-self bias. The researchers had another group of participants respond to the questions under varying time restrictions. The respondents then participated in a social-judgment task designed to assess the degree to which they ascribe morally good and bad behavior to the true self. Those who scored lower on the good-true-self bias scale (i.e., they thought people were more a mix of good and bad qualities) should presumably be less prone to give socially desirable responses under time pressure.

However, what the researchers found was that individuals scoring high on the good-true-self measure gave highly socially desirable answers in general, but especially so when they were given ample time to deliberate. In contrast, it was low scorers who adjusted their responses by responding in a more socially desirable way under time pressure.

In other words time pressure does not bring out a person's good "true self.

Under time pressure, people may default to their desire to appear virtuous, even if it means misrepresenting themselves, Protzko concluded.

He and his colleagues plan to examine previous studies that used the quick-answer technique to see how much results might be driven by participants giving socially desireable answers.

The study was supported by the Fetzer Franklin Fund. All materials have been made publicly available via the Open Science Framework. This article has received badges for Open Data, Open Materials, and Preregistration. The complete Open Practices Disclosure for this article can be found at http://journals.sagepub.com/doi/suppl/10.1177/0956797619867939.

http://bit.ly/2OJUBOD

Blood test raises hopes of tackling 'silent killer'

A new blood test devised by a team at the University of Dundee, detects the presence of desmosine an amino acid that diseased aortas release into the blood and urine.

It is the 'silent killer' that claimed the life of Albert Einstein and affects 1% of men over the age of 65, but researchers at the University of Dundee believe they may be able to reduce the number of fatalities caused by abdominal aortic aneurysms.

Aneurysms are the swelling and weakening of the arterial wall. Aortic aneurysms occur in the aorta, which delivers blood from the heart to organs. Aneurysms are often called a silent killer, because patients can display no symptoms until the aneurysm bursts. Around 80% of all patients with a ruptured aneurysm die from the condition.

A team from the University's School of Medicine have devised a test that detects the presence of desmosine, an amino acid that diseased aortas release into the blood and urine. They believe this can improve the diagnosis and monitoring of aortic aneurysms while possibly aiding effort to develop new therapies to slow down their progression.

Men aged 65 and over are most at risk and may be invited for ultrasound screening. If an aortic aneurysm is detected, they will be asked to attend regular follow up checks but, as aneurysms do not expand at a linear rate, this means rapid growth between screenings may be missed.

Furthermore, the size of an aneurysm does not always correlate to how close it is to rupturing. However, the Dundee researchers believe that measuring the level of desmosine is a more effective way of identifying which patients are in most urgent need of treatment.

Dr Anna Maria Choy, Senior Clinical Lecturer and Honorary Consultant Cardiologist at the University, said, "At the moment, patients are offered surgery when the aneurysm reaches a size where it is felt to be in danger of rupturing. The problem is that aortic aneurysms can progress quite unpredictably and rapidly between tests. Sometimes they stay the same for a long time then have sudden expansion and they can also rupture when not of a particularly significant size.

"All this means we need to find a better way to detect and monitor aneurysms as it is a terrible amount of uncertainty for patients and their families to live with. We established that desmosine was released into the blood when this disease was present so we looked at whether testing for this might add to the screening.

"Looking at a retrospective collection of samples from aneurysm patients, we found that not only was this effective in detecting aneurysms, it improved predicting complications and outcomes. This could potentially help to save lives by picking up danger signs missed by the current screening programme and identifying which patients should be offered surgery."

Ruptured aortic aneurysms cause 5,000 deaths in the UK each year, and are responsible for 1 in 75 deaths of men over 65. The incidence is growing as the population ages while smokers, diabetics and people with hypertension are among other at-risk groups.

Desmosine derives from elastin protein. As suggested by its name, elastin provides blood vessels with their unique elastic character to expand and stretch. When someone develops an aneurysm, this protein gets broken down and is released into blood and urine.

The Dundee team and their co-investigators from Edinburgh, Leicester and Singapore checked the desmosine levels of patients with aneurysms ranging from the very mild to extremely severe. They found it was not just an effective indicator of the size of the aneurysm but also the likelihood of the patient developing complications.

Dr Jeffrey Huang, a principal investigator who developed the desmosine assay, said, "Where available, screening programmes have helped reduce the number of fatalities but it is quite resource-intensive. It is potentially more cost-effective and patient-friendly to go to your GP for a simple blood test rather than going to hospital for an ultrasound.

"More importantly, our test has shown to be more effective in predicting outcomes than size alone so there is the potential to save lives."

At the moment there is no medical intervention known to slow the progression of aneurysms but Dr Choy and Dr Huang believe the test they have developed can help to guide the development of therapies through clinical trials by giving faster and clearer readings of the levels of desmosine and therefore aortic destruction.

"Next we want to test this research in women who experience a higher mortality rate event though they are less likely to be diagnosed with an aneurysm," continued Dr Choy. "It may also prove significant for people with genetic diseases that lead to diseased aortic walls. The bottom line is that in any disease of the aorta we think this amino acid may have a role to play in detection, prediction and follow up."

The research was funded by the Scottish Government Chief Scientist Office and Tenovus Trust Scotland and was published by the Journal of the American Heart Association.

http://bit.ly/318W97f

A Man Heard 'Scratching' Noises in His Ear. It Was a Spider.

After feeling a tickle in his ear, the man made a horrifying discovery.

By Rachael Rettner - Senior Writer

A man who felt a tickling and scratching sensation in his ear soon discovered something horrifying: A spider had crawled into his ear.

The man, 27-year-old Liam Gomez, of Kent, England, woke up with an earache and vertigo, which prompted him to call in sick to work, according to Fox News. He put some olive oil in his ear as a home remedy to help with the pain, and then went back to sleep.

Soon, he felt a tickle in his ear, but he thought this was just from the oil. However, "when I woke up a couple hours later, I could still feel the sensation, but also hear a faint scratching sound, so I decided to investigate with a cotton bud," Gomez told South West News Service (SWNS).

That's when part of a spider came out of his ear.

"My initial reaction was just to get the bloody thing out of me as fast as possible – I was obviously revolted as I hate spiders," he told SWNS. "Once I'd calmed down a bit I did think, 'Well, that's one for Facebook!'"

Gomez used a bobby pin and a cotton swab to get the spider out of his ear, and he counted the legs to make sure he'd retrieve them all. (Spiders have eight legs.)

Gomez had swept a spiders nest from his door the night before the incident. After removing the spider, Gomez did not go to the doctor, and he's hoping for no more surprises in his ear: He now sleeps with earmuffs on.

Cases of insects crawling into people's ears are more common than you might think, Live Science previously reported. Doctors have removed all sorts of critters from people's ears, including

cockroaches, ticks and fruit-fly larvae. Just last month, and woman in Missouri was found to have a brown recluse spider in her ear, which doctors successfully removed.

http://bit.ly/2MHk88z

More evidence linking common bladder medication to a vision-threatening eye condition

New study shows about a quarter of patients with significant exposure to the drug show signs of retinal damage

SAN FRANCISCO - A drug widely prescribed for a bladder condition for decades, now appears to be toxic to the retina, the light sensing tissue at the back of the eye that allows us to see. After an initial report last year that Elmiron (pentosan polysulfate sodium) may be associated with retinal damage, three ophthalmologists conducted a review of patients at Kaiser Permanente in Northern California. They found that about one-quarter of patients with significant exposure to Elmiron showed definite signs of eye damage, and that this medication toxicity could masquerade as other known retinal conditions, such as age-related macular degeneration or pattern dystrophy. The research will be presented today at AAO 2019, the 123nd?Annual Meeting of the American Academy of Ophthalmology.

Interstitial cystitis causes chronic pain in the bladder and pelvis area. More than 1 million people in the United States, mostly women, are estimated to have the condition. Elmiron is the only FDA-approved pill to treat it. As a mainstay of treatment for decades, hundreds of thousands of people have likely been exposed to the drug.

Last year, Nieraj Jain, M.D., of Emory Eye Center in Atlanta, Ga., reported that six patients who had been taking Elmiron for about 15 years had developed unusual changes in their macula, the central part of the retina responsible for delivering clear, crisp, central vison. Because nothing in the patients' medical history or diagnostic tests explained the subtle, but striking pattern of abnormalities, Dr. Jain and his colleagues raised a warning flag that long-term use of Elmiron may damage the retina.

Robin A. Vora, M.D , Amar P. Patel, M.D., and Ronald Melles M.D., ophthalmologists at Kaiser Permanente, heeded that warning and looked at their population of patients. They initially found one woman on long-term treatment who was misdiagnosed as having a retinal dystrophy. This worrisome case prompted them to examine Kaiser's entire database of 4.3 million patients.

They found 140 patients who had taken an average of 5,000 pills each over the course of 15 years. Of those 140 patients, 91 agreed to come in for an exam. Drs. Vora, Patel, and Melles took detailed images of the back of their eyes and then divided the images into three categories: normal, possible abnormality, definite abnormality. Twenty-two of the 91 patients showed clear signs of drug toxicity. The rate of toxicity rose with the amount of drug consumed, from 11 percent of those taking 500 to 1,000 grams to 42 percent of those taking 1,500 grams or more.

"It's unfortunate," said Dr. Vora. "You have a patient with a chronic condition like interstitial cystitis, for which there is no cure and no effective treatment. They get put on these medications because it's thought to have few side effects and few risks, and no one thinks about it again. And year after year, the number of pills they're taking goes up and up."

Because it's unclear how much medication is too much, Dr. Vora recommends patients who show no signs of toxicity be screened for retina damage at least once a year. For those who do show some signs of damage, he recommends they speak with their urologist or ob/gyn about discontinuing the medication.

Good news is that if identified early, the damage may be mitigated by stopping the medication. In the late-stage, toxicity can mimic late-stage dry atrophic age-related macular degeneration and result in permanent vision loss.

http://bit.ly/2MF8AT3

Immune system lends the brain a hand

Study adds fuel to growing evidence that the immune system does more than fight disease.

Paul Biegler reports.

Researchers have discovered that the immune system helps out the brain, in the absence of any disease, by making a chemical messenger that boosts memory.

The study was in mice, but senior author Bruno Silva-Santos, from the University of Lisbon, Portugal, says the finding could lead to dietary recommendations to improve memory in people. The study is part of a rising tide of research upending the traditional view that the immune system exists only to fight infection and tumours.

The authors point out that disease is relatively rare, and so maintaining a complex system of immunity would impose a big cost if busting microbes and cancer were the only benefit.

Already, they say, immunity is known to have non-disease roles in temperature control and bone repair. But to accept that the immune system could be a major player in the everyday workings of the brain, another shibboleth in medicine must fall by the wayside.

"The brain was seen as an immune privileged organ, meaning that it would be completely shielded by the blood brain barrier and completely hermetic to the peripheral immune system," explains senior author Julie Ribot, in a linked video.

Recently, says Ribot, it has been found that lymphatic vessels, which transport infection-fighting white blood cells, are present in the lining of the brain, called the meninges. "This is really important," says Ribot, "because it suggests that actually the brain and the immune system do constantly communicate, even when we are not sick."

The presence of a workaday brain-immune relationship is born out in recent studies showing white cells, called T lymphocytes, are key for spatial learning and social behaviour. But the team had a hunch there was an even broader connection.

They believed a type of lymphocyte known as a gamma delta T cell, which is resident in the meninges, could be crucial for memory. So they devised some clever experiments in mice that were specifically engineered to lack gamma delta cells.

When they put those mice to the test in a maze, the critters' short-term memory – the bit that helps you remember what you had for lunch today, but not last week – was shot.

The finding was pleasingly consistent with the researchers' theory, but how those gamma delta cells were helping memory came as a curve ball. "We thought gamma delta cells would be pro-cognitive," says Silva-Santos.

"What was very surprising was that … the molecule they secrete to endow cognition is actually IL-17," he says.

Surprising, explains Silva-Santos, because IL-17 (interleukin-17) is what's known as a "pro-inflammatory cytokine". It's something of a bad boy, known to cause inflammation and contribute to disease, notably multiple sclerosis.

But IL-17, the researchers found, is also a trigger for brain derived neurotrophic factor, (BDNF) a prolific neuron fertiliser that enhances signalling between brain cells in the hippocampus, a major memory centre. The team now thinks IL-17 has to be kept in the Goldilocks zone – too much and you get inflammation and disease, too little and memory suffers.

Silva-Santos has some ideas on how we might one day get IL-17 just right. "What will be important to know is what are the factors that regulate these basal levels of IL-17... so that we can, for instance through diet, because we have realised that vitamins can regulate this process ... have enough IL-17 in our brains, in our meninges, to guarantee proper short term learning," he says.

The study appears in the journal *Science Immunology*.