https://wb.md/2whotdy

Incidental Pancreatic Cysts: Majority Don't Progress to Cancer

To study the frequency of incidental pancreatic cysts in asymptomatic individuals, the authors of a paper published in Gut performed a magnetic resonance cholangiopancreaticography (MRCP) examination in 1077 participants enrolled in a population-based cohort study.[1]

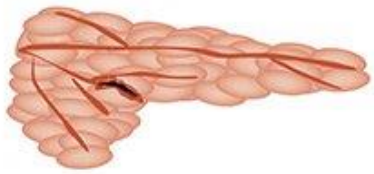
Albert B. Lowenfels, MD

Of the original group, 676 people underwent a repeat examination 5 years later. At the time of the initial exam, 49% had at least one cyst ≥ 2 mm in diameter. The yearly incidence of new cysts during the follow-up period was 2.6% per year. The frequency of cysts was strongly related to participants' age (P = .001) but was unrelated to body mass index or gender.

Viewpoint

With the advent of high-resolution scanning equipment, pancreatic cysts are being detected with increasing frequency. This study reveals that almost 50% of asymptomatic individuals with a mean age of 58 years harbored cysts ≥ 2 mm in diameter. Cyst presence was strongly related to age: By 75 years of age, 75% of participants had one or more cysts. This implies that assessing the significance and managing cysts will become an increasing problem in subsequent decades, because the number of older people is increasing rapidly in most countries.

Despite the publication of guidelines concerning the management of pancreatic cysts with respect to the potential risk for pancreatic cancer, surgeons still have difficulty deciding when or when not to operate on patients with these lesions.[2,3] Of the 1077 persons included in the study, one person whose initial imaging scan did not reveal a cyst went on to develop pancreatic cancer. The cysts detected in this study were mostly small, with a mean cyst size of 5.2 mm, with only 26 cysts (3.8%) being larger than 1 cm.



Intraductal tumor mucosa

This study suggests that a large proportion of asymptomatic persons will harbor a small pancreatic cyst but that the threat of pancreatic cancer is low.

References

1. Kromrey ML, Bülow R, Hübner J, et al. Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study. Gut. 2018;67:138-145. Abstract

2. Tanaka M, Fernández-del Castillo C, Adsay V, et al; International Association of Pancreatology. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology. 2012;12:183-197. Abstract

3. Vege SS, Ziring B, Jain R, et al; Clinical Guidelines Committee; American Gastroenterology Association. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. 2015;148:819-822. Abstract

http://bit.ly/2KFfK81

Researchers find that lipid accumulation in the brain may be an early sign of Parkinson's disease

Elevated levels of certain types of fat molecules in the brain may be an early sign of Parkinson's disease

Belmont, MA - A collaborative team of researchers at McLean Hospital, a Harvard Medical School affiliate, and Oxford University has found that elevated levels of certain types of lipids (fat molecules) in the brain may be an early sign of Parkinson's disease (PD). This finding could have significant implications for identifying patients who may be at risk for developing PD and for the early treatment of the disease. The detailed findings are available in the April 29 online edition of *Neurobiology of Aging*.

Parkinson's disease is a degenerative, progressive disorder characterized by the dramatic reduction of nerve cells, particularly dopamine neurons that are involved in movement initiation, in an area of the brain called the substantia nigra. For many years now, the loss of these nerve cells has been attributed to the toxic accumulation of the protein alpha-synuclein. In the past 15 years, however, researchers have

been studying an interesting relationship between the risk of developing PD and a group of disorders called lysosomal storage diseases--particularly Gaucher disease, which is caused by mutations that lead to loss of function in the glucocerebrosidase (GBA) gene.

The GBA gene normally produces an enzyme that breaks down lipids, but in the childhood disorder Gaucher disease, a near total lack of this enzyme activity leads to massive and usually fatal elevations of lipids inside cells. Notably, people who do not develop Gaucher disease but are carriers of one defective gene copy have a 7-to-10-fold risk of developing PD with age.

"This means that lipid accumulation may also be important in PD, and scientists at the Neuroregeneration Research Institute at McLean Hospital have previously shown that there is an elevation of a class of lipids, called glycosphingolipids, in the substantia nigra of patients with PD," said Ole Isacson, MD, PhD, professor of Neurology and Neuroscience at Harvard Medical School, co-director of the Neuroregeneration Research Institute at McLean Hospital, and co-senior author of the study.

Since aging is the most significant risk factor for developing PD, teams from McLean Hospital and the University of Oxford laboratory of Professor Frances M. Platt, PhD, FMedSci, collaborated to measure the levels of glycosphingolipids in the aging brain, using young and old mice. They found that the same glycosphingolipids that are increased in the brains of Parkinson's disease patients are also elevated in the brains of aging mice. These findings show that both genetics (GBA gene mutation) and aging can cause the same lipid elevations in the brain that are demonstrated in Parkinson's disease pathology.

"These results lead to a new hypothesis that lipid alterations may create a number of problems inside nerve cells in degenerative aging and Parkinson's disease, and that these changes may precede some of the more obvious hallmarks of Parkinson's disease, such as protein aggregates," said Penny Hallett, PhD, study lead author and co-director of McLean's Neuroregeneration Research Institute. "This potentially provides an opportunity to treat lipid changes early on in Parkinson's disease and protect nerve cells from dying, as well as the chance to use the lipid levels as biomarkers for patients at risk."

http://bit.ly/2KEy3KJ

Warning issued on child virus

Three epidemics of little known infant disease revealed.

Australia is in the grip of an emerging viral disease that affects babies and can lead to intensive care admissions, according to the *Medical Journal of Australia*.

A team of scientists led by Allen Cheng, of the Infection Prevention and Healthcare Epidemiology Unit at Melbourne's Monash University, reveal that a little-known pathogen called human parechovirus has now officially caused epidemics every two years since 2013.

There are 17 different types of parechovirus, of which three – known as HPeV1, 3 and 6 – are associated with humans. Most infections result in no or mild symptoms, such as gastroenteritis and rash, but those caused by HPeV3 are associated with more severe outcomes and have been the drivers behind outbreaks in 2013-14, 2015-16 and now 2017-18.

Children aged up to six months are the primary victims. Symptoms include meningoencephalitis, seizures and septic shock. There are no effective treatments against the virus itself, and hospital care is directed at management of immediate symptoms and complications.

"It is now recognised as a leading cause of sepsis-like illness and central nervous system infection, particularly in young infants," write the authors.

Australia is currently experiencing the third epidemic of the disease. In December 2017, more than 200 infants were hospitalised with HPeV3 infection. Cheng and his colleagues report that infants under three months are at high risk, with those under 28 days and premature births in the most danger of complications.

Between 20 and 50% of infants hospitalised required intensive care.

Cheng's team recommend preventative parenting when a child falls ill to help halt the spread of parechovirus. "Hand hygiene, cough etiquette

and staying away from childcare and school while unwell should be emphasised," they write.

They also strongly advise long periods of follow-up monitoring after recovery.

"Because of the evidence of adverse neurodevelopmental outcomes following severe HPeV infection, we recommend that all children hospitalised with HPeV infection should be followed up by a paediatrician at least until school entry, and preferably afterwards, to monitor development and learning, and manage complications including seizures," they conclude.

http://bit.ly/2IioXF2

Pill for breast cancer diagnosis may outperform mammograms

A pill that makes tumors light up when exposed to infrared light

ANN ARBOR--As many as one in three women treated for breast cancer undergo unnecessary procedures, but a new method for diagnosing it could do a better job distinguishing between benign and aggressive tumors.

Researchers at the University of Michigan are developing a pill that makes tumors light up when exposed to infrared light, and they have demonstrated that the concept works in mice.

Mammography is an imprecise tool. About a third of breast cancer patients treated with surgery or chemotherapy have tumors that are benign or so slow-growing that they would never have become life-threatening, according to a study out of Denmark last year. In other women, dense breast tissue hides the presence of lumps and results in deaths from treatable cancers. All that, and mammograms are notoriously uncomfortable.

"We overspend $4 billion per year on the diagnosis and treatment of cancers that women would never die from," said Greg Thurber, U-M assistant professor of chemical engineering and biomedical engineering, who led the team. "If we go to molecular imaging, we can see which tumors need to be treated."

The move could also catch cancers that would have gone undetected. Thurber's team uses a dye that responds to infrared light to tag a molecule commonly found on tumor cells, in the blood vessels that feed tumors and in inflamed tissue. By providing specific information on the types of molecules on the surface of the tumor cells, physicians can better distinguish a malignant cancer from a benign tumor.

Compared to visible light, infrared light penetrates the body easily--it can get to all depths of the breast without an X-ray's tiny risk of disrupting DNA and seeding a new tumor. Using a dye delivered orally rather than directly into a vein also improves the safety of screening, as a few patients in 10,000 can have severe reactions to intravenous dyes. These small risks turn out to be significant when tens of millions of women are screened every year in the U.S. alone.

But it's not easy to design a pill that can carry the dye to the tumor.

"To get a molecule absorbed into the bloodstream, it needs to be small and greasy. But an imaging agent needs to be larger and water-soluble. So you need exact opposite properties," Thurber said.

Fortunately, they weren't the only people looking for a molecule that could get from the digestive system to a tumor. The pharmaceutical company Merck was working on a new treatment for cancer and related diseases. They got as far as phase II clinical trials demonstrating its safety, but unfortunately, it wasn't effective.

"It's actually based on a failed drug," Thurber said. "It binds to the target, but it doesn't do anything, which makes it perfect for imaging."

The targeting molecule has already been shown to make it through the stomach unscathed, and the liver also gives it a pass, so it can travel through the bloodstream. The team attached a molecule that fluoresces when it is struck with infrared light to this drug. Then, they gave the drug to mice that had breast cancer, and they saw the tumors light up.

The research is described in a study in the journal *Molecular Pharmaceutics*, titled, "Oral administration and detection of a near-infrared molecular imaging agent in an orthotopic mouse model for breast cancer screening."

This work was done in collaboration with David Smith, the John G. Wagner Collegiate Professor of Pharmaceutical Sciences at the U-M College of Pharmacy. It was supported by the Foundation for Studying and Combating Cancer and the National Institutes of Health.

http://bit.ly/2IhxWqe

What your body odour says about you

Smells emanating from you can reveal anything from your health status to your personality or political taste.

April 30, 2018 by Karl Gruber, Particle

For many animals, their life depends of their sense of smell. It helps them find food, avoid predators or identify potential mates. For humans, too, the sense of smell plays an important role in different aspects of our lives.

For example, we use our nose to find the best food and avoid rotten morsels. We use perfumes, soaps and other toiletries with pleasant smells to make us more attractive to the opposite sex. But there is much more that can be learned from our body odours.

You may not be aware of it, but there are all sorts of smells produced by your body that convey different types of information. For example, if you are sick or stressed, your body may emit a particular scent. Even certain personalities are linked to particular scents.

Our body, it seems, has a lot to say through our scents.

The scent of age

Have you ever heard that "old people smell"? Well, it is actually true. Old people do have a distinct smell, but it is not bad at all. A study from 2012 compared body odour samples from the armpits of 44 individuals from three different age groups from people in their 20s to folks as old as 95. The study found that older participants (75 to 95 years old) had a distinct scent, which was not strong nor unpleasant—just characteristic of their age group.

"Elderly people have a discernible underarm odour that younger people consider to be fairly neutral and not very unpleasant," said Johan Lundström, a sensory neuroscientist at the Monell Chemical Senses Center in Philadelphia, USA, who led the study, in a press release. "This was surprising given the popular conception of old age odour as disagreeable. However, it is possible that other sources of body odours, such as skin or breath, may have different qualities."

The authors speculate that there might be an evolutionary reason why we are able to distinguish people of different age by their smell. "Similar to other animals, humans can extract signals from body odours that allow us to identify biological age, avoid sick individuals, pick a suitable partner and distinguish kin from non-kin," said Johan.

Evolution has also shaped another age-related odour in humans: the scent of babies. A 2013 study confirmed a well known fact about babies: they smell delicious! Literally. The study found that the smell of 2-day-old babies activated a special part of the brain associated with rewards. This is the same brain region involved with identifying a delicious treat or a drug, and the effect was more pronounced in mothers.

"What we have shown for the first time is that the odour of newborns, which is part of these signals, activates the neurological reward circuit in mothers. These circuits may especially be activated when you eat while being very hungry but also in a craving addict receiving his drug. It is in fact the sating of desire," said Johannes Frasnelli, lead author of the study.

Researchers speculate that their findings suggest that newborn odour may be a way to create an emotional link between mother and child, which leads to important functions like breastfeeding and protection.

Old age and yummy babies are just two of the secrets body odours reveal. But there are more.

The scent of disease

Certain diseases, like various types of cancers, seem to leave a particular odorous signature in the body of patients, which can be detected by a sensitive nose—like the one of a dog.

In fact, several human cancers, such as breast, melanoma, lung, ovary, colorectal, bladder and prostate cancers, can be detected by dogs. These cancers produce an odour signature that can be detected in things like urine, breath, blood and stools of patients. The scent is strong enough that dogs can then be trained to detect it with surprisingly accuracy.

Even other diseases such as Parkinson's disease may leave a signature that dogs can detect.

"The full potential of dogs to detect human disease is just beginning to be understood," said Claire Guest, Chief Executive of Medical Detection Dogs in a recent news report. "For hundreds of years, dogs have guarded us, rescued us when we're lost and provided unparalleled emotional support. Is it so hard to believe that they can detect the odour of human disease?" she asks.

"Dogs have an extraordinary sense of smell. They can detect parts per trillion—that's the equivalent of one drop of sugar in two Olympic-sized swimming pools," said Claire.

But disease-sniffing dogs can be hard to find. Luckily, a team from the University of Liverpool and University of the West of England (UWE) have developed a more practical way to detect cancer. They have created an apparatus, called Odoreader, which can detect bladder cancer as well other types of cancer.

"We have developed a device that can give us a profile of the odour in urine. It reads the gases that chemicals in the urine can give off when the sample is heated," explained Norman Ratcliffe, from the Institute of Biosensor Technology at UWE. In their study, the device was 100% effective at detecting urine samples from cancer patients.

Scents from babies, old people or disease sounds cool. But did you know even your personality could have its own scent, and your sensitivity to certain odours might influence who you vote for?

The scent of personality

According to a 2012 study, people with certain personalities could be identified from their scent alone. Neurotics and dominant people seem to give the stronger whiff!

In their study, researchers collected sweat samples by asking 30 male and 30 female participants, the odour donors, to wear a cotton T-shirt for 3 days straight. Then, 100 men and 100 women, the odour raters, assessed the scent of these smelly T-shirts. These odour ratings were compared to self-assessed personality tests made by the odour donors.

The results showed a strong relationship between odour and three personality types: extroversion, neuroticism and dominance. In other words, people who considered themselves neurotic, dominant or extrovert had particular body odours that odour raters consistently identified in this study. Other personalities tested, such as agreeableness, conscientiousness and openness to experience, did not seem to have any associated scent.

So, now we know that certain personalities smell and can be detected by other people. A more recent study found an even more intriguing link: people who are quick to feel yucky about body odours might also feel drawn to authoritarian figures. The study went as far as exploring this idea during the 2016 US presidential campaign.

In the study, researchers asked whether people's sensitivity to body odour, something called BODS or body odour disgust sensitivity, was related to the intention of voting for Donald Trump. "We showed a positive association between BODS scores and support for Donald Trump, who, at the time of data collection, was a presidential candidate with an agenda described as resonating with authoritarian attitudes," the authors said in their study.

So what is the logic here? The authors speculate that people who are more sensitive to body odours (high in BODS scores) may have a stronger fear of disease. Unknown folk, for example, could represent a potential source of disease in the mind of someone scoring high in BODS.

"Our reasoning was that sensitivity to body odours should covariate with attitudes that may be fuelled by a motivation to prevent us from intergroup contact because of the fear of contamination. So, people higher in BODS could have more sensitivity to cues of disease and be more motivated to keep unfamiliar groups distant," says Marco Tullio Liuzza, from the University of Catanzaro, who led the study.

So, next time you judge someone's personality, age or health … think that it might all be in your nose. And that might not be a bad thing.

https://wb.md/2HUOocw

Prostate Cancer on the Rise; Time to Revisit Guidelines?

Is the increase in invasive prostate cancer rates related to the 2012 USPSTF recommendations?

Arefa Cassoobhoy, MD, MPH

Hello. I'm Dr Arefa Cassoobhoy, a practicing internist, Medscape advisor, and senior medical director for WebMD. Welcome to Medscape Morning Report, our 1-minute news story for primary care.

In 2012, the US Preventive Services Task Force recommended against routine prostate cancer screening of asymptomatic men to detect early disease. Since then, invasive prostate cancer rates have been rising. Is this increase related to the 2012 USPSTF recommendations?

To find out, a recent study[1] looked at outcomes in more than 19,000 men with prostate cancer before and after the recommendations. Although the incidence of low-grade disease and surgical volume both dropped, they saw an increase in more aggressive prostate cancer, higher prostate-specific antigen (PSA) levels, and older age at diagnosis. Similarly, in another study[2] involving more than 1 million men who had undergone radical prostatectomy, rates of high-stage disease increased after 2012.

PSA screening recommendations are controversial, and the new data encourage us to revisit our screening approach in higher-risk patients.

References

1. Ahlering T, Huynh L, Kaler K, Williams S, et al. Unintended consequences of decreased PSA-based prostate cancer screening. Eur Urol Suppl. 2018;17:e269.

2. Huynh L, Ranasinghe O, Ahlering T. Step-wise increase in high-risk pathological outcomes as a consequence of decreased screening: A population-based analysis. Eur Urol Suppl. 2018;17:e268.

https://wb.md/2FMZcaN

Everything You Need to Know About Shingrix, and How Shingrix Differs From Zostavax

About the new, highly protective shingles vaccine, Shingrix

Kathleen Dooling, MD, MPH

Hello. I'm Dr Kathleen Dooling, a medical officer and shingles disease expert at CDC. I'm here to talk to you about the new, highly protective shingles vaccine, Shingrix. It is more than 90% protective against shingles, even among the elderly.[1,2] CDC now recommends Shingrix as the preferred shingles vaccine for immunocompetent adults age 50 and older.[3] Today I'm going to focus on two important aspects of Shingrix recommendations: first, proper vaccine administration; and second, how to counsel patients about possible reactions.

CDC recommends two doses of Shingrix, with the second dose given 2-6 months after the first.[3,4] The effectiveness of only one dose has not been studied, so to get full protection, patients should complete the two-dose series. Even if a patient previously received Zostavax, CDC recommends that they receive two doses of Shingrix. You should administer Shingrix intramuscularly in the deltoid region of the upper arm.[4] This is very important, because if Shingrix is incorrectly administered subcutaneously, the patient is more likely to develop a reaction.[1,2]

Shingrix is supplied as two components: the lyophilized antigen and the adjuvant solution. Both components should be stored in the refrigerator between 2˚ and 8˚ C, and the vaccine should be reconstituted prior to use.[4] You should not freeze Shingrix; once frozen, the vaccine is no longer viable. The vaccine storage and administration of Shingrix is quite different from that for Zostavax, a live attenuated shingles vaccine that CDC has recommended since 2006.

The second point I'd like to discuss today is reactions, or possible reactogenicity, associated with Shingrix. In clinical trials of more than 30,000 people, Shingrix was not associated with serious adverse events.[1,2] However, local and systemic reactions were common among those who got the vaccine. More than 75% of people who got Shingrix reported at least some pain at the injection site.[1,2] About 17% of patients who got Shingrix reported grade 3 reactions, which are severe enough to prevent normal activities. One in 10 reported grade 3 reactions due to pain or injection-site redness or swelling of at least 4

inches in diameter.[1,2] Also, about 1 in 10 people who got Shingrix reported systemic effects that limited activity, such as myalgia, fatigue, headache, shivering, fever, or gastrointestinal illness.[1,2]

CDC recommends counselling your patients about the possible reactions to the vaccine before administering Shingrix. Advise patients not to engage in strenuous activities for a few days after vaccination. If reactions do occur, you can suggest that patients take over-the-counter ibuprofen or acetaminophen to help relieve pain and inflammation. In clinical trials, a reaction to the first dose did not predict a reaction to the second dose.[1,2] Therefore, you should encourage patients to complete the two-dose series, even if they experience a reaction to the first dose. Most reactions to Shingrix are self-limited and resolve in 2-3 days. Report any clinically significant reactions online to the Vaccine Adverse Event Reporting System.

For more information, you can access the herpes zoster vaccine recommendations published in the *Morbidity and Mortality Weekly Report*[3] or visit CDC's shingles vaccine website.

As a healthcare provider, your recommendations on vaccination have the biggest impact on the choices your patients make. So help protect your patients ages 50 and older against shingles and its complications by strongly recommending shingles vaccination. Thank you.

Web Resources

Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines

Shingles Vaccine Information for Healthcare Professionals

References

1. *Lal H, Cunningham AL, Godeaux O, et al.; ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015;372:2087-2096. Abstract*
2. *Cunningham AL, Lal H, Kovac M, et al.; ZOE-70 Study Group. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Engl J Med 2016;375:1019-1032. Abstract*
3. *Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. MMWR Morb Mortal Wkly Rep. 2018;67:103-108. Article Accessed April 10, 2018.*
4. *Food and Drug Administration. Shingrix [package insert]. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2017. Package insert Accessed April 10, 2018.*

https://bbc.in/2IhCmxk

Critical window for learning a language

There is a critical cut-off age for learning a language fluently, according to research.

If you want to have native-like knowledge of English grammar, for example, you should ideally start before age 10, say the researchers.

People remain highly skilled learners until 17 or 18, when ability tails off.

The findings, in the journal Cognition, come from an online grammar test taken by nearly 670,000 people of different ages and nationalities.

The grammar quiz was posted on Facebook to get enough people to take part.

Questions tested if participants could determine whether a sentence written in English, such as: "Yesterday John wanted to won the race," was grammatically correct.

Users were asked their age and how long they had been learning English, and in what setting - had they moved to an English-speaking country, for example? About 246,000 of the people who took the test had grown up speaking only English, while the rest were bi- or multilingual.

The most common native languages (excluding English) were Finnish, Turkish, German, Russian and Hungarian.

Most of the people who completed the quiz were in their 20s and 30s. The youngest age was about 10 and the oldest late 70s.

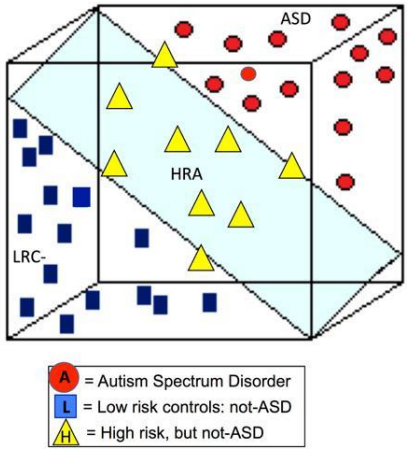
When the researchers analysed the data using a computer model, the best explanation for the findings was that grammar-learning was strongest in childhood, persists into teenage years and then drops at adulthood.

Learning a language is often said to be easy for children and to get more difficult as we age. But late learners can still become proficient, if not seamlessly fluent, say the researchers.

It is unclear what causes the drop in the optimal learning rate seen at about age 18. The researchers suggest it could be because the brain becomes less changeable or adaptable in adulthood.

Study co-author Josh Tenenbaum, a professor of brain and cognitive sciences at the Massachusetts Institute of Technology in the US, said: "It's possible that there's a biological change. It's also possible that it's something social or cultural.

"There's roughly a period of being a minor that goes up to about age 17 or 18 in many societies. After that, you leave your home, maybe you work full time, or you become a specialised university student. All of those might impact your learning rate for any language."



That doesn't mean learning another language in adulthood is futile.

Learning another tongue is said to be good for your brain and might even delay the onset of dementia, according to some studies.

Prof Marilyn Vihman, from the University of York's department of language and linguistic science, said: "The suggestion that you can't reach native-like ability if you don't start early is questionable.

"Such cases are rare, but they do occur and are documented. "There are cases of people in their 20s who learn a new language and can pass as spies. "There are two, three or four documented cases like that.

"I don't think there is a critical age as such, just a plateau that sets in after the teen years for most but not all speakers."

Dr Danijela Trenkic, also from the University of York, pointed out that the study dealt with only one aspect of language - grammar.

"You can be an excellent communicator, even if you don't sound like a native speaker or don't get all your sentences grammatically correct."

http://bit.ly/2Ij8rEE

EEG signals accurately predict autism as early as 3 months of age

Early diagnosis by 'digital biomarkers' may allow early intervention, better outcomes

Autism is challenging to diagnose, especially early in life. A new study in the journal *Scientific Reports* shows that inexpensive EEGs, which measure brain electrical activity, accurately predict or rule out autism spectrum disorder (ASD) in infants, even in some as young as 3 months.

"EEGs are low-cost, non-invasive and relatively easy to incorporate into well-baby checkups," says Charles Nelson, PhD, director of the Laboratories of Cognitive Neuroscience at Boston Children's Hospital and co-author of the study. "Their reliability in predicting whether a child will develop autism raises the possibility of intervening very early, well before clear behavioral symptoms emerge. This could lead to better outcomes and perhaps even prevent some of the behaviors associated with ASD."

Calibrated Severity Scores (CSS), part of the Autism Diagnostic Observation Schedule (ADOS), measure ASD symptom severity based on clinical assessment. This figure illustrates the CSS scores that were predicted for each of the participants, based on machine learning algorithms applied to EEG data.
William Bosl, Ph.D.

The study analyzed data from the Infant Sibling Project (now called the Infant Screening Project), a collaboration between Boston Children's Hospital and Boston University that seeks to map early development and identify infants at risk for developing ASD and/or language and communication difficulties.

William Bosl, PhD, associate professor of Health Informatics and Clinical Psychology at the University of San Francisco, also affiliated with the Computational Health Informatics Program (CHIP) at Boston Children's Hospital, has been working for close to a decade on algorithms to interpret EEG signals, the familiar squiggly lines generated by electrical activity in the brain. Bosl's research suggests that even an EEG that appears normal contains "deep" data that reflect brain function, connectivity patterns and structure that can be found only with computer algorithms.

The Infant Screening Project provided Bosl with EEG data from 99 infants considered at high risk for ASD (having an older sibling with the diagnosis) and 89 low-risk controls (without an affected sibling).

The EEGs were taken at 3, 6, 9, 12, 18, 24 and 36 months of age by fitting a net over the babies' scalps with 128 sensors as the babies sat in their mothers' laps. (An experimenter blew bubbles to distract them.) All babies also underwent extensive behavioral evaluations with the Autism Diagnostic Observation Schedule (ADOS), an established clinical diagnostic tool.

Bosl's computational algorithms analyzed six different components (frequencies) of the EEG (high gamma, gamma, beta, alpha, theta, delta), using a variety of measures of signal complexity. These measures can reflect differences in how the brain is wired and how it processes and integrates information, says Bosl.

The algorithms predicted a clinical diagnosis of ASD with high specificity, sensitivity and positive predictive value, exceeding 95 percent at some ages.

"The results were stunning," Bosl says. "Our predictive accuracy by 9 months of age was nearly 100 percent. We were also able to predict ASD severity, as indicated by the ADOS Calibrated Severity Score, with quite high reliability, also by 9 months of age."

Bosl believes that the early differences in signal complexity, drawing upon multiple aspects of brain activity, fit with the view that autism is a disorder that begins during the brain's early development but can take different trajectories. In other words, an early predisposition to autism may be influenced by other factors along the way.

"We believe that infants who have an older sibling with autism may carry a genetic liability for developing autism," says Nelson. "This increased risk, perhaps interacting with another genetic or environmental factor, leads some infants to develop autism -- although clearly not all, since we know that four of five "infant sibs" do not develop autism."

Helen Tager-Flusberg, PhD, of Boston University was the third co-author on the paper. The study was supported by National Institute of Mental Health (R21 MH 093753), the National Institute on Deafness and Other Communication Disorders (R21 DC08647 R01 DC 10290) and the Simons Foundation.

http://bit.ly/2HU0syK

Use of ibuprofen and similar NSAIDs may shorten life of patients

Non-aspirin non-steroidal anti-Inflammatory medications have a negative impact on overall and progression-free survival time for patients, according to a study published in the journal Kidney Cancer

Amsterdam, NL - Ibuprofen, aspirin, and other non-steroidal anti-inflammatory medications are among the most commonly utilized medications in the United States. Primarily for treating pain, inflammation, and preventing cardiovascular disease, NSAIDs' promising anti-cancer properties have been highlighted by a growing body of data in recent years. However, a new study in the journal Kidney Cancer indicated that non-aspirin NSAID use was associated with shorter overall survival in patients with metastatic renal cell carcinoma (mRCC).

Few studies have evaluated the effect of NSAIDs on patients with localized renal cell carcinoma (RCC); none have had characterized outcomes for patients with mRCC. To explore the effect of NSAIDs on outcomes of patients with mRCC, researchers investigated their use in 4,736 patients from a pooled database of patients treated on phase II-III clinical trials of targeted therapy agents.

According to the lead investigator Rana R. McKay, MD, Assistant Professor of Medicine, University of California San Diego, Moores Cancer Center, La Jolla, CA, USA, "The clinical trials database utilized in our analysis is a powerful tool to investigate clinically relevant questions. In the era of drug repurposing, evaluating the impact of agents that have the potential to demonstrate anti-cancer activity in patients is clinically meaningful. Our study, which is the largest to date investigating the impact of NSAIDs on mRCC, demonstrates that the use of non-ASA (non-aspirin) NSAIDs reduced overall or progression-free survival time for patients with metastatic disease, compared to patients who do not use NSAIDs."

The association of the use of non-ASA NSAIDs with reduced survival was consistent when looking at untreated or previously treated patients, and also when looking at the type of targeted therapy received, either vascular endothelial growth factor (VEGF) or mammalian target of rapamycin (mTOR) targeted therapy. This may be explained by non-ASA NSAIDs' kidney-specific toxicity profile and their potency, which can cause increased blood pressure and decreased renal function.

The study also concluded that aspirin did not provide a survival advantage or have an apparent anti-cancer effect for mRCC patients, even though previous epidemiological data demonstrates that aspirin use decreases incidence, metastasis, and mortality risk in several cancers. They point to NSAID nephrotoxicity as a possible cause and posit that the dose required for tumor-growth inhibition may be larger than the dose needed for the analgesic effect or cardiovascular disease prevention.

The anti-tumorigenic mechanism of NSAIDs has been largely attributed to their cyclooxygenase (COX) inhibitory activity, which leads to the suppression of prostaglandin synthesis, and ultimately decreases inflammation, although there are some differences in the inhibitory actions of ASA and non-ASA NSAIDs. In RCC, COX-2 expression is present in the majority of the tumors and correlates with poorer survival and other negative factors.

The investigators advise that "while thought-provoking, these results should be interpreted cautiously as hypothesis-generating rather than definitive and highlight the need for studies investigating the mechanisms of action underlying our observation." They also recommend: "Prior to starting a new medication in any patient, a discussion needs to take place regarding the potential risks and benefits of that agent. This is especially true for non-aspirin NSAIDs in patients with RCC."

http://bit.ly/2Im65VW

Researchers Succeed in Keeping Disembodied Pig Brains Alive

The organs showed neural activity for up to 36 hours, adding fuel to discussions about the ethics of future neuroscientific research.

By Catherine Offord | May 1, 2018

A team of US researchers has kept disembodied pig brains alive in a comatose-like state for up to 36 hours, according to a report published last week (April 25) by *MIT Technology Review*. First revealed by Yale University neuroscientist Nenad Sestan at a meeting held on March 28 at the National Institutes of Health, the results have increased the urgency of the ethical debate surrounding the future of brain research.

Although other groups have managed to keep disembodied brainstems and hearts of rodents alive, the current project is noteworthy for the scale of the brain being preserved, and its apparent success. The results have yet to be published in a scientific journal.

The researchers achieved the feat by experimenting with more than 100 pig brains obtained from a slaughterhouse, Sestan disclosed at the meeting (via *MIT Technology Review*). While maintaining circulation to the organs with a setup of pumps and heated-up blood, the team observed normal-like patterns of cell activity, even though the brains were only attached to the setup several hours after the pigs were killed—meaning at least some cell death and damage to the organs would be likely.

“These brains may be damaged, but if the cells are alive, it’s a living organ,” Steve Hyman, director of psychiatric research at the Broad Institute in Cambridge, Massachusetts and one of the scientists briefed on the work, tells *MIT Technology Review*. “It’s at the extreme of technical know-how, but not that different from preserving a kidney.”

The reaction to the news has been mixed, *The Guardian* reports. Frances Edwards, a neuroscientist at University College London, notes that the technique could allow researchers to study animals’ neural

networks in greater detail and develop better imaging techniques. But it's unlikely to be replicated in humans, she adds.

"It would be a major, pretty much impossible step even to get this far with a human brain," she tells *The Guardian*. "In the pig, you are taking a healthy animal and able to control exactly when and how it dies and immediately take out the brain." In humans, instead, "by the time the brain is accessible it would be well and truly compromised."

Nevertheless, several researchers argue that the time to consider the ethical implications of such research being carried out with human tissue is now, while brain preservation techniques, along with the development of brain surrogates such as chimaeras and brain organoids, are under development.

Writing last week (April 25) in *Nature*, Sestan, along with Hyman, biologist George Church, and 14 others, urged colleagues and the public to address questions such as "Who, if anyone, should 'own' ex vivo brain tissue, brain organoids or chimaeras?" and "Do ex vivo human brain models challenge our understanding of life and death?"

Neurobiologist Colin Blakemore of the School of Advance Study at the University of London tells *BBC News* that he seconds the authors' message. "It is very, very important that there should be a public discussion about this," he says, "not least because the researchers who have some investment can tell the public why it would be so important to develop such techniques."

http://bit.ly/2wj24fR

Single injection treats hemophilia B for life, in proof-of-concept study

In mice that hemophilia B can be treated for life with one single injection

LA JOLLA - For most people with hemophilia B, whose bodies can't properly form blood clots, constant injections to replenish their clotting factors are a way of life. But now, Salk researchers have demonstrated in mice that hemophilia B can be treated for life with one single injection, containing disease-free liver cells that can produce their missing clotting factor. The finding, published in the journal Cell Reports on May 1, 2018, could drastically change what it means to be diagnosed with hemophilia B, and could pave the way toward similar treatments for other, related genetic disorders.

Hemophilia B is caused by defects in the gene for a protein called clotting factor IX (FIX). Hemophiliacs may make reduced amounts of the protein, or lack a functional version altogether, leading to life-threatening delays in blood clotting. Currently, patients are treated with injections--as often as a few times a week--containing FIX made in animal cells and then purified. But the approach is expensive, time-consuming and can become less effective over time.

Recently, Salk scientists developed a new approach, treating mice genetically engineered to have hemophilia B with strands of messenger RNA encoding the FIX gene. Like the standard treatment, however, this required repeat injections each time levels of the messenger RNA ran low. So the scientists wanted to try a more permanent approach: transplanting healthy liver cells, capable of producing FIX, into patients.

"The appeal of a cell-based approach is that you minimize the number of treatments that a patient needs," says Suvasini Ramaswamy, a former Salk research associate in the Verma lab and first author of the new paper. "Rather than constant injections, you can do this in one shot."

Since donor livers are often in short-supply, the researchers instead turned to stem-cell strategies to produce the healthy liver cells. They collected blood samples from two human patients with severe hemophilia B, who are unable to produce FIX. Then, in the lab, they reprogrammed the cells into induced pluripotent stem cells (iPSCs), which have the capability to turn into many other cell types, including liver. Using CRISPR/Cas9, a tool that can alter genes, they then repaired the mutations in each patient's FIX gene. Finally, they coaxed those repaired cells to develop into liver precursor cells called hepatocyte-like cells (HLCs) and transplanted them into mice with hemophilia B.

Rather than perform surgery on hemophilic mice--a risky undertaking when their blood can't always clot--the team transplanted the HLCs through the spleen to distribute the cells uniformly in the liver.

Not only did the new HLCs produce FIX, but they produced enough of the protein to allow the mice to form normal blood clots, and the cells continued to survive--and produce FIX--for at least a year after the transplantation.

In people with hemophilia, using their own cells to generate healthy HLCs, then transplanting them back into their bodies, could help avoid the immune complications that often accompany cell therapies. But more work is needed to translate the findings to the clinic.

"A lot of things have to happen before this can go into humans," says Ramaswamy. Already, she adds, the work demonstrates the value in combining stem-cell reprogramming and new gene-modifying approaches to treat genetic diseases.

The work and the researchers involved were supported by grants from the National Institutes of Health, the National Cancer Institute, the National Institute of Neurological Disorders and Stroke, the Waitt Foundation, Ipsen, the H.N. and Frances C. Berger Foundation, the Glenn Center for Aging Research, the Leona M. and Harry B. Helmsley Charitable Trust, and the California Institute for Regenerative Medicine.

http://bit.ly/2wnpGjM

Wood you like a drink? Japan team invents 'wood alcohol'

Raw material? Japanese researchers say they have invented a way to produce alcoholic drinks from cherry trees and other types of wood

Discerning drinkers may soon be able to branch out after Japanese researchers said Tuesday they have invented a way of producing an alcoholic drink made from wood.

The researchers at Japan's Forestry and Forest Products Research Institute say the bark-based beverages have woody qualities similar to alcohol which is aged in wood barrels. They hope to have their "wood alcohol" on shelves within three years.

The method involves pulverising wood into a creamy paste and then adding yeast and an enzyme to start the fermentation process.

By avoiding using heat, researchers say they are able to preserve the specific flavour of each tree's wood.

So far, they have produced tipples from cedar, birch and cherry.

Four kilogrammes (8.8-pounds) of cedar wood gave them 3.8 litres (eight pints) of liquid, with an alcohol content of around 15 percent, similar to that of Japan's much-loved sake.

Researchers experimented with both brewed and distilled versions of the new beverage, but "we think distilled alcohol appears better", researcher Kengo Magara told AFP.

Wood fermentation is already used to produce biofuel but the product contains toxins and is flavourless, making it far from a suitable cocktail component. "But our method can make it drinkable, and with a wood flavour, because it does not require high heat or sulphuric acid to decompose the wood," Magara said.

The institute has a broad mandate for scientific study related to Japan's extensive woods and forests, but Magara acknowledged "wood alcohol" might not be the most obvious application for their research resources. "We thought it would be interesting to think that alcohol could be made from something around here like trees," Magara said. "It's a dream-inspired project."

The government institute aims to commercialise the venture with a private-sector partner and to have the lumber liquor on shelves within three years. "Japan has plenty of trees across the nation and we hope people can enjoy wood alcohols that are specialised from each region," Magara said.

https://bbc.in/2JXMJ6C

Doctors paying for sons to have HPV cancer jab

Regularly paying hundreds of pounds for their teenage sons to receive a vaccination against cancer

By Anna Collinson Reporter, Victoria Derbyshire programme

Doctors and health professionals are regularly paying hundreds of pounds for their teenage sons to receive a vaccination against cancer

that girls already receive for free on the NHS, the Victoria Derbyshire programme has been told. Is boys' health being put at risk?

"Had the HPV vaccine been available when I was a boy, I believe I would not have developed throat cancer more than 30 years later," said Jamie Rae, 53.

"I'm basing this on the overwhelming majority of research I have seen over the years and countless experts I have spoken to.

"That's why I'm desperate for boys to be able to receive it."

HPV is the name given to a large group of viruses. It is very common and can be caught through any kind of sexual contact with another person who already has it.

Doctors say 90% of HPV infections go away by themselves - but sometimes infections can lead to a variety of serious problems.

For boys, this includes cancer of the anus, penis, mouth and throat.

Since 2008, girls aged 12 to 18 across the UK have been offered HPV vaccinations as part of the NHS childhood vaccination programme.

It is currently not offered to boys of the same age, but it can be done privately, costing several hundred pounds.

Mr Rae founded the Throat Cancer Foundation after the treatment he received in 2010. He said at the time there was little information on HPV and he did not want anyone to go through his experience.

"I had radiotherapy for 35 days except weekends. I felt extreme burning in my neck and mouth and I was covered in sores. The pain was excruciating," he explained. "It's a lengthy recovery time. You have to teach yourself to swallow again and you get a dry mouth all the time."

His foundation is part of HPV Action - which represents more than 50 groups and charities that are calling for both genders to receive the vaccination on the NHS.

'Indefensible'

Mr Rae said the current disparity between boys and girls was "appalling".

"Lots of doctors are having their boys vaccinated because they can afford it, as are those who are better informed," he said. "But what about those who can't afford it? Cases of throat cancer are soaring. It's indefensible.

"Every day that goes past where boys are not being vaccinated condemns them to a whole host of diseases that we could prevent."

HPV Action says around a dozen countries including Australia, Canada and the US are already vaccinating boys or are planning to do so in the near future.

The government's vaccination advisory committee is currently reviewing whether boys should receive the HPV vaccination.

A spokesperson for the Department of Health and Social Cares says it will carefully consider its advice once they've received it.

Campaigners hope there will be a decision this year, possibly as soon as June.

A debate is taking place on Wednesday at Westminster Hall about the issue.

The argument for vaccinating boys against HPV

- ***About 15% of UK girls eligible for vaccination are currently not receiving both doses, a figure which is much higher in some areas***
- ***Most older women in the UK have not had the HPV vaccination***
- ***Men may have sex with women from other countries with no vaccination programme***
- ***Men who have sex with men are not protected by the girls' programme***
- ***The cost of treating HPV-related diseases is high - treating anogenital warts alone in the UK is estimated to cost £58m a year, while the additional cost of vaccinating boys has been estimated at about £20m a year***

Source: HPV Action

Prof Francis Vaz, a head and neck surgeon at University College London Hospital, paid privately to vaccinate his three sons.

He explained this was because he wanted to protect them from certain cancers like anus, penis, mouth and throat. He said he saw on a daily basis that cancers driven by the HPV virus had been increasing in the past decade.

"I regularly see the bad end of that spectrum, so I thought the vaccination would be suitable for my sons," he said. "It's just

unfortunate it wasn't available for them on the NHS. I was happy to pay for it because I think it's a good vaccine."

He said he made a conscious decision to spend £450 on three injections per son - you can pay less if you have two vaccines. "I'm aware that I'm in the know - and that there are people out there that can't afford it or aren't aware. It seems unfair."

He said for those who are concerned about vaccinating their child, it is a decision for parents to make. "I wouldn't suggest anyone should force a vaccine on any individual, but if this vaccine was exceptionally dangerous it wouldn't be distributed to as many people as it is."

'Very frustrating'

Prof Vaz said he understood there may be many factors explaining why boys were currently not receiving the vaccine, but cost had to be one of them.

The NHS argues only vaccinating girls indirectly protects boys because vaccinated girls will not pass HPV on to them. This is called herd immunity. However, many doctors argue this does not work because boys may go on to have a male partner, have a female partner who has not had the jab or visit a country where they do not provide HPV vaccinations.

"You hope with herd immunity it'll work and protect the boys - but that doesn't work," he explained. "People can fall through the net, though the net has been cast reasonably wide, it currently doesn't protect everyone."

Prof Chris Nutting also vaccinated his two sons, who were aged 13 and 14. "I specialise in treating throat cancer," he explained. "Fifty per cent of cancers I treat are caused by viruses which could be vaccinated against. It's very frustrating."

Decision call

Prof Nutting said the main argument against giving boys the jab is cost - extending the scheme will cost £20m. "The Department of Health should be making a decision. They have put it off for years," he said.

Peter Baker, of HPV Action, said HPV was as dangerous for boys as girls as it caused a number of different cancers in both sexes. "There's no obvious reason why the vaccination is split between the genders. More women get cancer through HPV then men - but the difference isn't huge," he said.

The government's vaccination advisory committee (JCVI) said it was still in the process of considering all the data and will wait until the process has concluded before making any statements. Public Health England also said it would not comment before the decision was made.

http://bit.ly/2wqiwO5

Why you shouldn’t freak out about tick and mosquito infections tripling

Sixty percent of the rise is from Zika, which mainly affected US territories in one year.

Beth Mole - 5/3/2018, 1:55 AM

The Centers for Disease Control and Prevention released an alarming report yesterday, declaring that cases of diseases spread by ticks, mosquitos, and fleas more than tripled in the US between 2004 and 2016. Unnerving headlines followed, emphasizing the tripling (e.g. *The Washington Post*) or some making claims that tick and mosquito infections are “spreading rapidly” (e.g. *The New York Times*).

But a look at the data tells a more nuanced, less alarming story.

The CDC’s data, published in the agency’s Morbidity and Mortality Weekly Report, clumps together cases of 16 different types of diseases spread by insects (called "vector-borne diseases"), which are each reported to the National Notifiable Disease Surveillance System (NNDSS). This system covers all US states as well as US territories. The agency noted in its press materials that this is the first time they’ve ever aggregated disease counts together like this for one analysis. (Why they chose to start this year is anyone’s guess. Perhaps because it allowed them to say things like “diseases tripled.” Who knows?)

Pack of pathogens

The 16 diseases include six tick-borne diseases; the big one is Lyme disease, but there's also spotted fever, and anaplasmosis and ehrlichiosis (counted together). There's also the relatively new babesiosis, and the rare tularemia and Powassan virus. Those last two affected just 230 and 22 people, respectively, in 2016.

CDC researchers examined nine mosquito-borne diseases, including West Nile virus, which is endemic to the US. Its case counts fluctuated with periodic outbreaks during the timeframe but didn't increase overall. CDC experts also netted counts of the newcomers in US-based mosquito-borne diseases—Zika, dengue, and chikungunya—as well as malaria and yellow fever, cases of which are entirely travel related. (There was no malaria or yellow fever transmission within the US during the 13-year period. And there was only one case of yellow fever in that time, which occurred in 2016.)

Researchers also looked at cases of rare mosquito-borne diseases, such as a collection of California serogroup viruses, St. Louis encephalitis virus, and eastern equine encephalitis virus. These did not significantly change over the 13-year period and caused 53, 8, and 7 illnesses, respectively, in 2016.

Last, the researchers looked at one flea-borne disease—plague. Perhaps surprising to some, plague is entrenched in rural rodent populations in many areas of the Western US and has been since the early 20th century (see map in gallery below). As such, there are a handful of cases in people each year, typically presenting as bubonic plague. Case counts usually range from one to fewer than 20. There were three cases in 2004 and four in 2016, with a high of 17 in 2006. There was no significant change in the rate of plague during the time frame, so the rest of the article will focus on the tick and mosquito-spread diseases.

So what *did* increase?

There are a lot of diseases here, each with its own factors and quirks. What accounts for this scary "tripling"? The short answer is: mostly Zika and Lyme disease.

Between 2004 and 2016, the 16 vector-borne diseases caused in total 642,602 cases of illnesses. The grand total of diseases for 2004 was 27,388, but that jumped to 96,075 in 2016.That means that there were an extra 68,687 disease cases in 2016 compared with 2004.

TABLE. Vectorborne disease cases reported to National Notifiable Disease Surveillance System — U.S. states and territories, 2004–2016*

	Year													
Disease	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Tickborne diseases														
Lyme disease†	19,804	23,305	19,931	27,444	35,198	38,468	30,158	33,097	30,831	36,307	33,461	38,069	36,429	**402,502**
Anaplasmosis/ Ehrlichiosis§	875	1,404	1,455	1,999	2,107	2,267	2,615	3,586	3,725	4,551	4,488	5,137	5,750	**39,959**
Spotted fever rickettsiosis¶	1,713	1,936	2,288	2,221	2,563	1,815	1,985	2,802	4,470	3,359	3,757	4,198	4,269	**37,376**
Babesiosis**	N	N	N	N	N	N	N	1,128	937	1,796	1,760	2,100	1,910	**9,631**
Tularemia	134	154	95	137	123	93	124	166	149	203	180	314	230	**2,102**
Powassan virus	1	1	1	7	2	6	8	16	7	15	8	7	22	**101**
Subtotal tickborne diseases	**22,527**	**26,800**	**23,770**	**31,808**	**39,993**	**42,649**	**34,890**	**40,795**	**40,119**	**46,231**	**43,654**	**49,825**	**48,610**	**491,671**
Mosquitoborne diseases														
Dengue viruses††	721	2,462	882	4,484	1,118	2,759	11,611	1,795	6,714	10,727	1,226	1,015	1,178	**46,692**
Zika virus	N	N	N	N	N	N	N	N	N	N	N	N	41,680	**41,680**
West Nile virus	2,539	3,000	4,269	3,630	1,356	720	1,021	712	5,674	2,469	2,205	2,175	2,149	**31,919**
Malaria**	1,458	1,498	1,476	1,411	1,257	1,456	1,778	1,726	1,504	1,594	1,654	1,397	1,958	**20,167**
Chikungunya virus	N	N	N	N	N	N	N	N	N	N	7,521	1,133	427	**9,081**
California serogroup viruses§§	118	80	69	55	62	55	75	137	81	112	96	70	53	**1,063**
St. Louis encephalitis virus	15	13	10	9	13	12	10	6	3	1	10	23	8	**133**
Eastern equine encephalitis virus	7	21	8	4	4	4	10	4	15	8	8	6	7	**106**
Yellow fever virus	0	0	0	0	0	0	0	0	0	0	0	0	1	**1**
Subtotal mosquitoborne diseases	**4,858**	**7,074**	**6,714**	**9,593**	**3,810**	**5,006**	**14,505**	**4,380**	**13,991**	**14,911**	**12,720**	**5,819**	**47,461**	**150,842**
Fleaborne disease														
Plague	3	8	17	7	3	8	2	3	4	4	10	16	4	**89**
Total vectorborne diseases	**27,388**	**33,882**	**30,501**	**41,408**	**43,806**	**47,663**	**49,397**	**45,178**	**54,114**	**61,146**	**56,384**	**55,660**	**96,075**	**642,602**

About 61 percent—or 41,680 cases—of that increase came from Zika; all of the Zika cases occurred in 2016. That was the only year that the NNDSS system collected case counts on Zika. That means that there is not enough data to establish trends for this disease's prevalence. Of those 41,680 cases in 2016, 36,512 were counted in US territories (Puerto Rico, US Virgin Islands, and American Samoa, which all had outbreaks). The remaining 5,168 were counted in US states, but 4,897 of them were travel-related. The last 271 cases were transmitted in US states, mainly in Florida and Texas.

Unexpected and explosive epidemics of emerging pathogens, such as Zika virus, are devastating and require resources to prepare for and control. That said, it's a bit misleading to say that vector-borne diseases *overall* tripled *throughout the US*, when the biggest cause of that

increase is one year of epidemic cases in specific territories—one that just happened to occur in the last year of the 13-year period analyzed.

Ars reached out to the CDC to ask why the data was framed this way. Dr. Ronald Rosenberg, a vector-borne disease expert and lead author of the new report got back to us saying: "Your point about Zika inflating the tally is well taken but we can say that about all the epidemic arboviruses [these types of insect-spread viruses], depending on the period you choose it could be up or down. What is significant is that we continue to have epidemics of not only those viruses known before 2004 but the two new ones [Zika and chikungunya]."

Uptick in tick-borne diseases

So, what about the rest of the increase? About 24 percent was from Lyme disease. But, that increase also requires an asterisk. Lyme disease case counts went from 19,804 in 2004 to 36,429 in 2016. But the CDC changed the way it counted Lyme disease cases back in 2008, adding "probable" cases into the "confirmed" case counts. Unsurprisingly, the number of Lyme disease cases peaked in 2009, with 38,468 cases. It has been below that level ever since (see graph in gallery above).

That said, there's no doubt that the incidence of Lyme disease is increasing—albeit at a slower pace. This has been going on for decades, as is the case for some other tick-borne diseases. A study by CDC researchers in 2008 looking at Lyme disease surveillance between 1992 and 2006 concluded that the number of reported cases doubled in that timeframe. They attributed the rise to "multiple reasons… including a true increase in the number of infections, enhanced surveillance, increased awareness among health-care professionals and the public, misdiagnosis, and reporting errors." The "true increase" in cases may be due to booms in tick populations, encroachment of human development into rural and suburban areas, and expansion of reservoir animal populations (that is, animals that harbor the pathogens before they're transmitted to humans, such as mice and squirrels in the case of Lyme disease).

Overall, the CDC researchers concluded that the 2008 report's findings "underscore the continued emergence of Lyme disease and the need for tick avoidance and early treatment interventions."

The gradual, continued increase of Lyme disease has in turn upped detection and surveillance of other tick-borne diseases, such as babesiosis, spotted fever, and anaplasmosis and ehrlichiosis. Those also saw increases in the current study, albeit at much lower levels than Lyme.

Overall, the bigger bites of tick-borne diseases and the buzz of periodic and emerging mosquito-borne diseases are urgent threats to public health. The CDC and local health authorities need more resources to monitor, anticipate, prevent, and control their spread. And the public needs to remain vigilant, including packing that bug spray as tick and mosquito-season is upon us. But most of the US is not seeing a sudden surge in these diseases—it's just that these truths make for less exciting headlines.

This post has been updated to include a response from the CDC.

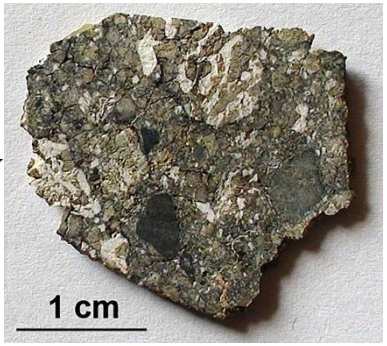
http://bit.ly/2IqvYGB

Meteorite find boosts hopes for moon water

A mineral in a moon rock means ice is just below the surface.

Richard A Lovett reports.

A rare mineral in a Saharan meteorite points to the presence of significant amounts of ice not far beneath the moon's surface, scientists say.



Small, but vitally important: a moon rock that strongly indicates the presence of water ice. **Masahiro Kayama and M. Sasaoka (SASAMI-GEO-SCIENCE)**

The meteorite, says Masahiro Kayama, a researcher from Tohoku University, Japan, is a chip from the moon that was blasted into space by an impact long ago. Scientists know it is of lunar origin, Kayama adds, because its chemistry, appearance, and isotope ratios match those of rocks brought back by Apollo astronauts.

They even know that it comes from a sprawling region known as Procellarum Terren, which spans much of the upper-left quadrant, as seen from Earth.

Such meteorites are rare – only 322 are currently known to exist, according to the official tally in the Meteoritical Bulletin Database – but they are important because many are from parts of the moon not visited by Apollo astronauts, says Melinda Hutson, curator of the Cascadia Meteorite Laboratory at Portland State University, in Oregon, US.

Kayama's meteorite, named NWA 2727, fell to Earth about 17,000 years ago. But it wasn't known to scientists until pieces of it were purchased from a Moroccan dealer in 2005. Now, Kayama and colleagues report in the journal *Science Advances* that it contains an unusual mineral called moganite.

Moganite is rare enough that it was unknown to science until 1984. It is similar to quartz, explains Kayama, but can only be formed from the evaporation of mineral-rich alkaline water. For moganite to have formed on the moon, he says, there had to have been an ice deposit not far beneath its surface, presumably brought in via an impact from a comet or water-rich asteroid.

Much of that water may have boiled off into space in the immediate aftermath of the impact, but some must have been trapped underground. Then, something else, perhaps a subsequent impact, stirred things up, melting the ice and creating conditions for the formation of moganite. Yet another impact later blasted pieces of this rock off into space, from which some eventually made their way to Earth.

What makes this exciting, Kayama adds, is that if there was sufficient near-surface water in one region to form moganite, additional water may well still be lurking elsewhere in the form of other ice deposits. These could be anywhere from a few centimetres to a few hundred metres below the surface.

Other scientists are excited. Only a few days ago, for example, Terik Daly, a planetary scientist at Johns Hopkins University, Baltimore, Maryland, published an article in the same journal describing laboratory experiments showing how water from an impact like Kayama's water-rich comet or asteroid could have been trapped indefinitely beneath the surface. "This paper picks up where my paper left off," he says.

The study is also important for future lunar exploration and colonisation. Kayama's team estimates that for moganite to form, the rocks below that part of the moon's surface must have contained enough trapped ice to make up at least 0.6% of their weight. That doesn't sound like much, but it's equivalent to 18.8 litres of liquid per cubic metre.

That is approximately the amount of ice found at the moon's South Pole by NASA's 2009 LCROSS mission, which fired a giant projectile at it and observed the vapours released by the impact.

The projectile was aimed at one of the moon's permanently shadowed polar "cold traps" where temperatures never rise above minus-240 degrees Celsius and traces of water vapour were expected to condense into ice deposits. "The fact that the amounts of water implied by [the new] study align with findings from the LCROSS mission provides added confidence in the results," says Daly.

Building a lunar base in such cold conditions would be difficult. Building a base in the more temperate climes of Procellarum Terren, however, would be far less challenging, and the moganite in NWA 2727 suggests that the resources might be there to make it easier than previously anticipated.

"Astronauts can get enough water [and from it, hydrogen and oxygen] for drinking, breathing, and fuel," Kayama says.

Hutson agrees. Only a few days ago, scientists were bemoaning NASA's decision to scrap plans for its Lunar Prospector mission, which was intended to send a rover to the moon in search of ice deposits. The new finding, she says, "will provide additional impetus for going back to the moon to search for water".

http://bit.ly/2IkjJZj

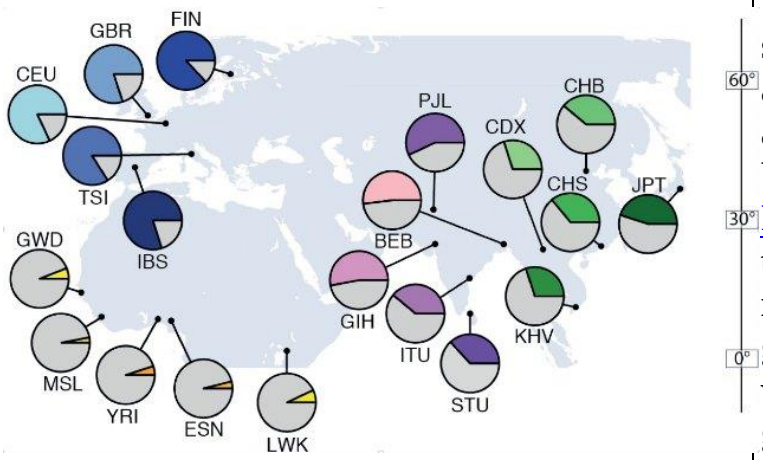
Genetic Adaptation to Cold Brought Migraines With It

Humans living in higher latitudes tend to have a variant of a gene involved in sensing cold temperatures, but it comes with a cost.

By Viviane Callier | May 3, 2018

A human genetic variant in a gene involved in sensing cold temperatures became more common when early humans migrated out of Africa into colder climates between 20,000 and 30,000 years ago, a study published today (May 3) in *PLOS Genetics* shows.

The advantage conferred by this variant isn't definitively known, but the researchers suspect that it influences the gene's expression levels, which in turn affect the degree of cold sensation. The observed pattern of positive selection strongly indicates that the allele was beneficial, but that benefit had a tradeoff—bringing with it a higher risk of getting migraines.



***Frequency of the adaptive allele in several human populations (from the 1000 Genomes dataset). Colors and letters represent different populations in the dataset, and the pie charts reflect the proportion of individuals in those populations who have the variant* TRPM8 *allele.* Felix M. Key, Mpi-Eva Multimedia Department And Colleagues**

"This paper is the latest in a series of papers showing that humans really have adapted to different environments after some of our ancestors migrated out of Africa," explains evolutionary geneticist Rasmus Nielsen of the University of California, Berkeley, who was not involved in the study. "There are a number of adaptations associated with moving into an artic climate, but none with as clear a connection to cold as this one," he adds.

Although studies have demonstrated some striking examples of recent human adaptation, for instance, warding off infectious diseases such as malaria or having the ability to digest milk, relatively little was known about the evolutionary responses to fundamental features of the environment, namely, temperature and climate.

"Obviously, humans lived in Africa for a long time, and one of the main environmental factors that changed as humans migrated north was temperature," explains population geneticist Aida Andres. So she and Felix Key the Max Planck Institute in Leipzig homed in on a gene, *TRPM8*, that encodes a cation channel in the neurons that innervate the skin. It is activated by cold temperatures and necessary for sensing cold and for thermoregulation. If there was a place to look for human adaptation, this gene looked like a good candidate.

Using the 1000 Genomes dataset and the Simons Genome Diversity Panel, the researchers investigated variants of this gene in populations throughout Africa, Europe, and Asia. They found that a single nucleotide polymorphism (SNP) in a regulatory region of the *TRPM8* gene was "highly differentiated between different populations in the world," Andres, now at University College London, says. And genotype correlated with latitude: 5 percent of people with Nigerian ancestry, versus 88 percent of people with Finnish ancestry, carry the cold-adapted variant.

Using models of population genetics, the researchers inferred that the cold-adapted allele had already existed in the ancestral African population, and that it became more common as people migrated northward. The geographic pattern was consistent with positive selection for the SNP at higher latitudes, Andres says.

"One of the interesting things about [this variant] is that it is relatively more common in Europe than in Asian people who live at the same latitude," notes Hawks. "We don't know why that should be. Maybe there's a historical factor here that isn't yet understood."

To find out when selection on this variant occurred, the researchers looked for the SNP in the genomes from ancient remains of hunter gatherers or farmers that lived 3,000–8,000 years ago in Eurasia. It turned out that the allele was already common among these groups at least 3,000 years ago.

The connection between *TRPM8* and migraine isn't clear, other than the association. "Selection is optimizing fitness," says anthropologist John Hawks of the University of Wisconsin-Madison who was not associated with the study. "It doesn't optimize health, it doesn't optimize happiness, so sometimes things are pushed by selection and they have negative side effects. This seems to be a case where a gene is pushed higher in frequency by selection for adaptation to cold, and it maybe has a bad side effect on increased susceptibility to migraines." It's also possible that the downside to having the cold-adaptive *TRPM8* allele is a modern phenomenon, and that the migraine risk didn't appear until more recently as environments have changed, says Nielsen.

F.M. Key et al., "Human local adaptation of the TRPM8 cold receptor along a latitudinal cline. PLOS Genet, 14:e1007298, 2018.

http://bit.ly/2HWJ0cX

Find pushes back hominin arrival in the Philippines seven hundred thousand years

Archaeologists unearth tools and bones that rewrite the settlement history of the region.

Andrew Masterson reports.

The discovery of stone tools near the skeleton of a long-extinct rhinoceros has pushed back evidence for hominin settlement in the Philippines by hundreds of thousands of years – long before the presence of *Homo sapiens*.

In a paper in the journal *Nature*, archaeologists led by Thomas Ingicco of the National Museum of Natural History in Paris, France, detail the results of recent excavations at a site called Kalinga in the Cagayan Valley of northern Luzon.

The team unearthed 57 stone tools, including flakes and possible hammer stones, in the vicinity of fossil bones and teeth from several different species, including the elephant-like stegodon, brown deer, turtles and monitor lizards. Most prominent, however, was an almost complete but dismembered skeleton of an extinct rhino, *Rhinoceros philippinensis*, showing clear signs of butchery.

Using a dating method known as electron-spin resonance, applied to tooth enamel and quartz, the finds were all dated to between 777,000 and 631,000 years ago.

Although the presence of ancient human ancestors in the Philippines has been hypothesised for decades, until now the oldest firm evidence of hominin occupation was a single metatarsal bone recorded in 2010 and dated to just 66,000 years ago. The bone, also found in northern Luzon, was identified as belonging to a "small bodied" *Homo sapiens*.

In the light of the new findings, Ingicco and colleagues suggest that this classification be revisited. The bone may indeed be from a comparatively recent migratory wave of *Homo sapiens*, they say, but may also be a direct descendent of the Kalinga tool makers.

As to which hominin species made the stone tools and butchered the rhino, the researchers say there is in insufficient evidence to make a determination, but nominate *Homo erectus* or Denisovans as possibilities.

They also raise the possibility that the ancestors of the Kalinga community may have arrived from across the sea, implying that they possessed the skills and knowledge to make simple water craft. Such a hypothesis, they concede, "still seems too farfetched to suggest", however, in light of increasing evidence of overseas dispersal, it "cannot currently be rejected".

http://bit.ly/2wiA1gF

Gut check: Metabolites shed by intestinal microbiota keep inflammation at bay

Researchers find inflammatory response in fatty liver disease is reduced by two tryptophan metabolites from gut bacteria

MEDFORD/SOMERVILLE - Researchers at Tufts University have elucidated a mechanism by which the "good" bacteria that reside in our gastrointestinal tract can help protect us from inflammation, and how their disruption (dysbiosis) can increase the susceptibility of the liver to more harmful forms of disease. Their study, now available in the journal *Cell Reports*, identified two key metabolites produced by the bacteria in mice that modulate inflammation in the host and could ultimately reduce the severity of non-alcoholic fatty liver disease.

Non-alcoholic fatty liver disease (NAFLD) is a prevalent condition in Western countries, affecting up to 25 percent of adults, tracking along with trends in obesity and diabetes. The severity of symptoms can vary, ranging from simple steatosis, which is benign and asymptomatic, to non-alcoholic steatohepatitis (NASH), which is characterized by liver inflammation, swelling and fibrosis and can lead to cirrhosis and liver cancer.

People who eat a high fat diet are more susceptible to NAFLD. Replicating that diet in mice, the researchers found that within just a few weeks, their intestinal microbiota changed character significantly, with some species of bacteria increasing and others decreasing. At the same time, an inventory of metabolites in the mouse's GI tract, serum and liver showed some metabolites known to be linked to intestinal microbiota to shift compared to mice on a low-fat diet. Three of those metabolites - tryptamine (TA), indole-3-acetate (I3A), and xanthurenic acid - were significantly depleted in high fat diet mice.

"That's bad news for the liver," said Kyongbum Lee, Ph.D., professor of chemical and biological engineering at the School of Engineering at Tufts. "We demonstrated that two of these metabolites - I3A and TA - attenuate the effects of inflammation in several ways. Their depletion clears the way for disease to progress toward more serious stages."

Some of those effects of I3A and TA include reducing the level of inflammation-inducing molecules (known as cytokines) like tumor necrosis factor alpha, interleukin-1-beta, and monocyte chemoattractant protein. The latter acts as an attractant for macrophages, which in turn produce more cytokines. All of these inflammatory agents are triggered by high levels of free fatty acid accumulation in the serum and liver - the hallmark of NAFLD, and the consequence of an unhealthy high fat diet.

Researchers also considered whether I3A and TA could be added back to the gut to help treat those with the more serious inflammatory stages of NAFLD. However, it was determined that high levels of TA are toxic.

"Our focus now is on I3A, where we will be exploring whether I3A or other microbiota metabolites can change the course of disease," said Lee.

Other contributing authors include Smitha Krishnan, Maria Choi, and Gautham Sridharan of the Tufts Department of Chemical and Biological Engineering, Nima Saedi and Martin Yarmush of the Center for Engineering in Medicine at Massachusetts General Hospital, David Sherr of the Boston University School of Public Health, and Robert Alaniz of Texas A&M University College of Medicine, and Yufan Ding and Arul Jayaraman of Texas A&M University Department of Biomedical Engineering.

The work was supported by the National Science Foundation (12645502, 1337760, 0821381) and the National Institute of Medical Sciences (GM106251).

Krishnan, S., Ding, Y., Saedi, N., Choi, M., Sridharan, G.V., Sherr D.H., Yarmush M.L., Alaniz R.C., Jayaraman A., Lee K. "IGut microbiota-derived tryptophan metabolites modulate inflammatory response in hepatocytes and macrophages," Cell Reports, (April 24, 2018) 23:1-13. DOI: 10.1016/j.celrep.2018.03.109

http://bit.ly/2KJ0oiT

A Cockroach Crawled Inside a Woman's Ear, and It Can Happen to You

Another day, another story about an insect crawling into a person's ear and making itself at home.

By Yasemin Saplakoglu, Staff Writer | May 4, 2018 04:24pm ET

Katie Holley, a Florida resident, woke up in the middle of the night to a weird sensation in her ear, "like someone had placed a chip of ice in my left earhole," she wrote in an essay published in Self magazine. At first, her husband tried to remove the invader with tweezers. But that strategy wasn't successful, so they went to the emergency room. There, the doctor confirmed her suspicion: A cockroach was in her ear canal. To get the insect out, he first killed it with lidocaine (a numbing agent) and then removed it using tweezers.

But in the days that followed, Holley had soreness in her ear and trouble hearing. When she returned to the doctor nine days later, she learned that she still had pieces — including the entire head — of the roach lodged in her ear.

If you're thinking "gross," you're not alone.

Unfortunately, insects crawling into ears appears to be more common than you'd hope, according to some doctors who talked to Self. (Not so common, though, that you should lose sleep over it).

While there are no recent studies that aim to quantify the icky instances, one small study, published in 2006 the South African Medical Journal, found that during a two-year period, the Tygerberg Hospital in Cape Town, South Africa, removed 23 insects (and one tick) from people's ears. Those insects included three beetles, eight flies and 10 German cockroaches.

And in 2014, emergency-room doctors in Taiwan found a batch of fruit-fly larvae in a woman's ear canal. The 48-year-old had sought medical care because she had severe ear pain, Live Science reported at the time.

Another case in Taiwan from 2012 involved a man who itched for two months because he had mites in his ears— a condition that's familiar enough to earn it a medical name: otoacariasis, according to a study published in 2016 in the Journal of Otology. (Otoacariasis isn't limited to mites; it can also be caused by ticks, the study said.)

If you do think you have an insect in your ear, take this advice from the National Institutes of Health (NIH): Try keeping the ear with the insect in it pointing upward in the hope it crawls or flies out or pouring mineral, olive or baby oil into your ear to suffocate the bug and let it potentially float out. And as Holley did, the NIH recommends visiting a doctor even if you pull out the insect on your own, because legs or other parts could be left behind and cause infections.