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The Overwhelming Safety of the HPV Vaccine

Misinformation Keeps Vaccination Rates Low

Paul A. Offit, MD

No vaccine has suffered more from misinformation and ill-founded concerns than the human papillomavirus (HPV) vaccine. Antivaccine activists have claimed that HPV vaccine causes chronic pain syndromes, chronic fatigue, sudden death, and a variety of autoimmune disorders. In addition, activists have gone so far as to claim that the HPV vaccine increases risky sexual behavior. These claims are often supported by the media as well as by substandard studies published in predatory journals. Indeed, on December 4, 2013, Katie Couric, in a segment titled "HPV Vaccine Controversy," interviewed two mothers: One claimed that the vaccine had caused her daughter to suffer chronic fatigue, the other that the vaccine had caused an otherwise unexplained death.

As a consequence of such fears, immunization rates for the HPV vaccine remain low. According to the Centers for Disease Control and Prevention (CDC), only 53% of girls and 44% of boys have received the recommended doses.[1] As currently constructed, the HPV vaccine—which contains the L1 surface protein from nine different strains—will prevent about 29,000 cases of HPV-associated cancers and 5000 deaths a year.[2] Unfortunately, because only about half of US adolescents have received this vaccine, every year about 15,000 people are destined to suffer and 2000 to die from a preventable cancer.

To the credit of the scientific and medical communities, millions of dollars have been spent on studies examining the safety of the HPV vaccine. Pre-licensure, about 30,000 people were studied for 7 years.[2] Post-licensure, more than 1 million people have been formally studied, examining all manner of chronic pain and fatigue syndromes as well as more than a dozen different rheumatologic diseases.[3-6] Not surprisingly, the HPV vaccine has not been found to cause any chronic or debilitating condition. Indeed, the HPV vaccine is probably the world's best-studied, modern-day vaccine.

Another Unwarranted Concern Debunked: Primary Ovarian Insufficiency

One concern recently raised by antivaccine activists is that the HPV vaccine causes primary ovarian insufficiency. How this concern was born remains a mystery. HPV doesn't infect the ovaries. And the HPV L1 surface protein doesn't mimic proteins on ovarian cells, which would at least make an autoimmune disease biologically plausible. Nonetheless, the fear persists. To address this concern, researchers at Kaiser Permanente Northwest examined a cohort of 199,078 female patients, finding 120 with a diagnosis of primary ovarian insufficiency.[7] The researchers found no statistically significant elevation of risk for ovarian failure following receipt of the HPV vaccine. They also didn't find an increased risk following receipt of the Tdap, MenACWY, or inactivated influenza vaccines.

The Kaiser Permanente study can now be added to the mountain of evidence that should reassure clinicians and parents that the HPV vaccine is safe. HPV, on the other hand, isn't safe. And until we dramatically increase immunization rates against this common, devastating infection, children will continue to suffer our ignorance.

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http://bit.ly/2Nx1R0e

UNM study shows medical cannabis effective in treating a wide range of health conditions

Researchers use mobile app to identify and track symptom relief

Utilizing new mobile application technology, researchers at The University of New Mexico found that medical cannabis provides immediate symptom relief across dozens of health symptoms with relatively minimal negative side effects.

In two recent studies titled, "Patient-Reported Symptom Relief Following Medical Cannabis Consumption," and "Effectiveness of Raw, Natural Medical Cannabis Flower for Treating Insomnia under Naturalistic Conditions" published in the journals, *Frontiers in Pharmacology and Medicines*, respectively, UNM Department of Psychology Associate Professor Jacob Miguel Vigil and UNM Department of Economics Assistant Professor Sarah See Stith, document that patients experienced statistically and clinically significant therapeutic benefits when they used cannabis for symptoms ranging from chronic pain to insomnia.

These studies analyzed data collected with the Releaf App, developed by co-authors Franco Brockelman, Keenan Keeling and Branden Hall and currently, the largest repository of user-entered information on the consumption and effects of cannabis use in the United States with nearly 100,000 recorded user sessions.

Since its release in 2016, the commercially developed Releaf App has been the only publicly available, incentive-free patient educational software program designed for recording how individual cannabis usage sessions correspond to immediate changes in symptom intensity levels and experienced side effects.

"If the results found in our studies can be extrapolated to the general population, cannabis could systematically replace multi-billion dollar medication industries around the world. It is likely already beginning to do so." - Jacob Vigil

This electronic assessment tool enables patients to monitor and manage their cannabis consumption decisions under naturalistic conditions while avoiding the limitations of retrospective survey collection methods (e.g., memory bias, social desirability effects) making it an ideal research tool for measuring real-world cannabis use.

In the first study, across 27 different health conditions with symptoms that ranged from seizure disorders to depression, users reported an average symptom reduction of nearly 4 points on a 1-10 scale following the consumption of cannabis in its various product forms, from concentrates to topicals.

The second study focused specifically on the use of raw natural cannabis flower, or 'buds' for treating insomnia, with similar degrees of effectiveness that varied according to characteristics of the flower and combustion methods. Both investigations were supported in part by the University of New Mexico Medical Cannabis Research Fund, which was designed to facilitate the types of biomedical cannabis-based research that historically have been difficult to fund through conventional governmental entities, such as the National Institutes of Health.

Most prescription medications carry a long list of unavoidable negative side effects and risks of serious health concerns and even death, allowing alternative forms of medication to compete for patient preferences and healthcare industry demands. Medical cannabis is rapidly gaining popularity with the largest expansions in

use among older people and patients with significant health conditions.

"Observational studies are more appropriate than experimental research designs for measuring how patients choose to consume cannabis and the effects of those choices," said Vigil. "By collecting massive amounts of patient-entered information on actual cannabis used under real-life circumstances we are able to measure why patients consume cannabis, the types of products that patients use, and the immediate and longer-term effects of such use. In other words, many of the important and practical research questions that randomized controlled trials fail to address."

Cannabis has been investigated as a potential treatment for a wide range of medical conditions from post-traumatic stress disorder to cancer, with the most consistent support for the treatment of chronic pain, epilepsy and spasticity. These studies hint at just how wide cannabis' therapeutic potential may be and are among the first to measure how characteristics of cannabis consumed by millions of people in the U.S. every day are likely to affect different types of health disturbances, both in symptom severity levels and experienced positive and negative side effects.

One of the most striking patterns in the current results was the breadth of symptoms that appeared to improve following cannabis consumption. More than 94 percent of cannabis users reported symptom intensity reductions following self-administered cannabis use across the various health conditions measured with the Releaf App. This may reflect the ability of the plant's phytocannabinoids to influence the human endocannabinoid system, which regulates both mental and physical health and behavioral systems.

According to the endocannabinoid deficiency theory, many mental and physical health disturbances result from the dysregulation of the body's innate endocannabinoid system (ECS), often described as a master network of chemical signals that promote physical and psychological homeostasis, or biological state-efficiency. The ECS consists of natural ligands (e.g., anandamide and 2-AG) and receptors (CB1 and CB2) that appear to play a major role in efficient regulation of a basic bodily systems including sleep, feeding (e.g., gut permeability and adipogenesis), libido and fertility, pain perception, motivation, happiness, anxiety, learning and memory, social functioning, autoimmune responses, cellular redox, and cancer pathophysiology.

"In other words and unlike conventional pharmaceutical approaches, which largely target specific neurotransmitter sites, cannabis may act to improve a broad spectrum of symptoms by regulating homeostatic functioning, perhaps best described as a system-modulating rather than symptom-modulating form of therapy," said Vigil. "The medicinal potential of this concept and practical application for treating so many and seemingly diverse health conditions is unlike that of any other single medication currently known to exist."

In addition to therapeutic benefits, these studies also showed that cannabis use is associated with frequent and numerous, yet generally non-serious side effects. Positive and context-specific side effects were far more commonly reported than negative side effects by the Releaf App users, with the most frequent reported side effects being positive (relaxed, peaceful, comfy) and the least frequent side effects being negative (paranoid, confused, headache).

Ultimately, cannabis could find a permanent place among our modern repertoire of medication options if it can treat users' health conditions more effectively and more safely than conventional pharmaceutical remedies. As in the case of insomnia, prescription sleep aids such as antidepressants (e.g., trazodone, amitriptyline, and doxepin), benzodiazepines (e.g., diazepam and lorazepam), gamma-aminobutyric acid (GABA) medications (zolpidem and eszopiclone), and anti-psychotics (aripiprazole, olanzapine, quetiapine and

risperidone) are associated with significant clinical drawbacks and heightened risk of morbidity.

The widespread apparent use of cannabis as a sleep aid and for treating myriad other health symptoms underscores the importance of further medical research regarding its risk-benefit profile and the effectiveness of cannabis as a substitute for other substances, including alcohol, over-the-counter and prescription sleep aids, and scheduled medications (e.g., opioids and sedatives).

According to Stith, "The economic impact of cannabis treatment should also be considered given the current burden of opioid and other high-risk prescriptions on healthcare systems, which have been forced to implement costly modifications to general patient care practices, including prescription monitoring programs, drug screening, and more frequent doctor-patient interactions.

"In addition, if the short-term risk-benefit profile of cannabis found in our studies reflects its longer-term therapeutic potential, substitution of cannabis for traditional pharmaceuticals could reduce the risk of dangerous drug interactions and the costs associated with taking multiple medications by allowing patients to treat a constellation of comorbidities with a single treatment modality. "

"If the results found in our studies can be extrapolated to the general population, cannabis could systematically replace multi-billion dollar medication industries around the world. It is likely already beginning to do so," Vigil added.

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Researchers unlock secret of deadly brain cancer's 'immortality'

New therapeutic target identified in glioblastoma could be effective against a common immortality mechanism in one third of human cancers

UC San Francisco researchers have discovered how a mutation in a gene regulator called the *TERT* promoter -- the third most common mutation among all human cancers and the most common mutation in the deadly brain cancer glioblastoma -- confers "immortality" on tumor cells, enabling the unchecked cell division that powers their aggressive growth.

The research, published September 10, 2018 in *Cancer Cell*, found that patient-derived glioblastoma cells with *TERT* promoter mutations depend on a particular form of a protein called GABP for their survival. GABP is critical to the workings of most cells, but the researchers discovered that the specific component of this protein that activates mutated *TERT* promoters, a subunit called GABP-ß1L, appears to be dispensable in normal cells: Eliminating this subunit using CRISPR-based gene editing dramatically slowed the growth of the human cancer cells in lab dishes and when they were transplanted into mice, but removing GABP-ß1L from healthy cells had no discernable effect.

"These findings suggest that the ß1L subunit is a promising new drug target for aggressive glioblastoma and potentially the many other cancers with *TERT* promoter mutations," said study senior author Joseph Costello, PhD, a leading UCSF neuro-oncology researcher.

Immortality is one of the key traits of cancer cells. In contrast to healthy cells, which are strictly limited in the number of times they are able to divide, cancer cells can go on dividing and multiplying forever, in many cases accumulating additional cancer-driving mutations as they go.

Normally, cellular life spans are set by structures called telomeres -- protective caps that sit at the ends of chromosomes like the aglets at the end of a shoelace. Telomeres shorten each time a cell divides, until eventually they are too short to protect the DNA any longer, a signal the cell has reached the end of its natural life span and should be retired like a balding car tire.

Tumor cells in most cancers get around this limitation by stealing the secret of immortality from long-lived stem cells, which can divide

indefinitely thanks to a telomere-extending enzyme called telomerase, the discovery of which led to a Nobel prize shared by UCSF's Elizabeth Blackburn, PhD. Normally only stem cells are allowed to cheat death in this way, but scientists estimate that as many as 90 percent of human cancers have activated telomerase, many through mutations in *TERT*, one of the two genes that encodes the telomerase complex, which enable them to grow and spread unfettered by the limitations of normal cells.

Efforts to treat cancers with drugs that block telomerase have mostly proven too toxic to patients because they interfere with telomere maintenance in stem cells such as those needed to maintain healthy blood.

But recent research has suggested that more than 50 types of human cancers may be caused not by a defective *TERT* gene itself, but by mutations in the *TERT* promoter -- a region of DNA where protein complexes called transcription factors can influence when and how the *TERT* gene is activated. These mutations enable a transcription factor called GABP to bind to the *TERT* promoter and activate it, other studies had found, which was strange because in healthy cells GABP and *TERT* usually have nothing to do with one another.

"This was really intriguing to us," Costello said. "You can't create a drug to target a promoter itself, but if we could identify how GABP was binding to the mutated promoter in these cancers, we might have a remarkably powerful new drug target."

Costello's team, led by graduate students Andrew Mancini and Ana Xavier-Magalhaes, studied human glioblastoma cell lines and primary tumor cells derived from advanced-stage glioblastoma patients and showed that the cells' mutations create two adjacent sequences of DNA in the *TERT* promoter that make a perfect landing pad for a particular form of the GABP transcription factor complex containing four subunits, one of which was GABP-ß1L.

The researchers showed that this GABP-ß1L-containing form of GABP is required to activate *TERT* and drive cancer growth, but that it appears not to be essential for healthy cells. When the researchers used multiple techniques, including CRISPR-based gene editing, to eliminate the GAPB1L subunit from glioblastoma cells in laboratory cultures, the cells' growth dramatically slowed. The researchers then implanted patient-derived glioblastoma cells into mice and showed that while unedited cells grew aggressively and quickly proved fatal for the animals, cells edited to lack GAPB1L grew much more slowly and were less lethal.

Costello said the next step will be to identify small-molecule drugs that could have a similar effect as the gene editing used in the current experiments, which was performed in collaboration with co-authors Pablo Perez-Pinera, PhD, of the University of Illinois, Urbana-Champaign and CRISPR pioneer Jennifer Doudna, PhD, of UC Berkeley and the Gladstone Institutes in San Francisco, who is also an adjunct professor of cellular and molecular pharmacology at UCSF.

"In theory what we have now is a therapeutic target that is not *TERT* itself, but a key to the *TERT* switch that is not essential in normal cells," Costello said. "Now we have to design a therapeutic molecule that would do the same thing."

A San Francisco-based company called Telo Therapeutics, founded by Costello and former graduate student Robert Bell, PhD, who is also a co-author on the current study, is currently conducting small molecule screens to find such a molecule in partnership with pharmaceutical giant GlaxoSmithKline (GSK).

"It's gratifying that GSK is willing to invest their significant resources into this early-stage finding," Costello said. "To me, it really speaks to promise of this target for so many different human cancers."

Authors: *Senior author Joseph Costello, PhD, is Karen Osney Brownstein Endowed Chair in Molecular Neuro-Oncology at UCSF, a professor in the Department of Neurological Surgery, and member of the UCSF Helen Diller Family Comprehensive Cancer Center. UCSF graduate student Andrew Mancini and former graduate student Ana Xavier-Magalhaes, PhD, were co-lead authors of the new study.*

Other authors were Kien-Thiet Nguyen, Josie L. Hayes, PhD, Andrew M. McKinney, Chibo Hong, PhD, Lindsey E. Jones, Kyle M. Walsh, PhD, and Robert J.A. Bell, PhD, of UCSF; Alexandra M. Amen, PhD, of UCSF and UC Berkeley; Christof Fellmann, PhD, of UC Berkeley; Jennifer A. Doudna, PhD, of UC Berkeley, the Gladstone Institutes, and the Howard Hughes Medical Institute; Wendy S. Woods, Michael Gapinske, Jun S. Song, PhD, and Pablo Perez-Pinera, PhD, of the University of Illinois, Urbana-Champaign; and Bruno M. Costa, PhD, of the University of Minho in Braga, Portugal. Doudna is also an adjunct professor at UCSF and executive director of the UC Berkeley-UCSF Innovative Genomics Institute. Bell is now CEO at Telo Therapeutics.

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Conflicts: *Costello and Bell are co-founders of Telo Therapeutics Inc. and have ownership interest.*

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Study reveals 'dark motives' behind brain teaser questions in job interviews

Brain teaser questions may be used because they give the interviewers power

A new *Applied Psychology* study asks why brain teaser questions are often used in employment interviews despite their known lack of validity and reliability. The authors provide evidence that these questions may be used because they give the interviewers power and speak to their 'dark personality traits.'

The study notes that companies such as Xerox, Microsoft, and Zappos are purported to ask applicants such questions as "Why is a tennis ball fuzzy?" "Why are manhole covers round?" and "How many cows are in Canada?" These oddball questions are not limited to employers in the United States, as several European employers have adopted the practice as well.

For the study, 736 participants were provided with various interview questions and asked if they would consider using them when hiring someone. They then completed questionnaires that assessed their personality traits.

Participants who would consider using brainteaser interview questions when hiring someone were more narcissistic, more sadistic, less socially competent, and believed more strongly in the power of intuition in the hiring process.

"Use of brainteasers in the hiring process provides little information about the suitability of the job applicant but considerable information about the callousness of the interviewer," said co-author Dr. Scott Highhouse, of Bowling Green State University, in Ohio.

Additional Information

Link to Study: https://onlinelibrary.wiley.com/doi/abs/10.1111/apps.12163

http://bit.ly/2x4DUnp

Study links widely used drug azathioprine to skin cancers

Study published in Nature Communications

A drug used to treat inflammatory bowel disease, arthritis and vasculitis as well as to prevent organ rejection in transplant patients has been identified as an important contributor to skin cancer development, in a research study carried out at the University of Dundee, Queen Mary University of London and the Wellcome Sanger Institute.

The research, published in Nature Communications, identified a `strong case for an association' between the drug azathioprine and the mutational signature found in cases of cutaneous squamous cell carcinoma (cSCC), a common form of skin cancer.

It was already known that use of azathioprine leads to increased photosensitivity to UVA light, probably contributing to development of skin cancers. This new study finds that use of azathioprine leaves

a molecular fingerprint in skin cancers, further implicating it in cSCC development.

Charlotte Proby, Professor of Dermatology in the School of Medicine at Dundee, said, "We recommend all physicians give appropriate advice on UVA avoidance including year-round sun protection for their patients on azathioprine."

Professor Proby and colleagues said they were not necessarily advocating withdrawal of azathioprine.

"As with all medications the risks must be balanced against the benefits, particularly with the need to treat potentially life-threatening diseases with an effective drug," she said.

"It is important that sun protection, skin surveillance and early diagnosis/lesion removal are part of the routine management of patients on azathioprine."

cSCC is a common skin cancer with more than 40,000 new cases diagnosed annually in the UK, with significant health economic implications.

Sophia Lowes, from Cancer Research UK, said, "It's important to protect your skin from the sun when it's strong, especially if you burn easily or are taking medications which make you more sun-sensitive. The most effective protection is to spend time in the shade and cover up with a hat, long-sleeved top and sunglasses. For the bits you can't cover, use sunscreen with at least 4 stars and SPF 15 or higher for protection against both UVA and UVB rays."

Importantly, this new study also reveals the molecular landscape of cSCC and highlights potential targets that may be developed for future therapeutic approaches to manage cSCC.

Different carcinogens leave a different `mutational signature' in a cancer. By studying these signatures, researchers can start to determine what the causes of a cancer are.

The researchers in the School of Medicine at Dundee, in collaboration with the Wellcome Sanger Institute and Queen Mary University of London, were able to carry out mutational signature analysis of cSCC tumours from 37 patients, many of whom had been on azathioprine. They found a new mutational signature, Signature 32, which correlated with time on azathioprine therapy.

Professor Gareth Inman, part of the research team at Dundee and now located at the Cancer Research UK Beatson Institute and the University of Glasgow, said, "Although patient numbers were small and these findings should be verified in a larger independent cohort, this molecular study provides a strong case for an association between this novel mutational signature and long-term azathioprine use."

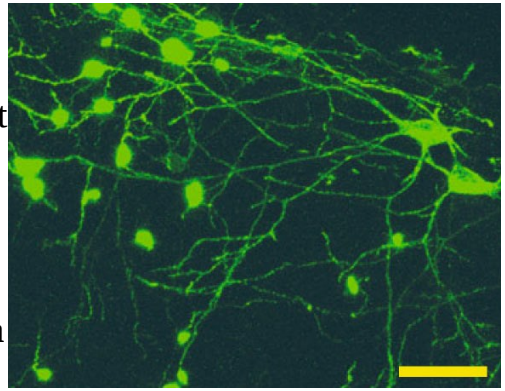
The research was funded by a grant from CRUK.

http://bit.ly/2NxvuOS

Neuroscientists Find 'Bravery Neurons' in Hippocampus

An international group of neuroscientists from Sweden and Brazil has found that some cells in a brain area called hippocampus play a key role in risk-taking behavior and anxiety.

The team, led by Uppsala University researcher Dr. Sanja Mikulovic and Dr. Richardson Leao, a scientist in the Brain Institute at the Federal University of Rio Grande do Norte, found that brain cells known as oriens-lacunosum-moleculare (OLM) interneurons, when stimulated, produce a brain rhythm that is present when animals feel safe in a threatening environment.



Microscopy image of OLM cells. Scale bar – 20 µm. **Mikulovic *et al*, doi: 10.1038/s41467-018-05907-w.**

The researchers also showed that anxiety and risk-taking behavior can be controlled by the manipulation of OLM cells.

"To find a pathway that quickly and robustly modulates risk-taking behavior is very important for treatment of pathological anxiety since reduced risk-taking behavior is a trait in people with high anxiety levels," they said.

"Adaptive (or normal) anxiety is essential for survival because it protects us from harm. Unfortunately, in a large number of people, anxiety can be dysfunctional and severely interfere with daily life."

"In these cases, doctors often rely on antidepressants to help patients recover from the dysfunctional state. However, these drugs act in the entire brain and not only in the areas where it is needed and may therefore have severe side-effects."

"Thus, to act in a single brain region and in a very specific group of cells to control anxiety may be a major breakthrough in treating anxiety and associated disorders like depression."

Another interesting finding in the study is that OLM cells can also be controlled by pharmacological agents.

In the past, the same team found that OLM cells were the gatekeepers of memories in the hippocampus and that these cells were very sensitive to nicotine.

"This finding may explain why people binge-smoke when they are anxious," Dr. Leao said.

"It is fascinating how different regions of the same brain structure control distinct behaviors and how they interact with each other," Dr. Mikulovic said.

"Identifying specific circuits that underlie either cognitive or emotional processes is crucial for the general understanding of brain function and for more specific drug development to treat disorders."

"The discovery of these neurons and their role in anxiety and risk-taking may open a path for the development of highly efficient anxiolytics and antidepressants without common side-effects, such as apathy."

The results appear in the journal *Nature Communications*.

Sanja Mikulovic et al. *2018. Ventral hippocampal OLM cells control type 2 theta oscillations and response to predator odor*. Nature Communications *9, article number: 3638; doi: 10.1038/s41467-018-05907-w*

https://wb.md/2x0Ukxq

Renowned Cancer Expert Fails to Disclose Millions From Industry

Did not disclose financial ties in dozens of research articles published in prestigious journals

Roxanne Nelson, BSN, RN

An internationally renowned breast cancer expert has failed to disclose millions of dollars that he received in payments from the pharmaceutical industry and extensive corporate relationships, according to an analysis by the *New York Times (NYT)* and *ProPublica*.

José Baselga, MD, PhD, currently physician-in-chief and chief medical officer, Memorial Sloan Kettering Cancer Center (MSKCC) in New York City, has not disclosed financial ties in dozens of research articles published in prestigious journals, including *The New England Journal of Medicine* and *The Lancet.*

According to the analysis, Baselga has held board memberships or advisory roles with Roche and Bristol-Myers Squibb, among others; has had a stake in start-ups during early-phase trials; and has played a key role in the development of new therapies that have helped to change the paradigm of breast cancer treatment.

Baselga also failed to abide by the financial disclosure rules that were set by the American Association for Cancer Research (AACR) when he was president of the organization and omitted payment he had received from companies connected to the research in his articles

published in the AACR's journal, *Cancer Discovery*. At the same time, he has been one of the journal's two editors-in-chief.

The *NYT/ProPublica* report notes that Baselga was paid more than $1.5 million in compensation by MSKCC in 2016, according to the hospital's latest available tax disclosures.

On top of that are consultation agreements made with industry.

Baselga received nearly $3.5 million from nine companies from August 2013 through 2017, according to the federal Open Payments database, which compiles disclosures filed by drug and device companies.

In addition, he has disclosed other investments and advisory roles in biotech start-up companies but has declined to provide detailed information about those interests, the report notes. If a product has not yet received regulatory approval, manufacturers do not have to disclose the payments that they made to physicians.

An analysis of Baselga's publications in medical journals since 2013, the year he joined MSKCC, showed that he failed to declare his disclosures in over 100 publications, or about 60% of the time. In 2017, he failed to list any potential conflicts of interest in 87% of the articles that he wrote or coauthored, the report maintains.

The investigation also reported that he put a positive spin on two clinical trials that were sponsored by Roche, when he presented their results at the 2017 and 2018 annual meeting of the American Society of Clinical Oncology (ASCO). Since 2014, he has received more than $3 million from Roche in consulting fees and for his stake in a company that they acquired.

Baselga has not disputed his relationships with at least a dozen companies and stated that the disclosure lapses were unintentional. He has also said he would correct his lack of disclosures for 17 articles, including those published in *The New England Journal of Medicine*, *The Lancet* and *Cancer Discovery*, but that he did not believe disclosure was required for dozens of other articles reporting early research.

MSKCC Responds

In response to the *NYT/ProPublica* article, an email was sent to all MSKCC staff by Craig B. Thompson, MD, president and chief executive officer, and Kathryn Martin, chief operating officer, saying that the institution and its faculty "need to do a better job" of disclosing relationships with industry.

"The matter of disclosure is serious," they wrote, adding that the issues surrounding author disclosures are complex and guidelines for reporting industry relationships are "nebulous" as to how and when to make voluntary disclosures.

The email further noted that they have asked Baselga to review his disclosures and to work with the various journals and organizations to correct the record, and this process has already begun.

"We need to work with journal publishers and professional societies to standardize the reporting process," they wrote. In addition, they noted, they have been in discussions with ASCO about the society's model as well as the value of having a common standard for oncology disclosures in journals and presentations.

Systemwide Problem

The issue of disclosing relationships with industry crosses all medical specialties. It received wide attention and spurred congressional action about 10 years ago, when several notable psychiatrists, including Charles Nemeroff, MD, PhD, from Emory University, Atlanta, Georgia, allegedly failed to accurately disclose payments from drug companies.

In January 2009, Sen. Charles Grassley (R, IA), then ranking member of the Senate Finance Committee, and Sen. Herbert Kohl (D, WI) reintroduced the Physician Payments Sunshine Act. The bill requires drug and medical-device manufacturers to disclose all payments and gifts to physicians if the annual total to an individual

is more than $100 per year, including funding given for continuing medical education and research grants.

That proposed legislation also required that the Department of Health and Human Services (HHS) establish procedures for drug companies to submit information and for HHS to make this information publicly available on a website no later than November 1, 2009. The federal government began requiring pharmaceutical manufacturers, as well as those making devices, to publicly disclose payments to doctors in 2013.

Career Path

A native of Spain, Baselga received both his MD and PhD degrees from the Autonomous University of Barcelona in 1982, and completed a fellowship in medical oncology at MSKCC. From 1996 to 2010, he was the chairman of the Medical Oncology Service and founding director of the Vall d'Hebron Institute of Oncology at the Vall d'Hebron University Hospital in Barcelona.

Relocating to the United States, he then served as the chief of the Division of Hematology/Oncology and associate director of the Massachusetts General Hospital Cancer Center in Boston from 2010 to 2012, before his current appointment at MSKCC.

His current research at MSKCC focuses on identifying mechanisms that limit the sensitivity to targeted therapy in solid tumors, in particular to PI3K/Akt/mammalian target of rapamycin inhibitors and anti-human epidermal growth factor receptor 2 agents.

http://bit.ly/2MlqW9r

Scientists develop new drug treatment for TB

Scientists at The University of Manchester have developed the first non-antibiotic drug to successfully treat tuberculosis in animals.

The team hope the compound -developed after 10 years of painstaking research will be trialled on humans within three to four years.

The drug- which works by targeting Mycobacterium tuberculosis' defences rather than the bacteria itself - can also take out its increasingly commonly antibiotic resistant strains.

The research funded by the Medical Research Council - is published today in the *Journal of Medicinal Chemistry*.

Although a vaccine for TB was developed 100 years ago, one in three people across the world are thought to be infected with the infectious disease. About 1.7 million die from the bug each year worldwide and 7.3 million people were diagnosed and treated in 2018, up from the 6.3 million in 2016.

It is most common in Africa, India and China, but on the rise in the UK with London often described as the TB capital of Europe.

Patients are forced to take a cocktail of strong antibiotics over 6 to 8 months, often enduring unpleasant side effects with a 20% risk that the disease will return.

But now The University of Manchester team's discovery has been proven effective in guinea pigs at Rutgers University in the United States.

The animals with acute and chronic TB infection were treated with the compound, which was discovered after investigating dozens of other derivatives and compounds thought to have similar properties.

Professor Lydia Tabernero is the project leader. She said: "The fact that the animal studies showed our compound, which doesn't kill the bacteria directly, resulted in a significant reduction in the bacterial burden is remarkable.

"For more than 60 years, the only weapon doctors have been able to use against TB is antibiotics. But resistance is becoming an increasingly worrying problem and the prolonged treatment is difficult and distressing for patients.

"And with current treatments, there's no guarantee the disease will be eliminated: antibiotics do not clear the infection and the risk of being infected with drug-resistant bacteria is very high.

"But by disabling this clandestine bacteria's defences we're thrilled to find a way that enhances the chances of the body's immune system to do its job, and thus eliminate the pathogen."

Mycobacterium Tuberculosis secretes molecules called Virulence Factors - the cell's secret weapon -which block out the immune response to the infection, making it difficult to treat.

The team identified one Virulence Factor called MptpB as a suitable target, which when blocked allows white blood cells to kill Mycobacterium Tuberculosis in a more efficient way

Professor Tabernero added: "The great thing about MptpB is that there's nothing similar in humans - so our compound which blocks it is not toxic to the human cells.

"Because the bacteria hasn't been threatened directly, it is less likely to develop resistance against this new agent, and this will be a major advantage over current antibiotics, for which bacteria had already become resistant. "TB is an amazingly difficult disease to treat so we feel this is a significant breakthrough.

"The next stage of our research is to optimise further the chemical compound, but we hope Clinical trials are up to four years away."

NOTES FOR EDITORS

Structure-based design of MptpB inhibitors that reduce multi-drug-resistant Mycobacterium tuberculosis survival and infection burden in vivo is published in Journal of Medicinal Chemistry

https://www.ncbi.nlm.nih.gov/pubmed/30153005.

http://bit.ly/2MmTXBC

A model to predict and quantify racism, sexism, and other unequal treatment

UC Berkeley Haas researchers show direct connection between stereotypes and unequal treatment

When a Starbucks employee recently called the police on two black men who asked for a bathroom key but hadn't yet ordered anything, it seemed a clear-cut case of racial bias leading directly to unfair treatment. Many outraged white customers publicly contrasted it with their years of hassle-free, purchase-free Starbucks pit stops.

But from a scientific perspective, making a direct connection between people's biases and the degree to which they treat others differently is tricky. There are thousands of ways people stereotype different social groups--whether it's assuming an Asian student is good at math or thinking an Irish colleague would make a good drinking buddy--and with so many variables, it's incredibly challenging to trace how someone is treated to any one particular characteristic.

"There is a tendency for people to think of stereotypes, biases, and their effects as inherently subjective. Depending on where one is standing, the responses can range from 'this is obvious' to 'don't be a snowflake,'" said Berkeley Haas Assoc. Prof. Ming Hsu. "What we found is that these subjective beliefs can be quantified and studied in ways that we take for granted in other scientific disciplines."

A new paper published this week in the Proceedings of the National Academy of Sciences cuts to the heart of messy social interactions with a set of computational models to quantify and predict unequal treatment. Hsu and post-doctoral researcher Adrianna C. Jenkins--now an assistant professor at the University of Pennsylvania--drew on social psychology and behavioral economics in a series of lab experiments and analyses of field work. (The paper was co-written by Berkeley researcher Pierre Karashchuk and Lusha Zhu of Peking University.)

"There's been lots of work showing that people have stereotypes and that they treat members of different social groups differently," said Jenkins, the paper's lead author. "But there's quite a bit we still don't know about how stereotypes influence people's behavior."

It's more than an academic issue: University admission officers, for example, have long struggled with how to fairly consider an applicant's race, ethnicity, or other qualities that may have presented

obstacles to success. How much weight should be given, for example, to the obstacles faced by African Americans compared with those faced by Central American immigrants or women?

While these are much larger questions, Hsu said the paper's contribution is to improve how to quantify and compare different discrimination across different social groups--a common challenge facing applied researchers.

"What was so eye-opening is that we found that variations in how people are perceived translated quantitatively into differences in how they are treated," said Hsu, who holds a dual appointment with UC Berkeley's Helen Wills Neuroscience Institute and the Neuroeconomics Lab. "This was as true in laboratory studies where subjects decided how to divide a few dollars as it was in the real-world where employers decided whom to interview for a job."

Rather than analyzing whether the stereotypes were justified, the researchers took stereotypes as a starting point and looked at how they translated into behavior with over 1,200 participants across five studies. In the first study involving the classic "Dictator Game," where a player is given $10 and asked to decide how much of it to give to a counterpart, the researchers found that people gave widely disparate amounts based on just one piece of information about the recipient (i.e., occupation, ethnicity, nationality). For example, people on average gave $5.10 to recipients described as "homeless," while those described as "lawyer" got a measly $1.70--even less than an "addict," who got $1.90

To look at how stereotypes about the groups drove people's choices to pay out differing amounts, the researchers drew on an established social psychology framework that categorizes all stereotypes along two dimensions: those that relate to a person's warmth (or how nice they are seen to be), and those that relate to a person's competence (or . These ratings, they found, could be used to accurately predict how much money people distributed to different groups. For example, "Irish" people were perceived as warmer but slightly less competent than "British," and received slightly more money on average.

"It turns out that, even though people are incredibly complex, these two factors were immensely predictive," Hsu says. "We found that people don't just see certain groups as warmer or nicer, but if you're warmer by X unit, you get Y dollars more." Specifically, the researchers found that disparate treatment results not just from how people perceive others, but how they see others relative to themselves. In allocating money to a partner viewed as very warm, people were reluctant to offer them less than half of the pot. Yet with a partner viewed as more competent, they were less willing to end up with a smaller share of the money than the other person. For example, people were ok with having less than an "elderly" counterpart, but not less than a "lawyer."

It's one thing to predict how people behave in carefully controlled laboratory experiments, but what about in the messy real world? To test whether their findings could be generalized to the field, Hsu and colleagues tested whether their model could predict treatment disparities in the context of two high-profile studies of discrimination. The first was a Canadian labor market study that found a huge variation in job callbacks based on the perceived race, gender, and ethnicity of the names on resumes. Hsu and colleagues found that the perceived warmth and competence of the applicants--the stereotype based solely on their names--could predict the likelihood that an applicant had gotten callbacks.

They tried it again with data from a U.S. study on how professors responded to mentorship requests from students with different ethnic names and found the same results.

"The way the human mind structures social information has specific, systemic, and powerful effects on how people value what happens to others," the researchers wrote. "Social stereotypes are so powerful

that it's possible to predict treatment disparities based on just these two dimensions (warmth and competence)."

Hsu says the model's predictive power could be useful in a wide range of applications, such as identifying patterns of discrimination across large populations or building an algorithm that can detect and rate racism or sexism across the internet--something these authors are deep at work on now.

"Our hope is that this scientific approach can provide a more rational, factual basis for discussions and policies on some of the most emotionally-fraught topics in today's society," Hsu said.

http://bit.ly/2CKQQnx

UBC breakthrough opens door to $100 ultrasound machine

New ultrasound transducer could dramatically lower the cost of ultrasound scanners

Engineers at the University of British Columbia have developed a new ultrasound transducer, or probe, that could dramatically lower the cost of ultrasound scanners to as little as $100. Their patent-pending innovation--no bigger than a Band-Aid--is portable, wearable and can be powered by a smartphone.

Conventional ultrasound scanners use piezoelectric crystals to create images of the inside of the body and send them to a computer to create sonograms. Researchers replaced the piezoelectric crystals with tiny vibrating drums made of polymer resin, called polyCMUTs (polymer capacitive micro-machined ultrasound transducers), which are cheaper to manufacture.

"Transducer drums have typically been made out of rigid silicon materials that require costly, environment-controlled manufacturing processes, and this has hampered their use in ultrasound," said study lead author Carlos Gerardo, a PhD candidate in electrical and computer engineering at UBC. "By using polymer resin, we were able to produce polyCMUTs in fewer fabrication steps, using a minimum amount of equipment, resulting in significant cost savings."

Sonograms produced by the UBC device were as sharp as or even more detailed than traditional sonograms produced by piezoelectric transducers, said co-author Edmond Cretu, professor of electrical and computer engineering.

"Since our transducer needs just 10 volts to operate, it can be powered by a smartphone, making it suitable for use in remote or low-power locations," he added. "And unlike rigid ultrasound probes, our transducer has the potential to be built into a flexible material that can be wrapped around the body for easier scanning and more detailed views--without dramatically increasing costs."

Co-author Robert Rohling, also a professor of electrical and computer engineering, said the next step in the research is to develop a wide range of prototypes and eventually test their device in clinical applications.

"You could miniaturize these transducers and use them to look inside your arteries and veins. You could stick them on your chest and do live continuous monitoring of your heart in your daily life. It opens up so many different possibilities," said Rohling.

The research was published recently in *Nature Microsystems & Nanoengineering*

http://bit.ly/2QnkrGs

A single gene mutation may have helped humans become optimal long-distance runners

In novel study, mice engineered to lack the same gene run stronger, longer and with less fatigue

Two to three million years ago, the functional loss of a single gene triggered a series of significant changes in what would eventually become the modern human species, altering everything from fertility rates to increasing cancer risk from eating red meat.

In a new paper, published in the September 12 issue of the *Proceedings of the Royal Society B*, researchers at University of California San Diego School of Medicine report on studies of mice engineered to lack the same gene, called *CMAH*, and resulting data that suggest the lost gene may also have contributed to humanity's well-documented claim to be among the best long-distance runners in the animal kingdom.

At roughly the same time as the *CMAH* mutation took hold, human ancestors were transitioning from forest dwellers to life primarily upon the arid savannahs of Africa. While they were already walking upright, the bodies and abilities of these early hominids were evolving dramatically, in particular major changes in skeletal biomechanics and physiology that resulted in long, springy legs, big feet, powerful gluteal muscles and an expansive system of sweat glands able to dissipate heat much more effectively than other larger mammals.

Such changes, say scientists, helped fuel the emergence of the human ability to run long distances relatively tirelessly, allowing ancestors to hunt in the heat of the day when other carnivores were resting and to pursue prey to their point of exhaustion, a technique called persistence hunting.

"We discovered this first clear genetic difference between humans and our closest living evolutionary relatives, the chimpanzees, more than 20 years ago," said senior author Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular Medicine at UC San Diego School of Medicine and co-director of the UC San Diego/Salk Center for Academic Research and Training in Anthropogeny.

Given the approximate timing of the mutation and its documented impact on fertility in a mouse model with the same mutation, Varki and Pascal Gagneux, PhD, professor of anthropology and pathology, began investigating how the genetic difference might have contributed to the origin of *Homo*, the genus that includes modern *Homo sapiens* and extinct species like *Homo habilis* and *Homo erectus*.

"Since the mice were also more prone to muscle dystrophy, I had a hunch that there was a connection to the increased long distance running and endurance of *Homo*," said Varki, "but I had no expertise on the issue and could not convince anyone in my lab to organize this long-shot experiment."

Ultimately, a graduate student named Jon Okerblom took up the task, building mouse running wheels and borrowing a mouse treadmill. "We evaluated the exercise capacity (of mice lacking the *CMAH* gene), and noted an increased performance during treadmill testing and after 15 days of voluntary wheel running," said Okerblom, the study's first author. The researchers then consulted Ellen Breen, PhD, a research scientist in the division of physiology, part of the Department of Medicine in the UC San Diego School of Medicine, who added observations that the mice displayed greater resistance to fatigue, increased mitochondrial respiration and hind-limb muscle, with more capillaries to increase blood and oxygen supply.

Taken together, Varki said the data suggest *CMAH* loss contributed to improved skeletal muscle capacity for oxygen utilization. "And if the findings translate to humans, they may have provided early hominids with a selective advantage in their move from trees to becoming permanent hunter-gatherers on the open range."

When the *CMAH* gene mutated in the genus *Homo* two to three million years ago, perhaps in response to evolutionary pressures caused by an ancient pathogen, it altered how subsequent hominids and modern humans used sialic acids -- a family of sugar molecules that coat the surfaces of all animal cells, where they serve as vital contact points for interaction with other cells and with the surrounding environment.

The human mutation causes loss of a sialic acid called *N*-glycolylneuraminic acid (Neu5Gc), and accumulation of its precursor, called *N*-acetylneuraminic acid or Neu5Ac, which differs by only a single oxygen atom.

This seemingly minor difference affects almost every cell type in the human body -- and has proved to be a mixed blessing. Varki and others have linked the loss of the *CMAH* gene and sialic acids to not just improved long-distance running ability, but also enhanced innate immunity in early hominids. Sialic acids may also be a biomarker for cancer risk.

Conversely, they have also reported that certain sialic acids are associated with increased risk of type 2 diabetes; may contribute to elevated cancer risk associated with red meat consumption; and trigger inflammation.

"They are a double-edged sword," said Varki. "The consequence of a single lost gene and a small molecular change that appears to have profoundly altered human biology and abilities going back to our origins."

Co-authors include: William Fletes, Hemal H. Patel and Simon Schenk, all at UC San Diego.

http://bit.ly/2Mp86yq

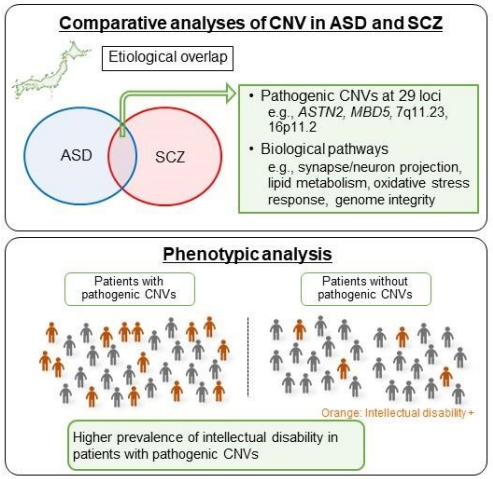
Overlapping copy number variations underlie autism and schizophrenia in Japanese patients

Common genetic variants may underlie autism spectrum disorder and schizophrenia across human populations

Common genetic variants may underlie autism spectrum disorder and schizophrenia across human populations, according to a study appearing September 11th in the journal *Cell Reports*. In line with previous studies in Caucasians, the researchers found that Japanese individuals with autism spectrum disorder and schizophrenia have overlapping copy number variations (CNVs)--inter-individual variations in the number of copies of a particular gene.

"The strength of our study is the systematic head-to-head comparison of pathogenic CNVs and biological pathways between autism spectrum disorder and schizophrenia," says senior study author Norio Ozaki of Nagoya University Graduate School of Medicine. "Previous studies in Caucasian populations found overlap in pathogenic CNVs between the two disorders, but their analyses were limited to a small number of genes and CNV loci."

Autism spectrum disorder and schizophrenia have complex inheritance patterns, with multiple genetic and environmental factors influencing disease risk. Available evidence points to genetic overlap between the two clinically distinct disorders. For example, they tend to co-occur at a higher rate than would be expected in the general population, and a large epidemiological study showed that a family history of schizophrenia in first-degree relatives is a risk factor for autism spectrum disorder. In particular, previous studies have revealed that these two disorders are associated with an increased burden of CNVs, and that rare CNVs in specific loci are shared risk factors for both disorders.



This visual abstract depicts the comparative analyses of CNV in autism and schizophrenia. **Itaru Kushima, Nagoya University Graduate School of Medicine**

However, the majority of the previous CNV studies were carried out in Caucasian populations, limiting the generalization of pathogenic CNVs and relevant biological pathways. Studies in populations other than Caucasians may also provide additional biological insights into the disorders. Moreover, the clinical features of patients with pathogenic CNVs have not been fully examined in non-Caucasian

populations. Until now, no studies have directly compared pathogenic CNVs and biological pathways between autism spectrum disorder and schizophrenia in non-Caucasian populations.

To address this gap in knowledge, Ozaki and his team performed comparative CNV analyses of 1,108 cases of autism spectrum disorder, 2,458 individuals with schizophrenia, and 2,095 controls in a Japanese population using a high-resolution technique called array comparative genomic hybridization. They confirmed an increased genome-wide burden of rare CNVs in autism spectrum disorder and schizophrenia and observed an overlap in pathogenic CNVs between the two disorders. Pathogenic CNVs, including those at 29 loci common to both disorders, were found in about 8% of the two types of patients, which was significantly higher than in controls.

"Genetic overlap has been suggested in epidemiological and molecular genetic studies," says first author Itaru Kushima of Nagoya University Graduate School of Medicine. "In line with this, our systematic and comprehensive investigation confirmed a significant overlap of pathogenic CNVs between autism spectrum disorder and schizophrenia in a Japanese population."

Additional analysis revealed that both disorders are associated overlapping biological pathways involved in the oxidative stress response, lipid metabolism, and genomic integrity. The researchers also identified 12 CNV loci potentially associated with these disorders in a Japanese population. Moreover, intellectual disability was strongly associated with pathogenic CNVs in both patient groups.

"The identification of shared pathways and disease-relevant genes provides biological insights into autism spectrum disorder and schizophrenia," Ozaki says.

Moving forward, the researchers plan to investigate CNVs in bipolar disorder and examine the overlap of pathogenic CNVs and biological pathways among the three disorders. In the near future, they will also conduct studies using CNV-based animal models, as well as induced pluripotent stem cells (iPSCs) derived from patients with pathogenic CNVs.

This research was supported by the Ministry of Education, Culture, Sports, Science and Technology of Japan and the Ministry of Health, Labour and Welfare of Japan; AMED, the UTokyo Center for Integrative Science of Human Behavior (CiSHuB); the International Research Center for Neurointelligence (WPI-IRCN) at The University of Tokyo Institutes for Advanced Study (UTIAS); Research Group For Schizophrenia; Program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers of Japan Society for the Promotion of Science; SENSHIN Medical Research Foundation; and The Uehara Memorial Foundation.

Cell Reports, Kushima et al.: "Comparative Analyses of Copy-Number Variation in Autism Spectrum Disorder and Schizophrenia Reveal Etiological Overlap and Biological Insights"
https://www.cell.com/cell-reports/fulltext/S2211-1247(18)31293-2

http://bit.ly/2CNE6qc

UCalgary researchers discover critical differences in the clots that cause a stroke

Findings will help inform physicians which treatment will work best for patients

There are two main treatments for stroke caused by a clot in a blood vessel in the brain. One treatment, mechanical thrombectomy, involves pulling the clot out with a specialized catheter that is inserted into the artery in the groin and guided by imaging to the clot. This procedure is only performed at hospitals that specialize in these techniques. The other treatment, which is more widely accessible, involves giving a patient a clot-busting drug that helps the body dissolve the clot.

Quick decision making on which treatment is best for which patient is critical because the clot deprives brain cells of oxygen causing them to die. For physicians, knowing which patients will benefit the most from the clot-buster Alteplase (also known as tPA) just got easier.

University of Calgary scientists with the Hotchkiss Brain Institute at the Cumming School of Medicine (CSM) have discovered that clots have different compositions and depending on where they are located

in the brain, administering tPA can be almost as effective as thrombectomy given sufficient time.

"We've known that, when administered quickly, tPA can be effective in stroke, but until now, we didn't realize how effective it can be and we didn't understand the specific reasons why it works better in some cases than others," says Dr. Bijoy Menon, MD, associate professor in the departments of Clinical Neurosciences, Radiology and Community Health Sciences at the CSM. "Our findings show that some clots are permeable, which allows the tPA to penetrate the blockage and dissolve it. We saw that within two hours, greater than 50 per cent of permeable blockages had dissolved."

The UCalgary study led out of the Foothills Medical Centre is the largest of its kind to date, involving nearly 600 patients at 12 medical centres in five countries (Canada, the Czech Republic, South Korea, Spain and Turkey). The findings are published in JAMA.

"Despite earlier research on the benefit of using tPA, we know there is still some reluctance in the medical community to use it. These findings should provide physicians with definitive evidence on the value of giving patients tPA as soon as they've confirmed the stroke is due to a clot," says Dr. Andrew Demchuk, MD, professor in the departments of Clinical Neurosciences and Radiology. "It's critical that anyone showing symptoms of a stroke be given a CT-angiogram as soon as possible to confirm the blockage. The scan will guide whether tPA is likely to dissolve the clot and may inform whether the patient also needs thrombectomy."

A CT-angiogram (computer tomography scan) is a common noninvasive diagnostic tool that allows physicians to see images of the blood vessels in the brain. Researchers found that clots in the carotid artery of the brain do not respond to tPA, and for these patients, thrombectomy is required.

"Strokes happen at anytime, anywhere. Knowing who needs thrombectomy can help physicians make better decisions on how to prioritize patient transfers to specialized centres for this procedure," says Menon. "Data gathered in Europe showed that up to one-third of hospital transfers aren't necessary."

"Stroke is an important health care problem and one of the leading causes of death and disability worldwide," says Dr. Brian H. Rowe, scientific director, Canadian Institutes of Health Research (CIHR) Institute of Circulatory and Respiratory Health, which supported this study. "Through continued scientific research, important discoveries like this one will improve our ability to match patients with the most effective treatment for this particular injury. This will help speed up recovery times, reduce the associated impacts such as paralysis, and it will improve patient outcomes and ultimately save lives."

Drs. Menon and Demchuk add that for the science community these findings will help researchers better design studies that target dissolving the clot with new clot busting drugs or combination treatments.

Led by the Hotchkiss Brain Institute, Brain and Mental Health is one of six strategic research themes guiding the university towards its Eyes High goals. The strategy provides a unifying direction for brain and mental health research at the university and positions researchers to unlock new discoveries and treatments for brain health in our community.

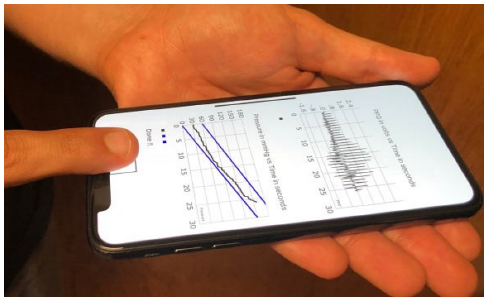
http://bit.ly/2x6FVj7

New Smartphone App Accurately Measures Blood Pressure from Fingertip

A team of researchers at Michigan State University has developed an iPhone X app that measures blood pressure via the 'oscillometric finger pressing method.'

"By leveraging optical and force sensors already in smartphones for taking selfies and employing 'peek and pop,' we've invented a practical tool to keep tabs on blood pressure," said Michigan State University's Professor Ramakrishna Mukkamala.

"Such ubiquitous blood pressure monitoring may improve hypertension awareness and control rates, and thereby help reduce the incidence of cardiovascular disease and mortality."



***Chandrasekhar* et al *invented a proof-of-concept blood pressure app that can give accurate readings using an iPhone.* Michigan State University.**

In a paper published in the journal *Science Translational Medicine* earlier this year, Professor Mukkamala and colleagues had proposed the concept with the invention of a blood pressure app and hardware. With the combination of a smartphone and add-on optical and force sensors, they produced a device that rivaled arm-cuff readings, the standard in most medical settings.

With advances in smartphones, the add-on optical and force sensors may no longer be needed.

Peek and pop, available to users looking to open functions and apps with a simple push of their finger, is now standard on many iPhones and included in some Android models.

"If things keep moving along at the current pace, an app could be available in late 2019," Professor Mukkamala said.

"Like our original device, the application still needs to be validated in a standard regulatory test."

"But because no additional hardware is needed, we believe that the app could reach society faster."

Internationally, this app could be a game-changer. While high blood pressure is treatable with lifestyle changes and medication, only around 20% of people with hypertension have their condition under control.

"This invention gives patients a convenient option and keeping a log of daily measurements would produce an accurate average," Professor Mukkamala said.

The new app is described in a paper in the journal *Scientific Reports*.

Anand Chandrasekhar et al. *2018. An iPhone Application for Blood Pressure Monitoring via the Oscillometric Finger Pressing Method.* Scientific Reports *8, article number: 13136; doi: 10.1038/s41598-018-31632-x*

https://nyti.ms/2OdXmEM

Parrots Think They're So Smart. Now They're Bartering Tokens for Food.

VA test of four different species shows they can accurately assign value to food and tokens, swapping lower value items for higher value food.

By James Gorman

Chalk up another achievement for parrots, with an odd twist that raises questions about whether the experimenters or the birds know best.

Anastasia Krasheninnikova and colleagues at the Max Planck Institute for Ornithology in Germany tested four species of parrots in an experiment that required trading tokens for food and recently reported their findings in the journal Scientific Reports.

Would the birds resist an immediate reward to trade for something better? Many species have shown the ability to hold off on an immediate treat — like a dry corn kernel — for something tastier later on, like a bit of walnut.

Chimpanzees, monkeys and cockatoos, among other species, can defer gratification. But using tokens for trading had not been tried before in birds, Dr. Krasheninnikova said.

Here's how it worked. First the birds, great green macaws, blue-throated macaws, blue-headed macaws and African grey parrots, learned that they could barter tokens for foods of different value — to the birds, that is.

A metal hoop could be traded for a piece of dry corn, the lowest value food, a metal bracket for a medium value sunflower seed and a plastic ring for the highest value food, a piece of shelled walnut.

The birds were then offered various choices, like a piece of corn or the ring. They all reliably chose to forego the corn and take the ring. Then they were able to trade the ring for a piece of walnut.

They also did well choosing a bracket instead of the corn, and in other situations where the token was of higher value than the food. The green macaws were consistently the best. The African greys, who have a reputation as very intelligent birds, did reasonably well on the obvious choices, but had some trouble when faced with a food and a token of the same value.

The right move, according to the experimenters, was to take the immediate reward of food. But the African greys, one in particular, often took the token. So instead of an immediate walnut it would get the ring and then trade it for a walnut.

Why take the extra step?

Dr. Krasheninnikova said the answer might lie in the way that African greys enjoy manipulating objects. “We know they’re very playful,” she said.

So maybe, those birds were making the right choice after all. They would get a moment to hold the ring, and still get the walnut in the end. After all, it was the humans who decided that it was better to get the food right away, not the parrots.

https://nyti.ms/2xbx8vh

Seeking Human Generosity’s Origins in an Ape’s Gift to Another Ape

Studying the behavior of our closest living relatives may help scientists better understand the human impulse for generosity.

By Carl Zimmer

How generous is an ape? It’s a hard question for scientists to tackle, but the answer could tell us a lot about ourselves.

People in every culture can be generous, whether they’re loaning a cellphone to an office mate or sharing an antelope haunch with a hungry family.

While it’s easy to dwell on our capacity for war and violence, scientists see our generosity as a remarkable feature of our species. “One of the things that stands out about humans is how helpful we are,” said Christopher Krupenye, a primate behavior researcher at the University of St. Andrews in Scotland.

This generosity may have been crucial to the survival of our early ancestors who lived in small bands of hunter-gatherers.

“When our own attempts to find food are unsuccessful, we rely on others to share food with us — otherwise we starve,” said Jan Engelmann, a researcher at Göttingen University.

To understand the origin of this impulse — known as prosociality — a number of researchers have turned to our closest living relatives. For example, a new study involving bonobo apes suggests that the roots of human generosity run deep, but only came into full flower over the course of the evolution of our species.

Roughly seven million years ago, our lineage split from the ancestors of chimpanzees and their cousin species, bonobos. Chimpanzees and bonobos share a common ancestor that lived about two million years ago.

These two closely related species of apes look almost identical to the untrained eye. But they have evolved some intriguing differences in their behavior, including which objects — food or tools — prompt them to behave with generosity.

Recently, Dr. Krupenye and his colleagues tested the generosity of bonobos that live in the Lola Ya Bonobo sanctuary in the Democratic Republic of Congo.

They proved to be generous — to a point.

The researchers designed an experiment that could provide strong evidence that bonobos could give things to each other simply out of

generosity — rather than being pressured into doing so, or expecting some sort of immediate payback.

"Would they do it if there was no benefit to them?" asked Brian Hare, a primatologist at Duke University who helped run the study.

For their experiment, the researchers took advantage of the fact that the Lola Ya Bonobo apes have learned to crack open palm nuts with rocks. Without a rock, they have to gnaw on the nuts for a long time to get them out of their shell.

The scientists put one bonobo in a cage with five nuts. In an adjacent cage, a second bonobo — a stranger to the first one — had two rocks, but no nuts. The cages were connected by a window.

The bonobos were free to bring gifts to the window to give to each other — or to ignore their neighbor.

The researchers found that the bonobos with the nuts proved generous. In 18 percent of the trials, the bonobos with the nuts handed one through the window to their neighbor, a rate that showed their willingness to give food to others.

But the bonobos in the other cage almost never returned the favor. They refused to pass one of their rocks through the window.

In another experiment, Dr. Krupenye got to experience their lack of generosity firsthand. Each bonobo would sit in a cage, with a mesh wall hanging in front of the door to the hallway. A colleague would slip a stick into the cage near the bonobo and leave.

Then Dr. Krupenye would come to the doorway and beg for the stick. He would reach out his arm, plaintively calling the bonobo's name.

The bonobos almost never handed Dr. Krupenye the stick. In fact, sometimes they seemed to tease him.

"They will put it through the mesh a little bit and then pull it back when I'm trying to reach for it," said Dr. Krupenye.

On Wednesday, Dr. Krupenye and Dr. Hare published their results with their co-author, Jingzhi Tan of the University of California, San Diego, in the Proceedings of the Royal Society.

"It's a really striking result," said Felix Warneken, a University of Michigan psychologist who was not involved in the study. What makes it surprising is that in studies involving chimpanzees in the same situations, they will do the opposite.

"Chimps are really reluctant to give food away," Dr. Warneken said. On the other hand, when it comes to tools, chimpanzees turn out to be generous. They'll give stones to other chimpanzees. In the stick-begging experiment, they'll help humans out. "The same species that will not help you get food will help you get an object," said Dr. Hare.

It's possible that the separate evolutionary paths of bonobos and chimpanzees have shaped their generosity. Chimpanzees live in habitats where food is often scarce. They have to compete for food, and groups of chimpanzees will sometimes even engage in warlike conflicts over territory.

Chimpanzees have also learned a lot of clever strategies for using tools to get food. In addition to cracking nuts with rocks, some chimpanzees kill monkeys with wooden spears. Others fish for termites with carefully fashioned poles.

Bonobos, by contrast, live in forests where food is far more abundant. "It's paradise — the stuff just falls off the trees," said Dr. Warneken. Adapting to this ecosystem, bonobos may have become more tolerant of each other. They recognize the value of food to others, and don't feel an urge to hoard it for themselves.

But bonobos also seem to be less adept with tools. In the wild, they've never been observed to crack nuts with a rock or fish termites with a stick. "They may just not have a deep-seated understanding of tools," said Dr. Warneken.

Chimpanzees may be unable to override their selfish tendencies about food. On the other hand, Dr. Warneken said, they may recognize the importance of tools for other chimpanzees.

Dr. Warneken and other researchers have carried out similar studies on children. They've found that even babies will spontaneously offer both food and objects to adults.

The work of Dr. Krupenye and others makes it clear that humans aren't unique in their generosity. It's possible that our common ancestor with bonobos and chimpanzees were already prosocial, at least to a limited extent. And now our generosity expands beyond what he and other scientists observe in our closest relatives.

"We're really good at realizing when other individuals could benefit from something," said Dr. Hare.

This versatility may have evolved early in our lineage, producing traits that encouraged more sharing. It leads toddlers to have generous inclinations without any coaching.

Dr. Warneken notes that around five years old, children become more aware of their prosocial actions. They know that being generous is good for their reputation.

It's possible that after our ancestors evolved the tendency to be generous, they then evolved a brain capable of understanding norms. In turn, humans came to see the benefits of being generous.

"It's no longer the same kind of motivation that we would find in other animals," he said. "Now there is some kind of obligation to share with others."

http://bit.ly/2NCewPk

Caffeine consumption may extend life expectancy for people with kidney disease

Consuming more caffeine may help reduce the risk of death for people with chronic kidney disease

A new study in *Nephrology Dialysis Transplantation* indicates that consuming more caffeine may help reduce the risk of death for people with chronic kidney disease.

An inverse relationship between coffee consumption and mortality has been reported in the general population. However, the association between caffeine consumption and mortality for people with chronic kidney disease remains uncertain. The researchers hypothesized that caffeine consumption might be associated with lower mortality among participants with chronic kidney disease.

The possible protective effect of caffeine might be related with effects at vascular level as caffeine is known to promote the release of substances, such as nitric oxide, that improve the function of the vessel.

About 89 percent of the adult USA population consumes caffeine daily. Approximately 14 percent of adults in the United States have chronic kidney disease. Chronic kidney disease is associated with increased health care costs and a higher risk of death. The prevalence of the disease is expected to continue to increase worldwide.

The study involved data from 4,863 American people observed from 1999 to 2010. Compared with people who consumed a smaller amount of caffeine-containing beverages, caffeine consumers were more likely to be male, non-Hispanic white, have a higher education level and higher annual income, be current or former smokers, have higher alcohol consumption, and have fewer previous strokes.

The results of the analysis suggest an inverse association between caffeine consumption and all-cause mortality among participants with chronic kidney disease. Comparing with people that consumed less caffeine, patients that consumed higher levels of caffeine presented a nearly 25% reduction in the risk of death over a median follow-up of 60 months.

According to Miguel Bigotte Vieira, one of the study's lead authors, "Our study showed a protective effect of caffeine consumption among patients with chronic kidney disease. The reduction in mortality was present even after considering other important factors such as age, gender, race, smoking, other diseases, and diet. These results suggest that advising patients with kidney disease to drink more caffeine may reduce their mortality. This would represent a

simple, clinically beneficial, and inexpensive option, though this benefit should ideally be confirmed in a randomized clinical trial." The author emphasized that this observational study cannot prove that caffeine reduces the risk of death in patients with chronic kidney disease, but only suggests the possibility of such a protective effect.

The paper, "Caffeine consumption and mortality in chronic kidney disease: a nationally representative analysis," will be available to the public here: https://academic.oup.com/ndt/article-lookup/doi/10.1093/ndt/gfy234 at midnight on September 12.

http://bit.ly/2OeHEcy

The Closest Exoplanet to Earth Could Be 'Highly Habitable'

Proxima Centauri b can sustain enormous areas of liquid water on its surface, raising prospects for life

By Adam Mann, Live Science Contributor

Just a cosmic hop, skip and jump away, an Earth-size planet orbits the closest star to our sun, Proxima Centauri.

Ever since the discovery of the exoplanet — known as Proxima Centauri b— in 2016, people have wondered whether it could be capable of sustaining life.

Now, using computer models similar to those used to study climate change on Earth, researchers have found that, under a wide range of conditions, Proxima Centauri b can sustain enormous areas of liquid water on its surface, potentially raising its prospects for harboring living organisms.

An artist's impression of the view from Proxima Centarui b, a newly discovered Earth-sized planet just four light-years away. It is unclear if there is intelligent life in the universe, but searches continue to find Earth-sized planets in the habitable zones of their respective stars. **NASA**

"The major message from our simulations is that there's a decent chance that the planet would be habitable," said Anthony Del Genio, a planetary scientist at the NASA Goddard Institute for Space Studies in New York City. Del Genio is also the lead author of a paper describing the new research, which was published Sept. 5 in the journal Astrobiology.

Proxima Centauri is a small, cool red-dwarf star located just 4.2 light-years from the sun. Despite its proximity, scientists still know very little about Proxima Centauri's planetary companion, besides that its mass is at least 1.3 times that of Earth and that it goes around its parent starevery 11 days. Therefore, Del Genio and his colleagues had to make some reasonable guesses about the exoplanet Proxima Centauri b — namely, that it had an atmosphere and an ocean on its surface — for their work to proceed.

Proxima Centauri b orbits in its star's habitable zone, meaning it's at just the right distance to receive enough starlight to keep its surface above the freezing temperature of water. But this zone is extremely close to the star, Space.com, a Live Science sister site, reported. So it's likely that the planet has become tidally locked due to gravitational forces. This means that the same side of Proxima Centauri b always faces its parent star, much like how the moon always shows the same side to Earth.

Previous simulations published in a 2016 paper in the journal Astronomy & Astrophysicsmodeled a hypothetical atmosphere on Proxima Centauri b and suggested that the star-facing hemisphere of the exoplanet might be baked under an intense glare, while a space-facing ocean would be frozen over. Therefore, only a circle of warm sea might exist on Proxima Centauri b — a scenario Del Genio's team calls "eyeball Earth."

But the new simulations were more comprehensive than prior ones; they also included a dynamic, circulating ocean, which was able to transfer heat from one side of the exoplanet to the other very

effectively. In the researchers' findings, the movement of the atmosphere and ocean combined so that "even though the night side never sees any starlight, there's a band of liquid water that's sustained around the equatorial region," Del Genio told Live Science.

He likened this heat circulation to our own planet's seaside climates. The U.S. East Coast is balmier than it would be otherwise, he said, because the Gulf Stream carries warm water up from the tropics. In California, by contrast, ocean currents bring cold water down from the North, and the West Coast is colder than it otherwise would be, Del Genio added.

The team ran 18 separate simulation scenarios in total, looking at the effects of giant continents, thin atmospheres, different atmospheric compositions and even changes in the amount of salt in the global ocean. In almost all of the models, Proxima Centauri b ended up having open ocean that persisted over at least some part of its surface. "The larger the fraction of the planet with liquid water, the better the odds that if there's life there, we can find evidence of that life with future telescopes," Del Genio said.

Ravi Kopparapu, a geoscientist at NASA's Goddard Space Flight Center in Greenbelt, Maryland, who was not involved in the study, agreed.

"I think it's exciting that some of these climate outcomes can be observed," Kopparapu told Live Science. Next-generation facilities, such as the Extremely Large Telescope currently under construction in Chile, might be able to witness heat coming off Proxima Centauri b and differentiate its possible surface conditions, he added.

https://wb.md/2N9wzqw

Medical, Recreational Marijuana Should Be Legal, Most Clinicians Say

Most respondents said medical and recreational marijuana should be legalized in the U.S.

Marcia Frellick

Most clinicians who responded to a *Medscape Medical News* poll said medical and recreational marijuana should be legalized in the United States.

The poll, which was posted May 9, was taken in light of Senate Minority Leader Chuck Schumer's (D-NY) then-impending legislation to decriminalize marijuana at the federal level.

He formally proposed the Marijuana Freedom and Opportunity Act, which would allow states to decide how they will treat marijuana possession, on June 27, and many states are debating changes to their laws.

Physicians were less likely than nurses/advanced practice registered nurses (APRNs), psychologists, and health/business administrators to approve of legalizing medical marijuana - 67% said yes to legalizing medical use.

Support for legalizing recreational marijuana was more consistent across groups, with the exception of health/business administrators, who were most often in favor of it: 53% of physicians said yes to legalizing recreational use.

Table 1. Should Medical Marijuana Be Legalized Nationally?

Response	Physician	Health Business/ Administration	Nurse/ APRN	Pharmacist	Psychologist
Yes	67%	88%	82%	71%	82%
No	28%	9%	13%	22%	13%
Unsure	5%	3%	6%	8%	5%

Table 2. Should Recreational Marijuana Be Legalized Nationally?

Response	Physician	Health Business/ Administration	Nurse/ APRN	Pharmacist	Psychologist
Yes	53%	72%	57%	54%	61%
No	41%	22%	33%	38%	30%
Unsure	6%	6%	10%	8%	9%

Tables 1 and 2 show the responses regarding medical marijuana and recreational marijuana, respectively.

According to the National Conference of State Legislatures, 31 states, the District of Columbia, Guam, and Puerto Rico now allow comprehensive public medical marijuana and cannabis programs. Nine states have legalized recreational marijuana.

Respondents who lived in states that had legalized medical marijuana at the time of the poll answered a question about whether they would recommend it to their patients, and percentages were low across the board.

Among physicians, 10% said they often recommend it; 24% said sometimes; 25% said rarely; and 41% said never.

Only 8% of nurses said they often recommend it; 31% said sometimes; 20% said rarely, and 41% said never.

Of pharmacist respondents, 4% often recommended it; 33% said sometimes; 15% said rarely; and 48% said they never recommend it.

Few Clinicians Use It Personally

Most providers do not use marijuana personally, either recreationally or medically.

Physicians (6%), nurses/APRNs (6%), and pharmacists (8%) were less likely to use the drug medically than psychologists (13%) and those in health business/administration (15%).

Physicians (9%) and nurses/APRNs (11%) were less likely to use it recreationally than were pharmacists (18%), health business/administrators (19%), and psychologists (20%).

Recreational use decreased by age for physicians and nurses. For physicians, the largest percentage who used the drug recreationally were aged 44 and younger (23%). The same was true for nurses/APRNs: 18% of that age group were recreational users.

Sample Size, Comments

Respondents included 417 physicians, 1054 nurses/APRNs, 171 people in health business/administration, 79 pharmacists, and 79 psychologists. The poll had drawn 60 reader comments by May 29.

Among the comments was this, from a family physician: "The big problem is good research on the acute effects of MJ. What is needed is the blood level at which MJ is intoxicating. As it stands now in many states researchers cannot legally do the research to find this level. Any good medical physiologist could come up with this answer within months. This would allow for the safe use of MJ."

A registered nurse wrote, "Cannabis is often a much healthier option for controlling many symptoms, notably chronic pain, anxiety, seizures, etc. This list is long and growing every day."

A psychologist responded, "We should remember that marijuana affects brain function. Hence, it affects personality and behavioral processes, more in some users than in others. Like anything else that alters consciousnesses, we should be wary of saying 'yes' to recreational use of the drug."

http://bit.ly/2NaXA2Q

Water in small dust grains can explain large amounts of water on Earth

Water trapped in dust grains from which the Earth formed can explain the current large amount of water on Earth.

This is suggested by scientists from the Netherlands, Germany and the United Kingdom, based on calculations and simulations. The research will appear in two articles in the journal *Astronomy & Astrophysics*.

For a long time scientists have struggled with an explanation for the large amount of water on Earth. A first scenario states that the water is delivered by comets and asteroids that hit the Earth. According to a second scenario, the Earth was born 'wet' and the water was already present on ten-kilometer-big boulders from which the Earth was built

up. However, the amount of water that these large boulders can contain is limited.

Now, an international team of scientists has devised and calculated a variant of the boulder-with-water scenario. The team shows that in the region where the Earth once originated, small to millimeter-sized dust grains can hold enough water. The water-rich dust grains then clump together to form pebbles and eventually kilometer-sized boulders. These boulders can then contain large amounts of water and they will eventually proceed to form Earth.

The new calculations also show that the small dust grains can collect enough water in 'only' a million years to explain the amount of water on Earth. A million years fits easily in the time it takes to form the larger boulders.

More information: *Warm dust surface chemistry in protoplanetary disks - Formation of phyllosilicates. Astronomy & Astrophysics, 2018.*

On water delivery in the inner solar nebula - Monte Carlo simulations of forsterite hydration. arxiv.org/abs/1808.06183

http://bit.ly/2NEMv9O

New evidence supports the hypothesis that beer may have been motivation to cultivate cereals

Stanford University archaeologists are turning the history of beer on its head.

September 12, 2018 by Melissa De Witte

A research team led by Li Liu, a professor of Chinese archaeology at Stanford, has found evidence of the earliest brewmasters to date, a finding that might stir an old debate: What came first, beer or bread? In a cave in what is now Israel, the team found beer-brewing innovations that they believe predate the early appearance of cultivated cereals in the Near East by several millennia. Their findings, published in the *Journal of Archaeological Science*: Reports, support a hypothesis proposed by archaeologists more than 60 years ago: Beer may have been a motivating factor for the original domestication of cereals in some areas.

'Oldest record of man-made alcohol'

Evidence suggests that thousands of years ago, the Natufian people, a group of hunter-gatherers in the eastern Mediterranean, were quite the beer connoisseurs.

Liu and her research team analyzed residues from 13,000-year-old stone mortars found in the Raqefet Cave, a Natufian graveyard site located near what is now Haifa, Israel, and discovered evidence of an extensive beer-brewing operation.

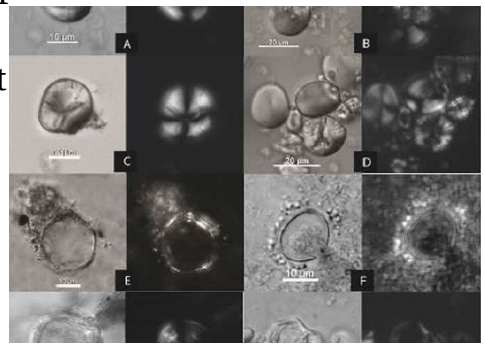
"This accounts for the oldest record of man-made alcohol in the world," Liu said.

The researchers believe that the Natufians brewed beer for ritual feasts that venerated the dead.

"This discovery indicates that making alcohol was not necessarily a result of agricultural surplus production, but it was developed for ritual purposes and spiritual needs, at least to some extent, prior to agriculture," Liu said about their findings.

In her lab analysis, Liu said she was surprised to discover evidence of beer brewing in the residue samples they gathered.

"We did not set out to find alcohol in the stone mortars, but just wanted to investigate what plant foods people may have consumed because very little data was available in the archaeological record," said Liu, who is the Sir Robert Ho Tung Professor in Chinese Archaeology at Stanford's School of Humanities and Sciences.



As Liu notes in the paper, the earliest bread remains to date were recently recovered from the Natufian site in east Jordan. Those could be from 11,600 to 14,600 years old. The beer finding she reports here could be from 11,700 to 13,700 years old.

Microscopic traces of ancient starches extracted from the Raqefet Cave (left) are compared to the references Liu and her research replicated in their beer brewing experiments. **Credit: Li Liu**

Ancient beer brewing

Ancient beer is far from what we drink today. It was most likely a multi-ingredient concoction like porridge or thin gruel, said Jiajing Wang, a doctoral student in the Department of East Asian Languages and Cultures and a co-author on the paper. Wang has helped Liu research ancient alcohol since 2015 when they first looked at 5,000-year-old brews in China before turning their attention to studying the Natufian culture.

In the Raqefet Cave, Liu and Wang unearthed residual remains of starch and microscopic plant particles known as phytolith, which are typical in the transformation of wheat and barley to booze.

The researchers believe that the Natufians used a three-stage brewing process. First, starch of wheat or barley would be turned into malt. This happens by germinating the grains in water to then be drained, dried and stored. Then, the malt would be mashed and heated. Finally, it would be left to ferment with airborne wild yeast.

All of these steps provided clues to help the researchers make their claim.

To test their hypothesis, the researchers conducted a series of experiments to recreate each step the Natufians would have taken to brew their beer. These brewing experiments allowed the researchers to study how starch granules changed during the brewing process and make comparisons to what they discovered.

Liu and Wang's brewing experiments showed a clear similarity to what the Natufians concocted.

The researchers also analyzed the artifacts that were excavated. They found that the traces left on the ancient stone mortar closely resembled their own lab experiments of pounding and crushing grain seeds, a process required for beer brewing.

Historical significance

The discovery of ancient brewing shed new light on Natufian rituals and demonstrate the wide range of technological innovations and social organization within their culture, the authors conclude in the paper. "Beer making was an integral part of rituals and feasting, a social regulatory mechanism in hierarchical societies," Wang said about their findings.

And those rituals were important to the Natufian culture, she said, noting that the discovery of beer-brewing at the graveyard signifies the emotional ties the hunter-gathers had with their ancestors.

More information: *Li Liu et al. Fermented beverage and food storage in 13,000 y-old stone mortars at Raqefet Cave, Israel: Investigating Natufian ritual feasting, Journal of Archaeological Science: Reports (2018).* *DOI: 10.1016/j.jasrep.2018.08.008*

http://bit.ly/2Mso9ve

Sugar pills relieve pain for chronic pain patients

Placebo benefits can be predicted by brain anatomy and psychological traits

- ***Doctors should consider treating chronic pain patients with sugar pills***
- ***Placebo pills relieve pain as effectively as drugs for half of chronic pain patients***
- ***Pain reduced by 30 percent***
- ***No need to fool patients, brain is primed to respond***
- ***Finding can result in vast cost savings for patients, health care system***

CHICAGO --- Someday doctors may prescribe sugar pills for certain chronic pain patients based on their brain anatomy and psychology. And the pills will reduce their pain as effectively as any powerful drug on the market, according to new research.

Northwestern Medicine scientists have shown they can reliably predict which chronic pain patients will respond to a sugar placebo pill based on the patients' brain anatomy and psychological characteristics.

"Their brain is already tuned to respond," said senior study author A. Vania Apkarian, professor of physiology at Northwestern University

Feinberg School of Medicine. "They have the appropriate psychology and biology that puts them in a cognitive state that as soon as you say, 'this may make your pain better,' their pain gets better."

There's no need to fool the patient, Apkarian said.

"You can tell them, 'I'm giving you a drug that has no physiological effect but your brain will respond to it,'" he said. "You don't need to hide it. There is a biology behind the placebo response."

The study was published Sept. 12 in *Nature Communications*.

The findings have three potential benefits:

- ***Prescribing non-active drugs rather than active drugs. "It's much better to give someone a non-active drug rather than an active drug and get the same result," Apkarian said. "Most pharmacological treatments have long-term adverse effects or addictive properties. Placebo becomes as good an option for treatment as any drug we have on the market."***
- ***Eliminating the placebo effect from drug trials. "Drug trials would need to recruit fewer people, and identifying the physiological effects would be much easier," Apkarian said. "You've taken away a big component of noise in the study."***
- ***Reduced health care costs. A sugar pill prescription for chronic pain patients would result in vast cost savings for patients and the health care system, Apkarian said.***

How the study worked

About 60 chronic back pain patients were randomized into two arms of the study. In one arm, subjects didn't know if they got the drug or the placebo. Researchers didn't study the people who got the real drug. The other study arm included people who came to the clinic but didn't get a placebo or drug. They were the control group.

The individuals whose pain decreased as a result of the sugar pill had a similar brain anatomy and psychological traits. The right side of their emotional brain was larger than the left, and they had a larger cortical sensory area than people who were not responsive to the placebo. The chronic pain placebo responders also were emotionally self-aware, sensitive to painful situations and mindful of their environment.

"Clinicians who are treating chronic pain patients should seriously consider that some will get as good a response to a sugar pill as any other drug," Apkarian said. "They should use it and see the outcome. This opens up a whole new field."

Other Northwestern authors are co-lead author Etienne Vachon-Presseau, Sara Berger, Taha Abdullah, Lejian Huang, Guillermo Cecchi, James Griffith and Thomas Schnitzer.

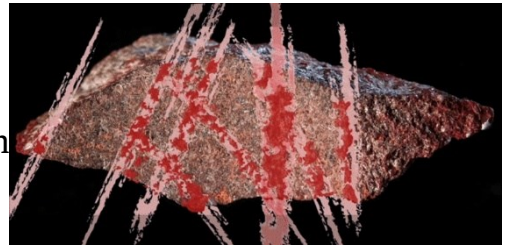
This study was funded by National Center for Complementary and Integrative Health grant AT007987 of the National Institutes of Health and the Canadian Institutes of Health Research and Fonds de Recherche Santé Québec.

https://go.nature.com/2p4TAm0

The earliest known drawing in history sends a message through 73,000 years

Cross-hatched crayon on a rock shard suggests early humans indulged in abstract art.

If a picture tells a thousand words, a cross-hatched design drawn on a fragment of rock some 73,000 years ago could speak volumes. The problem will be understanding what it tells us. The design, reported in *Nature* this week (C. S. Henshilwood *et al. Nature* https://doi.org/10.1038/s41586-018-0514-3; 2018), occurs on a lentil-shaped rock flake, and was found in Blombos Cave, on the southern shore of South Africa, by archaeologist Christopher Henshilwood and his colleagues. The flake bears an abstract design drawn, the authors say, using a crayon made of red ochre.



Ancient people used ochre crayon to draw on this rock. **Henshilwood et al., Nature 2018**

It is hard to claim that the design is beautiful, dazzling or engrossing. But the artwork is destined to be priceless and famous, because it seems to be the earliest evidence for a drawing in the archaeological

record, by some margin. Apart from some cave paintings from Spain dated to around 64,000 years ago — presumably the work of Neanderthals (D. L. Hoffmann *et al. Science* **359**, 912–915; 2018) — the next instance of drawing came around 40,000 years ago with cave paintings found at opposite ends of Eurasia: in the spectacular art decorating the walls of caves in Spain and France, and the more recently discovered cave art in Sulawesi in Indonesia (M. Aubert *et al. Nature* **514**, 223–227; 2014). Despite being located 12,000 kilometres apart, cave paintings such as these contain images that we instantly recognize as figurative art, including a range of animals, and stencils of hands that speak to us, millennia later, as signs of human self-awareness.

"Even nowadays we sometimes don't understand the reasoning behind an artist producing a piece of art" **Download MP3**

A key distinction of this latest piece is that it is a drawing — a design made by applying pigment — rather than an engraving, made by scratching or cutting a design into a surface. Engraving has a longer prehistory than art. The earliest engravings known are on pieces of shell from Trinil, Java, dated to around 540,000 years ago, well before modern humans evolved, and presumably made by *Homo erectus*. Other ancient engravings have been found around the world; all are extremely simple: just lines, sometimes cross-hatched. There is nothing remotely similar to what we would recognize as imagery, and there is insufficient evidence to say whether they might represent something utilitarian, such as tally sticks or calendars. So, were these Palaeolithic hashtags actually designs intended to convey meaning, or mindless graffiti? Some might have been the unintentional result of another action, such as cutting food items, just like the scratches left on a chopping board after slicing a loaf.

A drawing, by contrast, is much harder to dismiss. To be sure, the one from Blombos is as cross-hatched as the engravings, but it could not have been created as the accidental by-product of another process. Although proving intentionality is extremely hard, the authors examine the evidence they have — including detailed study of the ochre residues — with forensic thoroughness. It seems clear that the drawing was a fragment of something bigger, because some of the lines look as if they continued on to pieces now long gone. In addition, the authors attempted to restage history, using pieces of ochre themselves to show that such drawings can be made using crayons carved out of ochre (rather than, say, by brushwork), and that creating the design on such a rock fragment is possible only by deliberate rotation of the design through an angle, much as later artists might rotate their canvas.

That the ancient artist chose to sketch with red ochre is less of a surprise. The mineral, largely consisting of iron oxide, has been used as a pigment since time immemorial. Its earthy red hues clearly meant a lot to the early modern human inhabitants of Blombos Cave and other nearby sites. They used it as an ingredient in paint, and perhaps even as a sunscreen. Between around 100,000 and 73,000 years ago, the people of the region produced artefacts tens of thousands of years in advance of humans anywhere else in the world, including finely worked stone and bone tools and engraved ochre pieces.

That the early *Homo sapiens* living there were able to produce such designs suggests they possessed relatively 'modern' cognition and behaviour. What we cannot know is why they made the marks, or what they represent; unlike images of animals or hands, the drawing's abstract nature offers no clues. And that raises a fascinating question about the history of art. Whereas the humans living in South Africa 100,000 years ago were using technology as yet undreamed of elsewhere, they had yet to invent figurative art. So, are the cave paintings of Lascaux and Sulawesi unconnected, independent inventions, or did modern humans create cave art somewhere else along the way, and then take it with them as they

moved through the world? What is clear is that they started a trend, one that eventually led to Piet Mondrian, Jackson Pollock, Bridget Riley and the many great artists of today.

Nature ***561***, *149 (2018) doi: 10.1038/d41586-018-06657-x*

http://bit.ly/2x50M6o

As massive Zika vaccine trial struggles, researchers revive plan to intentionally infect humans

Cases of Zika are so low it may be impossible to tell whether the vaccine works

By Jon Cohen Sep. 12, 2018 , 12:30 PM

In 2016, as the mosquito-borne Zika virus spread through the Americas and cases of infected women having brain-damaged babies mounted, investigators raced to develop a vaccine. Now, a $110 million vaccine trial is underway at 17 sites in nine countries, but it faces an unexpected, and ironic, challenge. Cases of Zika have plummeted to levels so low that most people vaccinated in the trial likely will never be exposed to the virus, which could make it impossible to tell whether the vaccine works.

"Right now, there are no infections, and certainly not enough to even think about an efficacy signal at this point," says Anthony Fauci, director of the U.S. National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, which launched the trial. Human trials of other Zika vaccine candidates at earlier stages are also in limbo, and last year one large vaccinemaker pulled the plug on development of its candidate.

But NIAID and others are pressing ahead, saying a vaccine might someday be needed. To make up for the lack of new cases, other investigators are turning to an unusual, and ethically complex, strategy. Starting next year, *Science* has learned, they plan to test a vaccine by deliberately infecting people with Zika.

Launched in March 2017, NIAID's placebo-controlled vaccine trial includes two sites in Brazil, where Zika hit hardest and where the brain damage known as microcephaly first surfaced.

From the beginning of the outbreak in 2015 until the start of this year, Brazil had about half of all 800,000 suspected and confirmed Zika cases in the Americas, according to the Pan American Health Organization in Washington, D.C. But from January through June, Brazil's Ministry of Health reported fewer than 7000 probable cases, in a nation of 200 million people.

"It's a good dilemma because we don't have Zika anymore," says Esper Kallás of the University of São Paulo in São Paulo, Brazil, principal investigator for the local NIAID site. "But it's a dilemma. Everybody is concerned about it. It's a lot of investment."

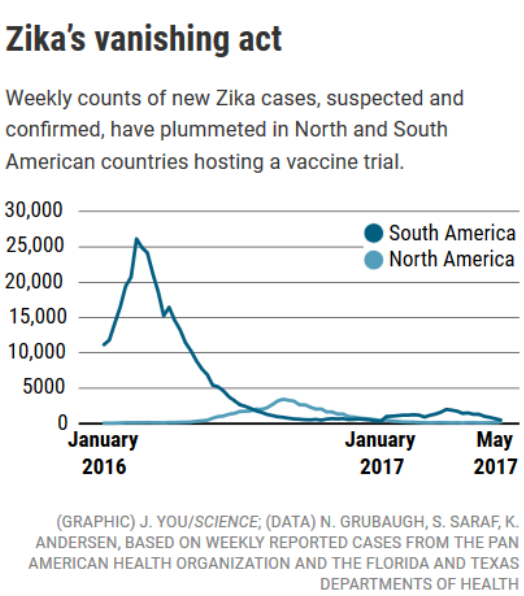
To date, 1380 participants have enrolled in the trial, which tests a vaccine containing a small circular piece of DNA that holds two Zika genes. From the outset, the researchers had planned to open new trial sites at infection hot spots, if needed. But new cases have dropped to a trickle throughout the Americas.

Weekly counts of new Zika cases, suspected and confirmed, have plummeted in North and South American countries hosting a vaccine trial.

Further complicating the trial, many people throughout Latin America and the Caribbean have already been infected with Zika and recovered, which has left them immune to the virus and hence ineligible for vaccine trials. "We have problems finding people to participate," Kallás says.

Indeed, nearly 50% of 2147 Nicaraguans studied in Managua—which is not a site in the NIAID trial—tested positive for antibodies to the Zika virus between January and September 2016, a group reported 27 August in the *Proceedings of the National Academy of Sciences*.

Kallás says evidence of efficacy could still emerge from areas of São Paulo that, inexplicably, have had little Zika. Those pockets, where less than 5% of the people test positive for Zika antibodies, remain susceptible to the outbreaks that could give the vaccine a real test. "There's this sense the epidemic will hit our region, but we don't know when," Kallás says. "We don't understand why it didn't happen already."



Given the drop in cases, a surer way to test any vaccine against Zika is to deliberately expose inoculated subjects to the virus. Researchers have used this strategy, known as a human challenge trial, for decades to test vaccines against diseases that either can be effectively treated or, like Zika, typically cause mild symptoms.

But in 2017, an ethics committee convened by NIAID and the Walter Reed Army Institute of Research in Silver Spring, Maryland, called it "premature" for Zika. They worried that people intentionally infected with the virus might transmit it to their sexual partners, primarily through infected semen. And they were confident that traditional field trials could test the efficacy of the leading vaccine candidates.

The report froze plans for a human challenge study, which NIAID had agreed to fund. "It was a great setback," says the study's leader, Anna Durbin of the Johns Hopkins University Bloomberg School of Public Health in Baltimore, Maryland. "If we had been allowed to go forward, we'd know today which vaccine candidates look good."

Now, the study is being considered again, as Zika disappears from the region and industry loses interest in bringing a vaccine to market. In a major blow, Sanofi Pasteur halted work on its vaccine, licensed from Walter Reed, in September 2017.

"There's a compelling reason to conduct a human challenge trial now," says bioethicist Seema Shah of Northwestern University's Feinberg School of Medicine in Chicago, Illinois, who chaired the 2017 ethics committee. But, she adds, "The details are complicated and it's important to have a rigorous review."

"If they're careful, we have no problems supporting it," Fauci says. Durbin plans to submit her new protocol for review in about a month, and in early 2019 hopes to start injecting Zika virus into people immunized with a vaccine containing live, but weakened Zika virus made by NIAID's Stephen Whitehead.

As a precaution, she plans to enroll only women at first, to avoid semen transmission from infected males. The volunteers will receive a low dose of Zika virus, and they will remain in clinics for the 2 weeks it typically takes to clear the infection.

Any vaccine that works in the challenge study theoretically could then be evaluated in a real-world outbreak—just as is occurring now with an unlicensed but promising Ebola vaccine.

The much larger NIAID trial could also pay off, even if it doesn't show whether the Zika vaccine is effective. It will yield data on safety and immune responses; combined with animal data on efficacy, the results might be enough for the U.S. Food and Drug Administration to license the vaccine, Fauci says.

But regardless of whether the trial leads to an approved vaccine, he has no regrets about launching it.

"Zika was a very ominous threat just a couple of years ago, and there is certainly the possibility that it is going to come back," Fauci says. "It's a risk that you'll spend this money and never use the vaccine, but balancing the importance of this infection and the impact it could

have, we felt it was a good decision to move ahead. And I would be happy to defend that anywhere."

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https://bbc.in/2QtCtan

Busting the myths around sex virus HPV

High levels of shame and ignorance are associated with HPV, the sexually-transmitted virus which affects 80% of people, a survey has discovered.

By Laurel Ives BBC Health

The government is rolling out HPV testing as part of routine screenings for cervical cancer.

Nearly half of the women surveyed believed their partner must have cheated if they had HPV, but the virus can remain dormant for years.

Campaigners fear women may not attend screenings because of the stigma.

The survey of 2,000 women was done by Jo's Cervical Cancer Trust last month.

It found that half of the women were embarrassed and "put off sex" as a result of contracting the virus.

Around 35% of the women had no idea what HPV is, and nearly 60% said they thought it meant they had cancer.

Laura Flaherty, 31, who was diagnosed with cervical cancer in 2016, is typical of the respondents.

"When I first saw on my letter that I had been diagnosed as being HPV positive, I didn't know what it was. When I Googled it I discovered it was a sexually transmitted infection, so I automatically thought my partner had been cheating.

"I knew nothing about it, and it felt dirty. I didn't realise it could lay dormant for so long and when I realised how common HPV is I was shocked. No-one I spoke to had heard of it, yet most of us are going to contract it."

Busting the HPV myths

Myth: You can only get the virus through sexual intercourse
Fact: HPV is usually sexually transmitted, but it can also be transmitted by any skin-to-skin contact in the genital and oral areas
Myth: HPV is a sign of being promiscuous
Fact: 80% of us will contract HPV virus at some point in our lives, it's easy to get and pass on and you can get it the first time you have any sexual contact.
Myth: HPV means I've got cancer
Fact: There are about 200 types of HPV. About 40 types affect the genital area, simply meaning they will live there, a few can cause unpleasant but harmless conditions like genital warts. Around 13 high-risk types can cause cervical cancer and other cancers of the genitals as well as mouth and throat cancer, but this is rare.
Myth: You'll know if you have HPV
Fact: HPV is symptomless and in most cases the immune system will clear the infection. Cervical screening picks up any abnormal cells

Source: Jo's Cervical Cancer Trust

The survey comes as a government initiative to test for HPV first in cervical screening, before other conditions, starts in Wales next week. It will roll out to England by 2019.

The change means that more women will be told that they have HPV.

Robert Music, Chief Executive, Jo's Cervical Cancer Trust, said: "Testing for HPV first is a far more effective way of identifying those most at risk of cervical cancer. This change to the programme does mean more women will be told they have HPV. "HPV can be confusing however, so we must normalise it to ensure people don't feel ashamed or scared about being told they have the virus."

HPV infection is rapidly declining in girls aged between 12 and 18 as a result of the HPV vaccine introduced in 2008.

Last year, the vaccine was extended to gay men aged 16 to 45, and in July the government announced that it will also be extended to boys, although no start date has yet been given.

There are no plans to extend the HPV vaccine to other adults over the age of 18, as the likelihood of already having the infection are high, and therefore the vaccine would be ineffective.

Dr Philippa Kaye, GP and author said: "GPs and health professionals will be having more conversations with patients about HPV as they come in to discuss their results. Understanding how it is transmitted and the relative risks will help reduce the stigma surrounding it."

http://bit.ly/2Ne3qcs

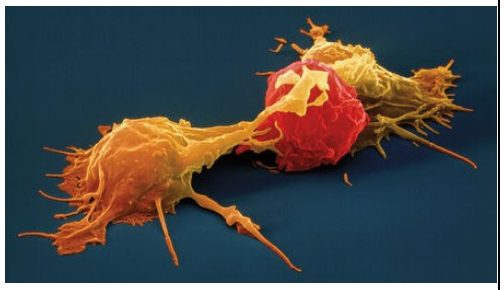
Engineered natural killer cells may be the next great cancer immunotherapy

Clinical trials of natural killer cells and macrophages equipped with cancer-homing receptor

By Mitch Leslie Sep. 13, 2018 , 1:05 PM

The cancer fighters known as CAR T cells have proved their prowess in recent years. Three therapies using the altered T cells against lymphoma or leukemia have won U.S. Food and Drug Administration approval, and hundreds of trials are now unleashing them on other malignancies, including solid tumors. But the cells may soon have company.

Researchers have equipped other immune guardians—natural killer cells and macrophages—with the same type of cancer-homing receptor, and the natural killer cells have made their debut in clinical trials.



Natural killer cells (yellow) attack a cancer cell. **Eye Of Science/Science Source**

CAR T cells—their name comes from the chimeric antigen receptor, or CAR, added to help the immune cells target cancer cells—inspired the new work. CAR natural killer (CAR NK) cells could be safer, faster to produce, and cheaper, and they may work in situations where T cells falter. CAR-carrying macrophages also have potential advantages, and one firm plans to launch the first clinical trials of these cells next year.

Although they aren't likely to replace CAR T cells, these alternative cancer fighters "could be an addition to the armamentarium of cell therapies," says hematologist and oncologist Katy Rezvani of the University of Texas MD Anderson Cancer Center in Houston. She is leading the first trial of CAR NK cells in the United States, which began in 2017, and organizing another that is due to start this year.

Making CAR T cells involves removing patients' own T cells and genetically altering them to attack cancer cells that carry a specific immune-stimulating molecule, or antigen. (All of the CAR T treatments approved so far target the CD19 protein on cancerous B cells, a type of immune cell.) The cells have produced impressive results in clinical trials—in one study, they triggered remissions in 83% of children with previously untreatable acute lymphoblastic leukemia. But some patients who have already undergone chemotherapy or radiation treatment may not have enough T cells left to donate. And these powerful immune warriors can trigger a potentially fatal flood of the immune system molecules known as cytokines or turn against normal body cells.

Perhaps the biggest shortcoming of CAR T cells, though, is they don't work well against solid tumors, says hematologist and oncologist Saar Gill of the University of Pennsylvania. Tumors rebuff T cells that try to enter, inhibit immune cells that do make it inside, and can curb production of antigens targeted by CAR T cells. Researchers are trying several approaches to improve CAR T cells' performance against solid tumors. But NK cells are a tempting alternative, scientists say.

"Natural killer cells are our first line of defense against cancer cells," Rezvani says. They scan other cells in the body and destroy any that are infected or otherwise abnormal, including tumor cells.

Researchers have been trying to harness the cancer-fighting activity of NK cells that don't carry CARs for more than 20 years, notes translational immunologist Jeffrey Miller of the University of Minnesota in Minneapolis. But upgrading them by adding CARs seems to boost their potency.

Earlier this year, for instance, stem cell biologist Dan Kaufman of the University of California (UC), San Diego, and colleagues reported that in mice, CAR NK cells perform about as well against ovarian tumors as CAR T cells do—and substantially better than unaltered NK cells. Mouse trials also suggest CAR NK cells may not cause some of the side effects of CAR T cells, such as excess cytokine release and neurological damage. CAR NK cells might also be less vulnerable to some of tumors' tricks for avoiding attacks. Because NK cells rely on other receptors to recognize tumor cells, not just the CAR, they may be able to detect a tumor even if it alters its antigens. In addition, Kaufman points out, it may be feasible to give patients multiple doses of CAR NK cells and hammer away at tumors, whereas the cost of CAR T cells limits patients to a single dose.

The first trials of CAR NK cells started in China in 2016 in patients with several kinds of cancers—early results from one suggest the cells are safe. Rezvani and colleagues' initial trial is pitting the cells against several varieties of lymphoma and leukemia. A European trial, which is testing CAR NK cells in patients with the brain cancer glioblastoma, launched this year. In the upcoming MD Anderson trial, patients with B cell lymphoma, a type of blood cancer, will receive stem cell transplants and chemotherapy before CAR NK cells, which the researchers hope will mop up any remaining cancer cells.

"I think the future is bright for CAR NK cells, but we are at the very beginning," says hematologist Mitchell Cairo of the New York Medical College in Hawthorne. One unknown is the best source for the cells. T cells from someone other than the patient can trigger a potentially fatal immune complication known as graft-versus-host disease, in which the transplanted cells attack the recipient's own tissues. But NK cells from a donor do not appear to cause that response, which opens a range of options. Although sieving NK cells from donors' blood is a possibility, the procedure is expensive and can harm the donors. Both MD Anderson trials instead rely on NK cells isolated from umbilical cord blood and then implanted with CARs. Donated umbilical cord blood is abundant and plenty of NK cells can be grown from it.

In contrast, the Chinese and European trials generated enough NK cells by turning to a cell line derived from a person with a type of lymphoma. These cells are staples of clinical trials, and despite their cancerous origin, they appear to be safe, says immunologist Torsten Tonn of the Technical University of Dresden in Germany, one of the researchers participating in the glioblastoma trial. Kaufman and colleagues are also exploring another possible source of NK cells: induced pluripotent stem cells, which are produced by nudging adult body cells to return to an unspecialized state.

All these approaches could lead to off-the-shelf CAR NK cells that avoid the need to extract and modify a cancer patient's own cells. The patient's immune system will eventually reject any foreign NK cells, Miller notes. But before that happens, Rezvani and other researchers think the donor NK cells will have a window of time during which they can combat cancer cells. The question, she says, is whether they will persist long enough to benefit patients.

Like NK cells, macrophages can destroy cancer cells, but the catch is that most macrophages inside a tumor are traitors, which help the tumor by quashing immune attacks against it, for example. "Tumors acquire macrophages to support their own growth and turn them into their minions," Gill says. But he and graduate student Michael Klichinsky have discovered that the procedure for equipping macrophages with a CAR prevents them from switching sides. The

duo helped found a company, Carisma Therapeutics in Philadelphia, Pennsylvania, that expects to begin clinical trials of CAR macrophages next year.

At least in the lab, adding a CAR to macrophages boosts their tumor-fighting abilities, just as it does for other immune cells, postdoc Meghan Morrissey of UC San Francisco and colleagues have also reported. But tumor immunologist Kim O'Neill of Brigham Young University in Provo, Utah, who leads another group trying to improve the cells' tumor-killing abilities, suggests macrophages could do the most good by recruiting other immune cells. T cells, for example, respond to the cellular debris leftover when a macrophage digests a tumor cell, so he envisions that patients would receive CAR macrophages along with CAR T cells. Like great detectives, even the most powerful cancer-fighting cells might benefit from a talented sidekick.

http://bit.ly/2NqaYTy

Plants communicate distress using their own kind of nervous system

Plants may lack brains, but they have a nervous system, of sorts.

By Elizabeth Pennisi Sep. 13, 2018 , 2:00 PM

Plants may lack brains, but they have a nervous system, of sorts. And now, plant biologists have discovered that when a leaf gets eaten, it warns other leaves by using some of the same signals as animals. The new work is starting to unravel a long-standing mystery about how different parts of a plant communicate with one another.

Animal nerve cells talk to each other with the aid of an amino acid called glutamate, which—after being released by an excited nerve cell—helps set off a wave of calcium ions in adjacent cells. The wave travels down the next nerve cell, which relays a signal to the next one in line, enabling long-distance communication.

But scientists were investigating something else when they stumbled on their discovery: how plants react to gravity. They developed a molecular sensor that could detect increases in calcium, which they thought might play a role. They bred the sensor, which glows brighter as calcium levels increase, into a mustard plant called Arabidopsis. They then cut one of its leaves to see whether they could detect any calcium activity.

They immediately saw a glow that got brighter, then dimmer, right next to the wound; then the glow appeared and disappeared farther away until the wave of calcium reached the other leaves (above), they report today in Science. Further study pinpointed glutamate as the trigger of the calcium wave.

Although plant biologists already know that changes to one part of a plant are sensed by the others, they had no idea how that information was transmitted. Now that they have seen the calcium wave and the role of glutamate, researchers can better monitor and—perhaps one day even manipulate—the plant’s internal communications.

http://bit.ly/2QyHxdi

Cladding tests show moisture may have sped up Grenfell flames

Tests on aluminium cladding panels have shown that water may have caused violent chemical reactions and accelerated flames

Tests on aluminium cladding panels, of the type used on the Grenfell Tower, have shown that the presence of water may cause violent chemical reactions and accelerate flames.

University of Portsmouth civil engineering student Laurence Casey carried out experiments in a specialist fire laboratory to find out why the panels could be a fire risk, despite having initially passed safety tests.

His investigation looked at the role water, in the form of steam, might have played in the spread of flames at the North Kensington tower block after the fire broke out on 14 June last year.

Mr Casey's research stemmed from initial experiments conducted by Professor Laurence Harwood, of the University of Reading, for the

BBC's Inside Out programme. Professor Harwood found that a violent reaction occurred when he directed a fine spray of water onto aluminium cladding sheets that had been heated to 300 C.

Mr Casey developed Professor Harwood's experiments with his own research to gather quantifiable data. Mr Casey said: "Prior to the laboratory tests, I had doubts about the reaction between the aluminium and steam occurring. Although aluminium is a highly reactive metal, the chemical reaction does not always develop when steam meets aluminium because of the protective oxide layers present on the surface. Once I had completed the tests, my doubts were lifted and I was confident the reaction took place. The results were shocking and to put things into perspective, the panels exposed to additional water produced more heat energy than burning petrol."

Using a cone calorimeter, which measures heat release, Mr Casey found that when water was applied to hot aluminium composite panels, a vast increase in the rate of heat release and heat of combustion occurred. This is thought to be a result of a chemical reaction producing hydrogen, a highly flammable gas, which subsequently burned, generating more heat and contributing to the acceleration of fire. The increase of heat energy released could pose a further risk to the ignition of flammable materials nearby, and could increase the rate at which the fire spreads across the façade.

He believes in the case of Grenfell Tower, this phenomenon would have then entered a chain reaction, with more steam being released from the burning polyethylene core within the panels, which impinged on nearby aluminium panels, triggering another chemical reaction and repeating the process whilst accumulating additional heat. This would have caused an out of control and ferocious fire

Professor Harwood has considered if weathering of the cladding could allow more water absorption in the insulating foam over time. The theory would be a possible explanation for the cladding passing initial tests but failing later ones. He also says that water from the fire brigade would not be a factor as the volume would quench the flames.

Laurence Casey says that without speculation, the source of the water vapour and the process of how it reaches the aluminium surface is unknown. Therefore, future research will investigate the effect of inherent water in polyethylene layer cladding systems, absorbed rain water and water from the initial quenching of flames.

The cladding used on the Grenfell Tower failed tests undertaken by BRE (British Research Establishment) during a fire safety programme launched after the tragedy. It has been concluded that this is primarily due to the use of a polyethylene inner core.

Mr Casey said: "This research raises the question whether some tests used to achieve compliance with certain building regulations are fit for purpose, and if they present the true fire performance of materials used in façade systems. There are several factors that need to be taken into account regarding the fire performance of a façade system; such as the type of insulation used, the presence of a cavity causing a chimney effect and we now know in the case of aluminium panels, the presence of water. These need to be tested in combination before any system is approved by regulatory authorities."

Graduate Mr Casey carried out the tests for his dissertation under the supervision of Dr. Laurie Clough, a teaching fellow in the School of Civil Engineering and Surveying at the University of Portsmouth. Professor Harwood was also involved providing advice as an external expert.

Professor Harwood has written to the Grenfell Tower Inquiry with his initial findings. He said: "This may explain why cladding removed from a number of buildings may have failed fire retardancy testing following the Grenfell Tower fire, despite the individual components having been found to be compliant with requisite fire regulations by the manufacturers."

This was a preliminary study and Mr Casey is hoping to continue investigating his results with more thorough studies. He said: "We need more concrete evidence and consistent testing methods to really understand the behaviour of aluminium during a building fire. But for a preliminary investigation, this is quite a significant result. There is clearly a knowledge gap in this area and Grenfell Tower is an example of the potential consequences of getting these things wrong."

https://wb.md/2xhBml8

DIY Artificial Pancreas Users Tweet it 'Changes Lives'

A patient-driven, do-it-yourself, open-source artificial pancreas system (OpenAPS) appears to safely improve glycemic control and quality of life among patients with type 1 diabetes, at least according to information gathered from Twitter.

Miriam E. Tucker

Findings from a 2-year qualitative "netnography" analysis of more than 3000 tweets carrying the hashtag #OpenAPS were published online September 10 in the *Journal of Diabetes Science and Technology* by Michelle Litchman, PhD, APRN, assistant professor at the College of Nursing, University of Utah Health, Salt Lake City, and colleagues.

Hacked open artificial pancreas system (OpenAPS). **University of Utah Health**

The OpenAPS movement was launched in 2015, when individuals in the type 1 diabetes community had become impatient with industry's attempts to develop an artificial pancreas. They hacked into older insulin pumps and current continuous glucose monitors (CGMs) and developed open-source code to allow the two devices to communicate, or "loop", for semi-automated insulin delivery. They tweeted their progress using the hashtag #WeAreNotWaiting.

This happened more than 2 years before the US Food and Drug Administration (FDA) approved the first hybrid closed-loop insulin delivery system, the Medtronic MiniMed 670G.

Today more than 750 people are believed to be using self-built artificial pancreas systems worldwide, despite the fact that they're not approved by regulatory bodies including the FDA.

"There is a large community that is actively exploring how they can manage their diabetes using off-label solutions...Healthcare providers, industry, and the FDA need to understand the wants and needs of people with diabetes in order to better serve them. OpenAPS was created out of a need for better solutions," Litchman said in a statement from her institution.

One endocrinologist who uses the OpenAPS system himself says it's not perfect but this new published study is a starting point to better track the progress of those who are using the "grassroots" technology. And physicians, he says, should be open-minded about it.

You Can't Hang Your Hat on a Twitter Study

Information gleaned from the hashtag tweets suggests that OpenAPS reduces HbA_{1c}, glycemic variability, and daily diabetes burden, and that users perceive it as safe. Other tweet themes were about interactions with healthcare providers concerning OpenAPS and how to adapt the technology to individual user needs.

The authors advise that clinicians "may want to consider becoming more informed about OpenAPS and other patient-driven innovations to support positive patient–provider interactions."

Asked to comment, endocrinologist Jeremy Hodson Pettus, MD, of the University of California, San Diego, told *Medscape Medical News*, "I think this whole do-it-yourself pancreas movement is very important. There are people using it and it's making a huge difference in their lives. I think it's important for more people to know about it, and hopefully it will become more mainstream and more available."

Regarding the new data, Pettus, who wears an OpenAPS system himself, noted, "It's not the most scientifically vigorous study. There are several biases, as those who tweet about it may not be representative...I tend to personally agree with the findings that the system has a real benefit, but I don't think you can hang your hat on a Twitter-based study."

Rather, Pettus says, the article will "get the word out and hopefully get more studies to follow it. Specifically, we need more controlled studies assessing pre- and post-glycemic control and quality of life. But in the absence of that and no real funding for a grass-roots effort, we have to start somewhere."

"OpenAPS Changes Lives"

Litchman and colleagues, of whom one is a user and co-developer of the technology and the other a parent of a child using the system, analyzed 3347 tweets using the hashtag #OpenAPS by patients, parents, caregivers, and care partners during 2016-2018.

Tweets from other individuals, including healthcare providers, were excluded. Only English-language tweets were included, but they came from 92 different countries. Overall, "the analysis resulted in one overarching theme: OpenAPS changes lives," the authors write.

Users indicated improvements in HbA_{1c}, with some tweets posting personal best values. Among those who provided them, HbA_{1c} results ranged from 4.9% to 6.8%. Individuals also tweeted about time in range and experiencing less glucose variability.

Users also frequently tweeted about the emotional impact the system had on individuals and their families, noting reductions in diabetes-related "burden" and "distress," with the automatic adjustments freeing them from constant mental tasks.

Similarly, Pettus says that in the year since he's been "looping," "it's allowed me to be lazier about my diabetes. If I go to bed high or low, things will correct. I have been able to ease up on the amount of mental energy I put into this disease."

Users also perceived the systems as safe, describing features within OpenAPS as including "extra security against untreated overnight hypos."

However, users didn't tend to view OpenAPS as a cure.

Similar to the Medtronic MiniMed 670G and other systems in development, users still must count carbohydrates, maintain the equipment, troubleshoot in case of failure (such as when cell coverage is unavailable), and with some CGMs, perform regular fingerstick calibrations.

And despite general support for the system's built-in safety mechanisms, some tweets expressed concerns about the reliance on older-model, out of warranty insulin pumps.

"Be Open-Minded About It"

Tweets reflected varying reactions from patients' healthcare providers to the use of OpenAPS. Some reported their providers were positive about the system based on the improved HbA_{1c} levels; however, others said their providers were resistant to the idea or unfamiliar with it.

But overall, users wanted their providers to be supportive and were willing to change physicians, if necessary. One tweet stated, "I couldn't imagine sticking with a doc that didn't support such advances."

Indeed, Pettus advises clinicians to "be open-minded about it. You don't have to necessarily recommend it or know all the nitty-gritty of it, but at least don't shut somebody down or naysay it if they show interest or if they come into your office on it."

Challenges and Future Course

Tweets also discussed the adaptability of the systems to meet individual needs, but others focused on difficulties in obtaining the necessary equipment and challenges in getting the systems to work.

Often, when someone tweeted about a difficulty, others responded by offering various types of help, including links to OpenAPS

directions, answers to specific questions, encouraging words of support, or connections to individuals or websites where OpenAPS supplies could be purchased.

Litchman and colleagues acknowledged the bias in their data source, noting "there may be individuals who tried OpenAPS and stopped due to technical challenges or untoward effects. However, this was not identified in the dataset."

Pettus said he doesn't think OpenAPS is currently a solution for the majority of people with type 1 diabetes, but more that it's a proof of concept. "This particular system as it stands now is not going to move the needle itself. But these grassroots technologies can become commercially available and are moving towards that. People may view artificial pancreas technology as kind of fringe, but it's already here. I think that's the point."

Lichtman has reported no relevant financial relationships. Pettus has reported consulting for Sanofi, Novo Nordisk, MannKind, and Insulet.

J Diabetes Sci Technol. Published online September 10, 2018. Abstract

http://bit.ly/2NflRoO

Bacteria in a Dinosaur Bone Reignite a Heated Debate

The discovery of modern microbes in a deeply buried fossil has complicated an already tangled dispute in paleontology.

Ed Yong

Around 76 million years ago, a massive herd of the horned dinosaur *Centrosaurus* died in what is now Alberta, Canada. While they were still alive, these creatures, like all other animals, would have had trillions of microbes living inside their bodies and on their skin. And even now, long after their demise, their remains *still* harbor life.

A Tyrannosaurus skull **Pawel Kopczynski / Reuters**

Within pieces of fossilized bone from a newly uncovered *Centrosaurus*, scientists led by Evan Saitta from the Field Museum have found a thriving community of unusual bacteria. These aren't ancient microbes, but modern ones that infiltrated the fossils and survived on the water and minerals inside them. "The bones provide a refuge," Saitta says. They are porous, and so "have space for the microbes to proliferate. They're full of phosphate and iron. They can wick up moisture."

When animals die, waves of microbes consume their corpses. Scientists have looked at how this "necrobiome" changes over the hours and days after an animal perishes. But Saitta's work suggests that microbes continue to colonize cadavers long after their flesh has decayed, after their bones have turned to stone, and after they've been buried several miles deep for millions of years.

That came as a huge surprise to Tullis Onstott, a microbiologist from Princeton who worked with Saitta, and who always thought of fossils as inert and inanimate. "I thought that dinosaur bone must be some kind of sealed sarcophagus," he says. "It's not, by any means. It's basically a condo for bacteria. Now the question becomes: Is this true for all dinosaur bones?"

The team's study, which has been uploaded as a preprint and has yet to be reviewed and published, complicates a heated debate that has rocked the world of paleontology for more than a decade. In the mid-2000s, Mary Schweitzer from North Carolina State University reportedly found blood vessels, cells, and traces of collagen protein from the thigh bones of two dinosaurs: a 68-million-year-old Tyrannosaurus and an 80-million-year-old *Brachylophosaurus*. Though a far cry from *Jurassic Park*, since no DNA had been discovered, the discovery was still an extraordinary one. If proteins really could survive that long, they would allow scientists to study dinosaurs at a molecular level, just as they do modern animals.

Others were skeptical. Most ancient proteins are hundreds of thousands of years old at most. A few exceptional molecules have lasted for 3 to 4 million years, protected either by exceptional cold

or unique minerals. The supposed collagen from Schweitzer's dinosaurs enjoyed no such protection, and would have been 20 to 30 times more ancient. Collagen is tough, but after such a long time, the chemical bonds that hold it together would likely have ruptured. Some critics argued that the proteins Schweitzer had detected weren't actually there, or that the cells she had seen were actually bacterial colonies. Others suggested that the molecules and tissues must have come from modern organisms that contaminated the samples.

Schweitzer's team addresses that last critique by taking extra care to stop external microbes from getting into its fossils. When it recently reanalyzed fragments from its *Brachylophosaurus*, the team even disassembled one of its analytical instruments and soaked its pieces in alcohol to kill any contaminating microbes.

But based on his new findings, Saitta now argues that such measures wouldn't have done anything to remove microbes living inside the bones themselves. And if such microbes prove to be common, researchers must take extra steps to prove that proteins in a dinosaur's bone actually belonged to the animal itself, and not to modern microbes that have infiltrated its remains.

His team tried to do that with their *Centrosaurus* specimen. Like Schweitzer's group, it took care to stop foreign microbes from landing in the samples. The scientists washed their gloves and face masks in alcohol. They sterilized their tools with bleach and a blowtorch. They extracted bones that were still encased in mudstone and wrapped them in sterilized foil. "Collecting bones aseptically is basically an impossible task because the techniques of paleontology haven't changed in the last 100 years, but I think we did a good job," Saitta says.

Once in its laboratory, the team pulverized the bone fragments and subjected them to a battery of chemical tests. And while it found plenty of amino acids—the building blocks of proteins—the profile of these molecules didn't match collagen. And they weren't ancient. When living things die, their amino acids gradually flip into a mirror-image state. By measuring the levels of these flipped versions, scientists can deduce how old proteins are. Those in the *Centrosaurus* were clearly modern. They likely came from microbes, and given the team's diligence, those microbes likely came from *inside* the bones.

The team found 50 times more microbial DNA within the bone fragments than in the mudstone immediately surrounding them. It could even see some of the cells under a microscope. "The concentration of bacteria in the bone was *huge*," Onstott says. "There's a very significant community in there."

This microbial community is dominated by just a few bacterial species that are very different than those in the surrounding sediment. Their exact identity is unclear, but around a third of the DNA is a close match for *Euzebya*, a bacterium that's been found in Etruscan tombs and in the skins of Japanese sea cucumbers. "It's not something I've widely encountered, so we're trying to figure out what they are," Onstott says. "There seems to be something in the bone that enhances this particular type of bacteria."

"It's slightly odd that no one's ever tried this before," says Matthew Collins from the University of York, who studies ancient proteins. Despite the collagen controversy, no one had looked directly for microbes inside the bones, and "surprise, surprise! There are microbes present. It doesn't disprove that researchers can get [original] proteins out of these dinosaur tissues, but it does cast shade on the interpretation."

Saitta and some of his colleagues take a harder line. They couldn't find any trace of ancient proteins in the *Centrosaurus* bones, which contradicts Schweitzer's discovery, or at least fails to replicate it. And since many bacteria can digest collagen, they say that the

presence of microbes in bone makes it even less likely that ancient proteins would have survived for tens of millions of years.

Others feel less strongly. Onstott notes that other dinosaur bones might have no microbes at all, or different communities of them. Some might contain species that help to *preserve* collagen over time. "I think the discovery of Cretaceous dinosaur proteins is still tentative, and we still don't have clear, unquestionable evidence," adds Enrico Cappellini from the University of Copenhagen. Nor is it clear, he says, that chemical signals that have been interpreted as dinosaur proteins came from bacteria.

Schweitzer doesn't think that the new study contradicts her work, either. "We never claimed that our bones have been preserved without a microbial influence," she says. That influence is neither surprising nor "mutually exclusive" with the preservation of actual dinosaur proteins—"a claim we support with multiple lines of evidence, rigorous data, and a plethora of controls."

Her team has used several techniques that Saitta's group did not, and that provide stronger evidence that its tissues and proteins couldn't have come from microbes. For example, it sequenced the proteins in question using mass spectrometry, and found matches to vertebrate proteins. It also showed that these tissues react to antibodies that specifically recognize vertebrate proteins not found in bacteria. Saitta and his colleagues "have not addressed these multiple lines of evidence, so they haven't refuted any of our hypotheses or negated any of our data," she says.

Her team also recently inoculated modern bones with bacteria and showed that the resulting colonies are very different, structurally and chemically, from the cells and blood vessels she has seen in dinosaur fossils. "There are no data to support a microbial source for the vessels and [bone cells] we have recovered," she says. "But there are abundant data to support that these are original to the dinosaur."

And so the debate continues. "I think it has ultimately been good for the field," says Beatrice Demarchi from the University of York. She means that scientists who are searching fossils for traces of ancient molecules have had to think hard about how to prove that their finds are authentic. Many of the techniques that they've adopted "should be applied routinely," Demarchi says, "and even more so when claims for really old proteins are made."

The debate has often been acrimonious, and Saitta hopes to avoid that this time round. "I don't want to create any animosity. I just want to do good science," he says. "There's a lot of interesting things going on in these bones, and if not for the dinosaur-protein claims, I wouldn't have thought to look into them."

We want to hear what you think about this article. Submit a letter to the editor or write to letters@theatlantic.com.

http://bit.ly/2xnAPhE

Study: Infants Use Same Gestures as Chimpanzees

Children used gestures to communicate, many of which are shared with chimpanzees

Great apes of all species — human and non-human — communicate using a combination of different types of signals: vocalizations, gestures, facial expressions and body postures. According to a **new study**, published in the journal ***Animal Cognition***, one- to two-year-old human children use many of the gestures observed in great apes. The study, led by University of St Andrews researcher **Catherine Hobaiter**, showed that children used 52 gestures to communicate, 46 (89%) of which are shared with chimpanzees. Like chimpanzees, children used them both singly, and in sequences, and employed individual gestures flexibly towards different goals.

Dr. Hobaiter and her colleagues from the UK, Uganda, Germany and Switzerland studied young children and chimpanzees.

Chimpanzees were observed in their habitat, the Budongo forest in Uganda, and young children were observed in their nursery and home environments.

Wild great apes use over 80 different gestures, and scientists have recently completed a 'great ape dictionary' to investigate what they mean.

"Wild chimpanzees, gorillas, bonobos and orangutans all use gestures to communicate their day-to-day requests, but until now there was always one ape missing from the picture — us," Dr. Hobaiter said.

"We used exactly the same approach to study young chimpanzees and children, which makes sense — children are just tiny apes."

The study authors were surprised by just how many gestures the children had in common with our ape cousins.

"We thought that we might find a few of these gestures — reaching out your palm to ask for something or sticking your hand up in the air — but we were amazed to see so many of the 'ape' gestures used by the children," Dr. Hobaiter said.

The researchers found that like young apes, the young children used these gestures in a similar way: combining them together to ask for different things.

They also found some differences — young children use pointing gestures far more than young apes, and waving your hand (to say hello or goodbye) seems to be uniquely human.

"Since chimpanzees and humans shared a common ancestor around 5-6 million years ago, we wanted to know whether our evolutionary history of communication is also reflected in human development," said study first author Dr. Verena Kersken, a scientist at the University of Göttingen in Germany.

"While humans developed language, it appears that we still have access to this shared ancient gestural heritage — and gestures continue to play an important role before language is fully developed."

http://bit.ly/2D3qmy5

Repeat vaccination is safe for most kids with mild to moderate reactions

Children who experience some type of adverse event following initial immunization have a low rate of recurrent reactions to subsequent vaccinations

Children who experience some type of adverse event following initial immunization have a low rate of recurrent reactions to subsequent vaccinations, reports a study in *The Pediatric Infectious Disease Journal*, the official journal of The European Society for Paediatric Infectious Diseases. The journal is published in the Lippincott portfolio by Wolters Kluwer.

"Most patients with a history of mild or moderate adverse events following immunization [AEFI] can be safely reimmunized," write Gaston De Serres, MD, of Laval University, Quebec, and colleagues. Although recurrent AEFIs can sometimes occur after repeat doses of vaccine, this study suggests that the risk of recurrent AEFIs after re-vaccination is relatively low, especially when the previous reaction was mild or moderate.

Safety of Repeat Vaccination after Initial Reactions - 'Passive Surveillance' Data In Quebec, healthcare professionals are legally required to report any "unusual or severe" AEFI related to a "passive surveillance" system similar to the Vaccine Adverse Event Reporting System (VAERS) used in the United States. The analysis included 5,600 patients with AEFIs reported to Quebec's passive surveillance database from 1998 through 2016, all of whom required further doses of the vaccine to which they reacted. (The analysis excluded seasonal influenza vaccine, which changes from year to year.)

Of 1,731 patients with available follow-up data, 1,350 patients were re-vaccinated: a rate of 78 percent. Most of the re-vaccinated children were under two years old; about one-half of the AEFIs were allergic-like reactions.

Sixteen percent of patients experienced some type of recurrent AEFI after re-vaccination. In more than 80 percent of cases, the recurrent reaction was no more severe than the initial reaction. The researchers analyzed potential risk factors for recurrent reactions, including:

- ***Patient Characteristics. Children under age 2 were more likely to be re-vaccinated and less likely to have recurrent reactions, compared to older patients. Recurrence risk was similar for males and females.***
- ***Type of AEFI. Recurrence rate was similar for patients with most types of initial AEFIs. The risk was highest (67 percent) for patients with large local reactions with "extensive limb swelling." For patients who had allergic-type reactions, the recurrence rate was 12 percent. Severe allergic events (anaphylaxis) were very rare after re-vaccination.***
- ***Severity of AEFI. Patients with more severe initial AEFIs were less likely to be re-vaccinated: only 60 percent of children with severe reactions were re-vaccinated, compared to 80 percent of those with less-severe reactions. Within this selected group, patients with severe AEFIs were less likely to have recurrences: eight versus 17 percent.***
- ***Type of Vaccine. The recurrence rate did not differ significantly for different types of vaccines. The re-vaccination rate was highest (90 percent) for children with AEFIs to diphtheria-tetanus-pertussis vaccines.***

Prior to this study, there have been limited data on the safety of reimmunizing patients who had a prior AEFI. The study is one of the largest to estimate the rate of recurrent AEFIs by type of reaction and type of vaccine - key information for healthcare providers and parents/caregivers making decisions about further immunization. The results support the safety of continued vaccination especially when the previous reaction was mild or moderate.

The study provides helpful information on the risk of recurrent reactions to specific vaccines and in patients with different types of initial reactions. Dr. De Serres and coauthors suggest that vaccine adverse event passive surveillance systems could be adapted to include "systematic and standardized follow-up" to provide more complete information on recurrence risk and other outcomes for children with AEFIs .

Click to read "Rate of Recurrence of Adverse Events Following Immunization: Results of 19 Years of Surveillance Ii Quebec, Canada" DOI: 10.1097/INF.0000000000002162

http://bit.ly/2NhwhUD

Inhaled steroids may increase risk of nontuberculous mycobacteria lung infections

NTM come in many different species and are widely dispersed in the environment

Patients using inhaled steroids to control asthma and other breathing problems may be at greater risk for developing nontuberculous mycobacteria (NTM) lung infections, according to new research published online in the *Annals of the American Thoracic Society*.

NTM are in the same family as tuberculosis, but NTM come in many different species and are widely dispersed in the environment. Although they cannot be spread from person to person, NTM are difficult to treat and can cause serious illness, and even death.

In "Association between Inhaled Corticosteroid Use and Pulmonary Nontuberculous Mycobacterial Infection," Stephen J. Ruoss, MD, and co-authors analyzed the medical records of 549 patients diagnosed with NTM lung infections in Northern California over a 10-year period.

They found that the odds of developing NTM pulmonary infection were 2.7 times greater in those patients who had filled three or more prescriptions for an inhaled steroid. They also found that the longer a person was on an inhaled steroid and the higher the dose, the more likely the patient was to develop an NTM lung infection.

"The increasing prevalence of NTMs is disconcerting because some of the most common types of NTM are harder to treat than multidrug-resistant TB," said Dr. Ruoss, senior study author and a pulmonologist and intensivist at Stanford University Medical Center in California. "The rapidly growing number of NTM infections has

occurred during a time when inhaled steroid use has increased, and we wanted to see if there was a potential connection."

According to the authors, the prevalence of NTM infection in the early 1980s was reported to be as many as 1.8 cases per 100,000 persons. More recent studies have shown that the prevalence in some regions of the country may now be over 40 cases per 100,000 persons. During this time, inhaled steroid use has grown. First used in the early 1980s in the U.S. to treat asthma, inhaled steroids are increasingly also used to treat COPD, or chronic obstructive pulmonary disease, and bronchiectasis, a chronic inflammatory condition that scars the airways.

Some studies have found that as many as three-quarters of COPD patients may be taking an inhaled steroid. While inhaled steroids are now commonly prescribed and used in COPD, it is likely only a modest number of patients who gain significant clinical benefit from this treatment, according to the authors.

"There have been some big studies that have shown a very modest, but statistically significant, benefit of inhaled steroid use in COPD patients," Dr. Ruoss said. "These studies have also shown that COPD patients who use these drugs are at a slightly greater risk of developing routine bacterial infections."

Because inhaled steroids appear to depress the immune system, they may contribute to the risk of respiratory infections, including NTM infections, the authors wrote.

"Inhaled steroids are standard therapy for those with asthma because the benefits have proven in studies and clinical practice to outweigh the risks," Dr. Ruoss said. "But as physicians, we should be careful using this class of drugs broadly in patients with COPD."

As with asthma patients prescribed an inhaled steroid, Dr. Ruoss recommends that physicians "concretely and objectively" assess whether their COPD patients are benefitting from the drug, and if so, work to prescribe the lowest effective dose if the patient cannot eventually be taken off the drug entirely.

For all their patients on inhaled steroids, Dr. Ruoss added, doctors should be "mindful of the increased risk for infections and monitor for routine and mycobacteria infections."

Study limitations include the fact that it was not a randomized, controlled trial so it cannot prove that inhaled steroids result in increased numbers of NTM lung infections.

"Study finds inhaled corticosteroids (#ICS), used to treat #asthma and #COPD, are associated with increased risk of nontuberculous mycobacteria (#NTM) #lung infections."

http://bit.ly/2NPSAjK

Art conservation using saliva wins chemistry Ig Nobel

This year's chemistry Ig Nobel prize has been awarded to three Portuguese conservation scientists who showed that human saliva is a good cleaning agent for paintings and historical artefacts.

By Emma Stoye 14 September 2018

Paula Romão, Adília Alarcão and César Viana's 1990 paper revealed how the trio collected saliva and measured how effective it was at removing dirt from 18th century gilded sculptures. They note that conservators have long been using their own saliva in preference to other solvents when working with delicate materials such as gold leaf and ceramics.

'I know that it seems quite improbable, but human saliva is indeed an effective cleaning agent for surfaces like paintings, sculptures and gilded wood. But don't try to use it on your kitchen counters,' Romão said in an acceptance video that was played at the awards ceremony at Harvard University. The cleaning action is in part due to an enzyme in saliva, α-amylase, which breaks down starch into simple sugars.

The Ig Nobel prizes are awarded annually to celebrate improbable scientific research across a variety of disciplines. Among this year's winners are Marc Mitchell and David Wartinger, who were awarded

the medicine prize for using roller coaster rides to hasten the passage of kidney stones, and an international team who won the biology prize for demonstrating that wine experts can smell the presence of a single fly in a glass of wine.

http://bit.ly/2NSztpy

Cancer Spreads from Organ Donor to 4 People in 'Extraordinary' Case

It's well known that organ transplants can pass infectious diseases from donors to recipients in rare cases. But even more rarely, transplants can transmit cancer, as a new case shows.

By Rachael Rettner, Senior Writer

In what's being described as an "extraordinary case," four people in Europe developed breast cancer after they received organs from the same donor, according to a new report.

Three of the patients died from the cancer, which underscores the "often-fatal consequences of donor-derived breast cancer," the authors wrote in their report, published in the July issue of the American Journal of Transplantation.

Undetected cancer

The 53-year-old organ donor died from a stroke in 2007, according to the report, written by researchers in the Netherlands and Germany. She had no known medical conditions that would have precluded organ donation, and multiple tests showed no signs of cancer. Doctors transplanted her kidneys, lungs, liver and heart into the donor recipients. (The heart-transplant patient died of unrelated causes shortly after the transplant.)

But 16 months later, a woman who received the lung transplant became ill and was found to have cancer in the lymph nodes in her chest.

An analysis of the cancer cells revealed that they were actually breast cancer cells, and DNA in the cancer cells showed that these cells had come from the organ donor. The lung recipient's cancer spread, and she died about a year after her cancer diagnosis, the report said.

At that time, the three other living patients who'd received the donations were notified. Doctors told them that the lung recipient had died from breast cancer tied to her transplant. These patients underwent tests for cancer, which were initially negative.

But in 2011, the liver-transplant patient was found to have breast cancer cells in her liver.

The patient didn't want to undergo another liver transplant, because she was afraid of potential complications. A radiation treatment for the cancer was initially helpful, but the cancer later returned, and that patient died in 2014.

The patient who received the left kidney was also later diagnosed with breast cancer in 2013 — six years after her transplant. The cancer had already spread to many other organs, and the patient passed away two months later.

A 32-year-old man who received the right kidney was also diagnosed with breast cancer cells in his transplanted kidney in 2011. But doctors were able to remove the kidney, and the patient stopped taking drugs to suppress his immune system.

He also underwent chemotherapy. The treatment was successful, and the man was still cancer-free 10 years after the transplantation surgery.

Low risk

Passing cancer through an organ transplant is "a very, very uncommon event," said Dr. Lewis Teperman, director of organ transplantation at Northwell Health in New Hyde Park, New York, who was not involved in the case. Indeed, transplant recipients have a chance of between 1 in 10,000 and 5 in 10,000 of this happening, according to the report.

"The organ supply is incredibly safe," Teperman told Live Science. That's because organ donors undergo rigorous screening, including

family history for disease, such as cancer, and multiple laboratory tests. In this case, the 53-year-old donor underwent a physical exam as well as an ultrasound of the abdomen and heart, a chest X-ray, and an examination of the airways.

Still, even with these robust procedures in place, "it's impossible to screen everything," and there's a very small chance that a donor will have an undetected disease that could be transmitted, Teperman said. In the current case, the patient had an undetected breast cancer.

The donor may have had "micro metastases" or groups of cancer cells that spread from the original cancer site but are too small to be detected with screening or imaging tests, the report said.

It's also easier for such cancer cells to grow in transplant patients, because the patients take drugs to suppress their immune systems. These drugs are needed so that patients' bodies do not reject the new organ, but any foreign cancer cells "would not be rejected either," Teperman said.

It's possible that a CT scan of the donor in this case may have caught the cancer, but the authors noted that it would be impractical to screen all donors in this way, according to The Independent. Routinely performing such tests could lead to the detection of false positives and the rejection of healthy donors, which would lead to a "decrease of the already scarce donor pool," the authors wrote in the study.

"You would have so many worries that you would never procure any organs," Teperman said.

The report concludes that the low rate of cancer transmission from transplantation "implies that current practices of donor screening for malignancy are effective." If cancer does pass from a donor to a recipient, doctors should consider removing transplants from all other patients who received organs from that donor, the researchers wrote.

https://bbc.in/2NKnJVW

'Aspirin-a-day risky in old age' - major study

Elderly people in good health should not take an aspirin a day, according to a major study in the US and Australia.

By James Gallagher Health and science reporter, BBC News

There are proven benefits of the drug for people after a heart attack or stroke. But the trial found no benefit for healthy people over the age of 70, and the pills increased the risk of potentially fatal internal bleeding. Experts described the results as very important and cautioned against self-medicating with aspirin.

People are prescribed aspirin after a heart attack or stroke because the drug thins the blood and reduces the chances of a repeat attack.

Some completely healthy people also choose to take aspirin to reduce their risk and there is continuing research into whether the drug can be used to cut the risk of cancer.

However, most research on the benefits of aspirin is performed on people in middle age and there is mounting evidence the dangers increase as we get older.

'No benefit'

The study was of 19,114 people in the US and Australia in good health, with no history of heart problems and over the age of 70.

Half were given a daily low-dose aspirin for five years. Three reports in the New England Journal of Medicine showed the pills did not reduce their risk of heart problems or have any other benefits.

They did increase the number of major stomach bleeds.

Prof John McNeil, from Monash University, said: "It means millions of healthy older people around the world who are taking low dose aspirin without a medical reason, may be doing so unnecessarily, because the study showed no overall benefit to offset the risk of bleeding. "These findings will help inform prescribing doctors who have long been uncertain about whether to recommend aspirin to healthy patients."

The study also discovered an increase in deaths from cancer, although the researchers think this needs further investigation as it goes against current findings in the field.

Prof Peter Rothwell, of Oxford University, a leading expert on the drug, said the findings were definitive. "Taking aspirin if you are otherwise healthy, over the age of 70, if you haven't had a previous heart attack or stroke, is really of very little benefit," he said. "And so self-medicating with aspirin in the absence of a definite medical indication isn't advisable."

The findings do not apply to people taking aspirin because of a heart attack or stroke - they should continue to follow their doctor's advice. And anybody who has been taking low-dose aspirin for a long time is advised not to stop overnight as that may also cause problems. Instead they should discuss any concerns with their GP, says Prof Rothwell.

https://nyti.ms/2D3hJDD

For Elderly Women With Breast Cancer, Surgery May Not Be the Best Option

Nursing home patients may be frail or have other diseases, leading some doctors to advise hormone therapy rather than operations.

By Paula Span

Annie Krause moved into a nursing home in Detroit in 2015, when she was 98 years old. She had grown frail. Arthritis, recurrent infections and hypertension had made it difficult for her to manage on her own.

When the facility's doctor examined her, he found a mass in Ms. Krause's breast and recommended a biopsy — standard procedure to determine what sort of tumor this was and, if it proved malignant, what treatment to pursue. Once diagnosed, breast cancer almost always leads to surgery, even in older women.

"If she were a passive person, she would have had a lumpectomy," said Ms. Krause's granddaughter, Dr. Mara Schonberg, an internist at Beth Israel Deaconess Medical Center in Boston. "But my grandmother was very strong-willed. She said no, no, no, she didn't want any procedure."

That didn't stop the doctor from recommending a biopsy, however.

Having spent years studying how best to inform older women about breast cancer, Dr. Schonberg said that patients' decisions — about screenings and treatments — have proved stubbornly resistant to change.

She told me about her family's situation in the wake of a recent study by researchers at the University of California San Francisco. Published in JAMA Surgery, it followed nearly 6,000 nursing home residents who underwent inpatient breast cancer surgery over a 10-year period.

It's the most common cancer operation for nursing home residents, the researchers reported. Yet Medicare data showed that as a group, these women did not fare well.

"The trajectories for these patients tends to be poor to begin with," said Dr. Victoria Tang, a geriatrician and the study's lead author. Almost by definition, women in nursing homes have serious health problems that already portend limited life expectancies.

The women in the study (average age 82) had high rates of diabetes, arthritis, heart failure and stroke. They needed considerable help with everyday tasks. Well over half were cognitively impaired.

Yet their surgeons tended to operate aggressively. Though about 11 percent had a lumpectomy, more than a quarter underwent a mastectomy, removal of the entire breast. In more than 60 percent, surgeons also removed underarm lymph nodes, a procedure usually conducted to help determine future treatment, but one that can cause pain and infection, with arm swelling that hampers mobility.

In younger and healthier groups, breast cancer surgery is considered low risk. “A lumpectomy is seen as routine, no big deal,” Dr. Tang said. “It can be done as an outpatient.”

But for these women, “the surgical treatment for breast cancer may have been worse than the breast cancer itself,” said Dr. Rita Mukhtar, a breast cancer surgeon and a co-author of the study.

Within a month after surgery, two to eight percent of the patients in the study had died, a very high mortality rate. Those undergoing lumpectomy — perhaps, the authors hypothesize, because those women were sicker and deemed less likely to survive more invasive surgery — were most likely to die.

Surgeons and hospitals (and Medicare) pay close attention to the 30-day mortality rate, but most patients and families expect more, months or years of extended life in exchange for the rigors of surgery. But within a year, 29 to 41 percent of these patients had died, depending on the type of surgery they’d had — another very high mortality rate.

Of those who survived a year, about 60 percent experienced a decline in function. “A lymph node dissection might disable you and leave you in pain, so you’re less able to dress or bathe or even feed yourself,” Dr. Tang said.

Of course, nursing home residents do decline and die, with or without surgery. But that, Dr. Mukhtar said, was the point.

“We’re taking people who are more likely to die of something else, and putting them through hospitalization and surgery, with all those risks,” she said, citing those including infection, falls and delirium. “By operating on them, we may be diminishing their quality of life for their remaining days.”

Given a clearer sense of the risks, patients and families might opt for less invasive treatments. Hormone therapy, like tamoxifen or aromatase inhibitors taken orally, slows the progression of certain kinds of tumors. Radiation may also control tumors, with fewer dangers than surgery.

In cases where a tumor grows through the skin and causes pain or bleeding, of course, surgery becomes a palliative response.

But it takes more than 10 years after screening to prevent a single breast cancer death for 1,000 patients screened, if they’re of average risk. So researchers say mammograms (and colon cancer screening, which involves a similar time lag) are most useful for those with life expectancies greater than a decade.

Few women in nursing homes will live that long. Many who develop breast cancer will experience no symptoms, and would never have known they had it without a physical exam or continuing mammograms.

Like any test or procedure, mammography involves risks: additional screenings, biopsies, complications of biopsies and treatment, and the anxiety the whole process creates.

The United States Preventive Services Task Force doesn’t recommend mammograms for women over 75 because there’s insufficient evidence to assess benefits and harms. Older women have largely been excluded from clinical trials.

Since many older women have been dutifully having mammograms for decades anyway, Dr. Schonberg developed a brochure called “Should I Continue Getting Mammograms?”

It explains procedures, helps women assess relevant health factors and points out that over age 75, screening 1,000 women prevents only one breast cancer death over 5 years, while generating 100 false positives. (There’s also a version for women over 85.)

Distributing the brochure to 45 women, Dr. Schonberg determined that it had some impact. After using it, women were more knowledgeable and more likely to discuss the decision with their doctors. Yet 60 percent still had another mammogram

She has since completed a broader study, being prepared for publication, involving 541 women over 75. Here, too, preliminary results show that the proportion who had another mammogram dropped only slightly after using the brochure, from 61 to 56 percent — a modest drop that demonstrates women's reluctance to discontinue screening.

These subjects were not nursing home residents, and it might make sense for them to use other yardsticks besides age in their decision-making.

Dr. Mukhtar has performed breast cancer surgery on patients in their 50s and 60s, for instance, who had serious medical problems beforehand, leading to troubling complications afterward. But she also operated on healthy patients in their 80s who recovered well.

Nursing home residents are already in poor health, however. "It's likely the surgery didn't help them live longer, and certainly not better," Dr. Schonberg said.

As for her grandmother, Annie Krause, she declined the biopsy and Dr. Schonberg supported her decision.

"In a 98-year-old, it probably is breast cancer," Dr. Schonberg said. "But she didn't want any more medical interventions. She was focused on optimizing her quality of life."

Ms. Krause died two years later, after a stroke.

http://bit.ly/2xpHZSz

Household cleaning products may contribute to kids' overweight by altering their gut microbiota

Common household cleaners may altering children's gut microbiota and make them overweight

Commonly used household cleaners could be making children overweight by altering their gut microbiota, suggests a Canadian study published in *CMAJ (Canadian Medical Association Journal)*.

The study analyzed the gut flora of 757 infants from the general population at age 3-4 months and weight at ages 1 and 3 years, looking at exposure to disinfectants, detergents and eco-friendly products used in the home.

Researchers from across Canada looked at data from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort on microbes in infant fecal matter. They used World Health Organization growth charts for body mass index (BMI) scores.

Associations with altered gut flora in babies 3-4 months old were strongest for frequent use of household disinfectants such as multisurface cleaners, which showed lower levels of Haemophilus and Clostridium bacteria but higher levels of Lachnospiraceae. The researchers also observed an increase in Lachnospiraceae bacteria with more frequent cleaning with disinfectants. They did not find the same association with detergents or eco-friendly cleaners. Studies of piglets have found similar changes in the gut microbiome when exposed to aerosol disinfectants.

"We found that infants living in households with disinfectants being used at least weekly were twice as likely to have higher levels of the gut microbes Lachnospiraceae at age 3-4 months; when they were 3 years old, their body mass index was higher than children not exposed to heavy home use of disinfectants as an infant," said Anita Kozyrskyj, a University of Alberta pediatrics professor, and principal investigator on the SyMBIOTA project, an investigation into how alteration of the infant gut microbiome impacts health.

Babies living in households that used eco-friendly cleaners had different microbiota and were less likely to be overweight as toddlers.

"Those infants growing up in households with heavy use of eco cleaners had much lower levels of the gut microbes Enterobacteriaceae. However, we found no evidence that these gut microbiome changes caused the reduced obesity risk," she said.

She suggests that the use of eco-friendly products may be linked to healthier overall maternal lifestyles and eating habits, contributing in turn to the healthier gut microbiomes and weight of their infants.

"Antibacterial cleaning products have the capacity to change the environmental microbiome and alter risk for child overweight," write the authors. "Our study provides novel information regarding the impact of these products on infant gut microbial composition and outcomes of overweight in the same population."

A related commentary provides perspective on the interesting findings.

"There is biologic plausibility to the finding that early-life exposure to disinfectants may increase risk of childhood obesity through the alterations in bacteria within the Lachnospiraceae family," write epidemiologists Dr. Noel Mueller and Moira Differding, Johns Hopkins Bloomberg School of Public Health, in a related commentary http://www.cmaj.ca/lookup/doi/10.1503/cmaj.181134.

They call for further studies "to explore the intriguing possibility that use of household disinfectants might contribute to the complex causes of obesity through microbially mediated mechanisms."

Dr. Kozyrskyj agrees and points to the need for studies that classify cleaning products by their actual ingredients. "The inability to do this was a limitation of our study."

The research study was funded by the Canadian Institutes of Health Research (CIHR) with funding from the Allergy, Genes and Environment (AllerGen) Network of Centres of Excellence for the CHILD study.

"Postnatal exposure to household disinfectants, infant gut microbiota and subsequent risk of overweight in children" is published September 17, 2018.

Podcast permanent link: https://soundcloud.com/cmajpodcasts/170809-res

Video: https://youtu.be/2OUXHwkpc28