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How did reading and writing evolve? Neuroscience gives a clue

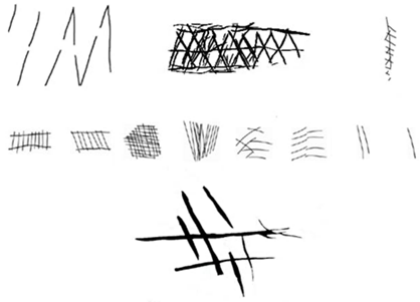
Determining how and why humans first began to make repetitive marks

Derek Hodgson

The part of the brain that processes visual information, the visual cortex, evolved over the course of millions of years in a world where reading and writing didn't exist. So it's long been a mystery how these skills could appear some 5,000 years ago, with our brains suddenly acquiring the specific ability to make sense of letters. Some researchers believe that the key to understanding this transition is determining how and why humans first began to make repetitive marks.

Recent extensive brain imaging of the visual cortex as people read text has provided important insights into how the brain perceives simple patterns. In my new paper, published in the Journal of Archaeological Science Reports, I analyse such research to argue that the earliest human-made patterns were aesthetic rather than symbolic, and describe what that means for the evolution of reading and writing.

Archaeologists have uncovered a growing number of ancient, engraved patterns produced by early humans as well as Neanderthals and *Homo erectus*. The marks predate the first representational art (drawings that represent something) by thousands of years.



Early marks. Top, left to right: Trinil shell, Blombos engravings (two examples). Middle: South Africa on ostrich eggshell. Bottom: Gibraltar by Neanderthals on rock surface. **Author provided**

Such motifs have been found in South Africa with engravings dating back to 100,000 years ago. Archaeologists have also found shell engravings made by *Homo erectus* some 540,000 years ago. One intriguing observation of these early marks is that they all feature grids, angles and repetitive lines.

The brain's pattern filter

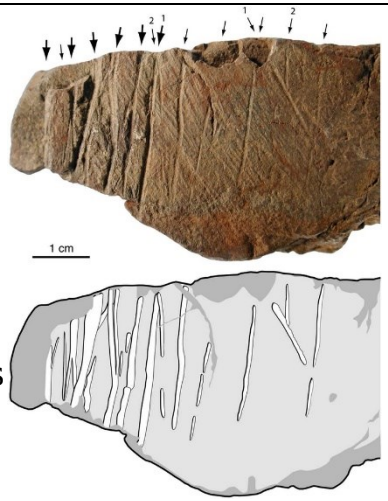
In 2000 I first suggested that the way the "early visual cortex" – the location where visual information from the eye first impacts the cortex – processes information gave rise to the ability to engrave simple patterns. We know that this area has neurons coding for edges, lines and "T" junctions. As distilled forms, these shapes preferentially activate the visual cortex.

It's easy to see how this may have come about. Lines, angles and intersections are the most abundant features embedded in the natural environment – they provide crucial first cues to the layout of objects. Our brain's ability to process them is shared by other primates, but the human brain is also able to respond to these cues proactively using "Gestalt principles" – rules that enable the mind to automatically perceive patterns in a stimulus. This helps it construct basic forms that are fed forward to the higher-order visual areas of the brain, which can process them in a way so we can experience them as real objects.

Symmetrical Acheulean tools. **Author provided**

At some point from around 700,000 years ago, this sensitivity to geometry and pattern perception enabled humans to start making refined "Acheulean tools", which exhibit a certain symmetry. This is unlikely to have been possible without an implicit knowledge of geometry.

The tool making then further promoted an enhanced sensitivity and bias towards patterns in the natural environment, which our ancestors projected onto materials other than the actual tools. For example, they started accidentally making marks on rocks, shells and materials such as ochre.



Engraving to writing

At some point, these unintentional patterns were intentionally copied on such materials – developing into engraved designs and later on into writing.

Ochre block from Klasies River in South Africa (c.100,000) where accidental striations may have been exploited to make cross shapes. **d'Errico et al. 2012. Journal of Archaeological Science. (Permission of Elsevier)**

But how was this possible? Neuroscientific research has shown that writing text involves the premotor cortex of the brain, which drives manual skills. My theory therefore suggests that reading and writing evolved when our passive perception for discerning things started to interact with manual dexterity.

Engraving from the Blombos cave in South Africa, about 77,000 years old. **https://originalrockart.wordpress.com/, CC BY-SA**

Writing and abstract patterns also activate so-called "mirror neurons" in the brain. These brain cells are remarkable because they fire both when we act and when we observe others acting – helping us identify with and understand others as if we ourselves were acting. But they also fire when we view patterns and see written text. This can therefore produce a sense of identification with a pattern – whether accidental or natural – in a way that inspires us to replicate it. And these marks were the first steps to writing and reading.

These developments therefore enabled the brain to reuse the visual cortex for an entirely new purpose. Ultimately, it could have created a new process in the brain that exploited the visual cortex, giving rise to a visual word form area and connecting with speech areas incrementally over time.

That said, some researchers believe that early marks were symbolic rather than aesthetic and that writing evolved from encoding information in them. However I argue this now seems increasingly unlikely. Early marks look similar to each other over an immense period of time. If the marks were symbolic, we would expect to see far more variation across space and time, just as we do in modern writing systems. But this is not the case.

All this points to the probability that the earliest marks were aesthetic in that they derive from the early visual cortex's preference for basic configurations. And it could have begun as early as *Homo erectus*, which lived from about 1.8m to 500,000 years ago.

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Brain Surface Area Reveals Overlap in Genes, Intelligence, Evolution

An analysis of the contours of more than 600 kids' brains points to links between cerebral surface area and heritability in regions of the brain important in cognition.

Carolyn Wilke

Over the course of human evolution, our brains expanded massively. One of the areas that ballooned over the past few million years is the cerebral cortex, the wrinkly outer layer of the brain. It processes sensory information, coordinates our motion, and is in charge of our

higher order functions, such as language processing and problem solving.

Scientists are scrutinizing the structure of the cortex for clues about its development throughout our lives and our evolution as a species and to understand where heredity intersects with intelligence.

A new study of hundreds of developing brains reveals a trifecta of overlap in regions of the cortical surface that develop from childhood to adulthood, expanded during evolution, and are connected to genetics. The scientists also found genetically mediated links between IQ test scores and surface area in regions related to intelligence, they report today (March 4) in the *Journal of Neuroscience*.

"I think it's a very, very strong work," says Rachel Brouwer, a neuroscientist at University Medical Center Utrecht in the Netherlands who was not part of the study. The authors pick up which regions of the brain where variability is most explained by genes, but by looking for connections with evolutionary expansion and neurodevelopment, "it is an attempt to link [heritability] to what it actually means in a broader picture," she says.

The study's authors analyzed brain scans captured by MRI from 677 children. The scans let them map the kids' brains, revealing the layout of their cortical puckers, grooves, and coils. By linking the brains' features to genetic variations in their sample, the researchers could probe how genes construct the brain during development and through evolution.

Using image processing tools, the researchers measured the thickness of the cortex and also its surface area. "It's a measure of if you basically took the cortex and you unfolded it . . . and like, rolled it out like a pizza," says J. Eric Schmitt, a neurogeneticist at the University of Pennsylvania School of Medicine, and one of the authors of the study.

The study's results pointed to the importance of the brain's surface area in development, which until recently hadn't received as much attention as total volume or cortical thickness, says Brouwer.

The researchers also dug into the heritability of these traits by comparing brains in a sample that included a large number of identical and fraternal twins, siblings, and family members. Using correlations to capture the shared fraction of genes based on the family relationship, they could tease out links between genetics and certain features of the brain.

Surface area and brain structure vary widely in humans and the researchers found that the brain's total surface area is highly heritable. Genetic factors accounted for 85 percent of the variation, similar to the results of earlier studies. "That's a huge fraction of the variability. . . . Genes are really, definitely dominant in patterning global surface area," says Schmitt.

The scientists also observed that cortical thickness and the brain's surface area were genetically linked in these kids, contrary to earlier findings in adults that were "interpreted to mean that different genetic factors underlie the development of surface area versus cortical thickness," says John Gilmore, a psychiatrist at University of North Carolina, Chapel Hill, who was not involved with this work. Previously, Gilmore, Schmitt, and colleagues showed a genetic coupling of cortical thickness and surface area in newborns in a study that inspired this project.

"If we can find out what are the actual genes that cause this coupling . . . and why it starts to grow apart when people get older, that would really help in our

The authors also zoomed in on regional differences in the brain. After chopping up the virtual brain surface into roughly 80,000 tiny triangles, they could compare surface areas in different regions of the brain across the study's subjects.

Merging these data with genetic information let the researchers see to what extent variations were connected to heredity at each point. When the scientists accounted for variations in total surface area, their analysis revealed where in the brain surface area was most related to an overall, or global, genetic factor.

These regions that were most influenced by heredity—large swaths of the frontal and temporal cortex, which are important in language processing and intelligence—overlapped strongly with parts of the brain that expanded during human evolution. These are the areas that are the most different from nonhuman primates, as discovered by other studies. "That led us to hypothesize that perhaps there's a shared genetic factor that's influencing all these regions that are evolutionarily novel," says Schmitt.

These regions are also the ones that change the most rapidly during childhood, which "suggests that maybe some of the genes that cause individual differences within human beings may be the ones that also evolved over time," says Schmitt. "I find that very interesting. I want to know what genes those are." This study doesn't pinpoint the actual genes that control the variations in brain surface area. To find those genes would require an even larger sample size, he says.

By analyzing their genetically descriptive brain maps alongside results from IQ tests they administered to the kids, the researchers could tease out which areas of the cortex tied to a higher performance on the test may be linked to heredity.

Their results highlighted a few areas, but one region of the brain really stood out as linking these threads—the supramarginal gyrus on the left side of the brain. "That's the receptive language center of the brain in almost everybody," explains Schmitt. The correlations are almost one, basically as high as they can get, which means there's almost perfect genetic overlap between IQ and surface area in that spot, he says.

It's not the first study looking for correlations with intelligence, and Schmitt says that while IQ is a useful and fairly reproducible metric, it's not a direct measure of intelligence. Even still, "seeing such a strong effect is pretty rare. . . . It's is a little bit of the holy grail of neuroscience," he says.

The results are interesting in part because there hasn't been much work on how surface area relates to intelligence, says Brouwer. Here, "most of the effects seem to be pretty global, so that means there is some global genetic factor that is good for your brain and your intelligence, for example," she says.

Although generally positive about the study's methods and findings, David Glahn, a psychologist at Boston Children's Hospital and Harvard University, is skeptical of how important the results regarding intelligence really are. "Yes, this looks like an important effect . . . [but] if you have a larger or smaller surface area, what does that really mean with reference to IQ? Are we talking two-to-three point difference? Or are we talking ten point difference?" he says. It makes sense that the authors see a relationship between the brains' anatomy and intelligence, but while many papers have also reported such relationships, others haven't, and the effects observed in adults aren't very strong, he says.

Schmitt acknowledges that the underpinnings of intelligence is a sensitive subject in neuroscience but feels comfortable surveying it through population-level studies. It's also a question he finds fascinating.

"What drives cognitive skills in humans is, I think, one of the fundamental questions that we have in neuroscience and it's actually one of the things that got me interested in neuroscience in the first place. Why do we have this thing that sucks up a huge amount of our energy? It's got to be doing something for us," says Schmitt.

J.E. Schmitt et al., "A comprehensive quantitative genetic analysis of cerebral surface area in youth," J Neurosci, doi:10.1523/JNEUROSCI.2248-18.2019, 2019.

https://wb.md/2HpMPpx

EU Panel Backs Dupilumab (*Dupixent*) for Severe Asthma

EMA's CHMP *has recommended as add-on maintenance therapy for patients aged 12 years and older*

Megan Brooks

The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has recommended dupilumab (*Dupixent*, Sanofi-Aventis) as add-on maintenance therapy for patients aged 12 years and older with severe asthma with type 2 inflammation characterized by increased blood eosinophil levels and/or increased fractional exhaled nitric oxide (FeNO) levels whose condition is poorly controlled with high-dose inhaled corticosteroids plus another medicine.

Dupilumab is an interleukin-4 (IL-4) and interleukin-13 (IL-13) inhibitor; both IL-4 and IL-13 are proteins that stimulate the type 2 inflammation that forms the basis of severe asthma. Dupilumab reduces inflammatory biomarkers, including FeNO, immunoglobulin E, and eotaxin-3.

"Therapeutic options are limited" for patients with poorly controlled, severe asthma despite adequate therapy, the EMA noted in a press statement. In three clinical trials conducted in 2888 patients, dupilumab was shown to reduce severe asthma exacerbations and improve lung function, the agency said.

The most common side effects of dupilumab are infections, eye disorders (conjunctivitis and related conditions), and injection site reactions.

Dupilumab is already approved in Europe for adults with moderate to severe atopic dermatitis who are candidates for systemic therapy.

The US Food and Drug Administration approved dupilumab for severe atopic dermatitis in 2017 and as add-on therapy for moderate to severe asthma in 2018.

Detailed recommendations for the use of dupilumab for asthma patients will be described in the updated summary of product characteristics, which will be published in the revised European public assessment report, and will be made available after a decision on this change to the marketing authorization has been granted by the European Commission.

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What makes people willing to sacrifice their own self-interest for another person?

Study's findings may have troubling implications for ethical behavior

- ***We're more likely to share resources with others when we feel like our lives and work are interdependent, researcher says***
- ***Collaboration effect operates by creating sense of indebtedness to the collaborator***

EVANSTON, Ill. --- In a new Northwestern University study, researchers show that people are more willing to sacrifice for a collaborator than for someone working just as hard but working independently.

"This suggests we're more likely to share our resources with others when we feel like our lives and work are interdependent with the lives and work of those other people," said lead author Mary McGrath, assistant professor of political science in the Weinberg College of Arts and Sciences at Northwestern and faculty fellow with the University's Institute for Policy Research. The effect appears to exist regardless of how much effort the partner puts in.

McGrath and co-author Alan Gerber of Yale University find evidence that this collaboration effect operates by creating a sense of indebtedness to the collaborator.

"When thinking about what might be driving the effect, my hunch was that this was driven by a sense of obligation to your collaborator, rather than just some general sense of goodwill -- that people felt like they owed the collaborator something," McGrath said. "I was

surprised by how starkly that was supported when looking into it: Indebtedness really stood out from all the rest of the possibilities. Interestingly, collaboration even had a borderline negative effect on saying you were motivated by a desire to do something nice for your partner -- in other words, there's a slight indication that collaboration made you less likely to be motivated by a sense of goodwill toward the other person."

Though an impulse to repay a collaborator may be pro-social in many scenarios, McGrath noted that giving preferential treatment to those who have contributed to your cause could have problematic implications for ethical behavior.

"A politician given a generous campaign contribution could feel an innate 'moral' compulsion to satisfy a debt owed to the donor, or a doctor receiving a research grant from a pharmaceutical company may feel a similar impulse to 'give something back,'" McGrath said.

McGrath said that there's been pioneering work in developmental and comparative psychology suggesting that collaboration in our evolutionary past may have played an important role in shaping an innately human sense of distributive justice -- that is, what we consider to be a "fair" distribution of resources.

"Certainly, an impulse to repay a collaborator is a good thing in many scenarios -- but giving preferential treatment contingent upon a contribution to your cause has some troubling implications in terms of ethical behavior," McGrath said. "Taken together with the work suggesting that collaboration in our evolutionary past may be responsible for our developing a distinctly human sense of justice and fairness, we arrive at this surprising implication: the development of human morality and our vulnerability to corruption potentially springing from the same source."

"Experimental evidence for a pure collaboration effect" published recently in *Nature Human Behaviour*.

http://bit.ly/2UvAqUv

Modern beer yeast emerged from mix of European grape wine, Asian rice wine yeast

New study shows that modern brewing strains were derived from a mixture of European grape wine and Asian rice wine strains

For thousands of years brewers made beer using specialized strains of the budding yeast Saccharomyces cerevisiae. The historical origins of brewer's yeast are not well understood, however, as brewing predates the discovery of microbes. A new study publishing March 5 in the open-access journal *PLOS Biology*, led by Justin Fay at the University of Rochester, shows that modern brewing strains were derived from a mixture of European grape wine and Asian rice wine strains. This finding points to the emergence of beer yeast from a historical East-West transfer of fermentation technology, similar to the transfer of domesticated plants and animals by way of the Silk Route.

The historical origins of any domesticated organism are often clouded by recent migration, gene flow and mixing with other groups. While analysis of ancient DNA has been a boon to reconstructing many historical events, ancient fermented beverages and the microbes used to produce them are not available. However, many beer strains are known to be polyploid--having more than two copies of their genome--which allows them to remain isolated from other populations and provides researchers with a living relic of their ancestors.

To reconstruct the history of beer strains, the researchers sequenced and compared the genomes of beer strains to a panel of reference strains from around the world. The beer strains formed four related groups: two ale, one lager and one group containing both beer and baking strains. All of these groups show mixed ancestry from both European grape wine strains and Asian rice wine strains. The strains also contain novel gene variants not present in any other population.

The origin of these novel variants is less clear, but their abundance suggests they were derived from an uncharacterized or extinct population. A complete reconstruction of the order and timing of events during the evolution of beer strains is difficult since their polyploid genome is not static. Changes in their polyploid genome have occurred during cell divisions, generating beer strain diversity and likely playing an important role in specialization to various brewing styles.

Peer-reviewed / Experimental Study / Cells In your coverage please use this URL to provide access to the freely available article in PLOS Biology:
http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000147
Citation: Fay JC, Liu P, Ong GT, Dunham MJ, Cromie GA, Jeffery EW, et al. (2019) A polyploid admixed origin of beer yeasts derived from European and Asian wine populations. PLoS Biol 17(3): e3000147. https://doi.org/10.1371/journal.pbio.3000147
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Could genetic breakthrough finally help take the sting out of mouth ulcers?

Scientists identify genes associated with mouth ulcers

A large breakthrough has been made in the genetic understanding of mouth ulcers which could provide potential for a new drug to prevent or heal the painful lesions.

Mouth ulcers affect up to 25 per cent of young adults and a higher proportion of children. Previous research has shown that mouth ulcers are partially heritable, but until now there has been little evidence linking specific genes or genomic regions to mouth ulcers.

The study, carried out by an international team of scientists and led by researchers at the University of Bristol, attempted to pinpoint areas of the genome associated with triggering mouth ulcers by looking systematically across the DNA code.

By looking at mouth ulcers in different populations in the UK, USA and Australia the researchers aimed to find genes which were consistently linked to mouth ulcers. The research is published today [Tuesday 5 March] in *Nature Communications*.

The team identified genetic variants associated with the condition by analysing genetic data derived from over 450,000 participants in the UK Biobank and replicated these findings in over 350,000 participants in USA-based data collection 23andMe.

They discovered 97 common genetic variations across the genome that predispose people to mouth ulcers. The study went on to look at three further studies, including Bristol's Children of the 90s (ALSPAC) study, which showed confirmatory results. These variations are enriched in genes that have previously been linked to regulation of the body's immune system.

Tom Dudding, Wellcome Trust Clinical Research Fellow in the Bristol Medical School: Population Health Sciences (PHS) and Bristol Dental School and joint-first author of the paper, said: "Currently, there are few satisfactory drug treatments for mouth ulcers as current medication options are non specific and can lead to side effects. The field has gone from very little genetic understanding of mouth ulcers to having up to 97 areas of the genome which may provide an excellent basis for future research.

"Importantly, our findings also show that several of the genes related to mouth ulcers are in pathways which are already targeted by drugs that are used to treat other diseases such as rheumatoid arthritis and psoriasis.

There is the potential that drugs like these could be used to treat mouth ulcers, although further work is required to demonstrate this."

Paper: *'Genome wide analysis for mouth ulcers identifies associations at immune regulatory loci' by T. Dudding, S. Haworth et al in* Nature Communications

https://nyti.ms/2Cd61DB

Eli Lilly Will Sell Half-Price Version of Humalog, Its Popular Insulin

The drugmaker Eli Lilly will begin selling a cheaper version of its most popular insulin, Humalog, in an effort to head off criticism about the rising costs of prescription drugs, the company said Monday.

By Katie Thomas

Lilly will begin selling an "authorized generic" of Humalog 100 for $137.35 per vial, a 50 percent discount off the list price. An authorized generic means that, except for the label, it is identical to the brand-name drug and manufactured in the same facilities. The new product, which the company said would be made available as quickly as possible, will be called Insulin Lispro and will be sold through a Lilly subsidiary, ImClone Systems.

Except for the label, an "authorized generic" version of Humalog will be identical to the brand-name insulin drug and manufactured at the same facilities. **Mauritius Images GmbH/Alamy**

"There are clearly patients who, despite many best efforts, are struggling to afford their insulin," David Ricks, the chief executive of Lilly, said in an interview Friday. "This is a step we can take to close part of that remaining gap."

The move offers a compromise to critics who have called on drugmakers to lower their list prices. Lilly will continue selling Humalog at its regular price to the insurers and employers who want to keep pocketing the large discounts, or rebates, they receive for purchasing brand-name drugs, while also making available a cheaper version to patients who pay for their insulin out of pocket.

As a result, people without health insurance should benefit most from the generic insulin, while those with drug coverage will either experience no change or see some decrease in their costs.

"This announcement is a great step forward to make insulin more affordable," said Derek Rapp, the chief executive of JDRF, a diabetes advocacy group that receives funding from Eli Lilly. He called on "all other insulin manufacturers to follow Eli Lilly in finding ways to bring down the price of this lifesaving drug."

But others, such as Elizabeth Rowley, the founder and director of T1International, a diabetes advocacy group that does not accept drug-industry funding, said Lilly and other companies could do more while still making a profit on their insulin products. "While half-price is certainly an improvement, it's still an unaffordable price for so many," she said.

Pharmaceutical companies have been under pressure to show they are doing something about the rising list price of their products, which consumers have increasingly been exposed to as insurers scale back on coverage. Multiple congressional inquiries have focused on insulin, and last week executives for seven major drugmakers testified on drug prices in a hearing before the Senate Finance Committee. President Trump has also made the issue a priority.

Critics have singled out insulin manufacturers because versions of the lifesaving diabetes treatment have been around since the 1920s, yet the three companies that control the market — Lilly, Novo Nordisk and Sanofi — have consistently raised list prices over the past decade. Outrage over the cost of insulin has driven much of the political conversation about high drug prices, with reports of patients dying because they could not afford it.

In February, the Senate Finance Committee sent Lilly a letter asking for more information about how it sets prices for its insulin products, including Humalog. The letter noted that taxpayers spend more than $1 billion a year for Humalog through Medicare and Medicaid and

said, “When one insulin product costs the taxpayer more than $1 billion in one year, the American people ought to know how the company prices its product.”

Sen. Ron Wyden, the ranking Democrat on the Senate Finance Committee, said in a statement Monday that the investigation into Lilly’s insulin prices would continue. “The company’s decision to offer a generic version of a several decade old drug will be part of the investigation,” he said.

The story of insulin, many say, is a salient example of how the drug pricing system is broken. Over the years, industry intermediaries known as pharmacy benefit managers have negotiated ever-deeper discounts for insulin, yielding savings for the insurers and employers that pay the bulk of drug costs. Insulin manufacturers have responded by raising their list prices in an effort, they say, to please the benefit managers, who keep a percentage of the discounts they pass along.

The list price of insulin has gone from about $20 per vial in 1996, when Humalog entered the market, to about $275 per vial today. Humalog patients typically use about two vials a month, Lilly said.

The result is a yawning gap between the list price of insulin — which people who are uninsured must pay — and the net price that insurers and employers pay.

Enrique A. Conterno, the president of Lilly’s diabetes division, said Friday that the list price of the authorized generic will be comparable to the net price the company regularly offered to insurers in exchange for standard placement on their formulary, or the list of covered drugs, although he did not specify a dollar amount. But he said the company provided deeper discounts to insurers that give Humalog preferred treatment, which typically means lower out-of-pocket costs for patients.

Mr. Ricks, Lilly’s chief executive, said the net price of Humalog — the amount the company keeps — has dropped by 8 percent over the past five years.

By releasing an authorized generic of Humalog, Lilly will permit its existing contracts with insurers to continue, while offering a more affordable alternative to people who pay out of pocket. The company said about 95 percent of Humalog patients pay less than $100 per month. Other drug companies have made similar moves while facing heat for their prices. In 2016, Mylan began selling an authorized generic of the EpiPen in response to outrage over the price of the allergy treatment. Last fall, Gilead announced it would do the same for two of its pricey hepatitis C drugs.

Offering an authorized generic for an expensive drug is “a really great solution for patients who don’t have health insurance, or who are paying a deductible or coinsurance,” or a percentage of a drug’s list price, said Stacie B. Dusetzina, who studies drug pricing at the Vanderbilt University Medical Center.

Lilly has offered a discount program since 2016 that allows consumers to buy Humalog at a significant discount, but Medicare beneficiaries and other people insured by government health care plans were not allowed to use it. The authorized generic will not carry those restrictions, and pharmacists will be able to automatically substitute it for Humalog without asking a doctor to write a new prescription.

Humalog 100 is the most common variety of Lilly’s short-acting insulin. The company said about 80 percent of patients taking Humalog use the vial or the KwikPen, which will both become available as authorized generics. (The list price of a five-pack of the generic equivalent of KwikPens will be $265.20.)

Humalog brought in nearly $3 billion in revenue in 2018 and is the company’s second-best-selling product, behind the diabetes drug Trulicity. Mr. Conterno said the company was considering releasing authorized generics for other insulin products. However, “we also want to see how this works,” he said. “I’ll be honest, we are entering unusual territory.”

http://bit.ly/2SZl4WM

Your Dumb Party Balloons Are Killing All the Seabirds

Forget about plastic straws: The deadliest ocean garbage for seabirds is balloons.

By Mindy Weisberger, Senior Writer

In a recent survey of over 1,700 dead seabirds, more than a quarter of the deaths were linked to eating plastic. Four in 10 of those deaths were caused by soft debris such as balloons (which are often made of plastic), even though it made up only 5 percent of the inedible trash in the birds' stomachs.

Swallowing plastic can be lethal for seabirds, and balloons are especially deadly. **Lauren Roman**

Seabirds frequently snap up floating litter because it looks like food; once swallowed, it can obstruct birds' guts and cause them to starve to death. If a seabird swallows a balloon, it's 32 times more likely to die than if it had gulped down a piece of hard plastic, researchers reported in a new study.

"Among the birds we studied, the leading cause of death was blockage of the gastrointestinal tract, followed by infections or other complications caused by gastrointestinal obstructions," lead study author Lauren Roman, a doctoral candidate with the Institute for Marine and Antarctic Studies at the University of Tasmania in Australia, said in a statement.

With an estimated 280,000 tons (250,000 tonnes) of floating marine debris worldwide, about half of all seabird species are thought to ingest plastic on a daily basis, the study authors reported. Birds are especially likely to swallow dangerous balloons because they closely resemble squid, according to the study.

The findings were published online March 1 in the journal Scientific Reports.

https://wb.md/2Hbvb9N

FDA Approves Esketamine Nasal Spray for Resistant Depression

The US Food and Drug Administration (FDA) has approved esketamine nasal spray* (Spravato, *Janssen Pharmaceuticals*) *for treatment-resistant depression.

Caroline Cassels

"There has been a long-standing need for additional effective treatments for treatment-resistant depression, a serious and life-threatening condition," Tiffany Farchione, MD, acting director of the Division of Psychiatry Products in the FDA's Center for Drug Evaluation and Research, said in an FDA release announcing the drug's approval.

"Controlled clinical trials that studied the safety and efficacy of this drug, along with careful review through the FDA's drug approval process including a robust discussion with our external advisory committees, were important to our decision to approve this treatment. Because of safety concerns, the drug will only be available through a restricted distribution system and it must be administered in a certified medical office where the health care provider can monitor the patient," Farchione added.

The potential risk for serious adverse outcomes associated with the drug, including sedation and dissociation and the potential for abuse and misuse, means it is only available through a restricted distribution system, under a Risk Evaluation and Mitigation Strategy. The patient self-administers the esketamine nasal spray under the supervision of a healthcare provider in a certified doctor's office or clinic. Patients are not permitted to take the drug home.

In addition, patients must be monitored by a healthcare provider for at least 2 hours after the drug is administered. During and after each use of the nasal spray device, the healthcare provider is required to check the patient and determine when the patient is ready to leave.

Prescribers and patients are also required to sign a Patient Enrollment Form that states that the patient understands they should make arrangements to safely leave the healthcare setting to get home. In addition, patients are cautioned that they should not drive or use heavy machinery on the day they receive the drug.

The FDA's decision comes on the heels of last month's 14-to-2 vote (1 abstention) from two FDA advisory panels — the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee — recommending the drug's approval.

As reported by *Medscape Medical News* at the time, several panel members noted that the drug may be a game changer for patients suffering from severe depression. The FDA's approval of the drug is based on safety and efficacy data from five phase 3 studies.

Results from both a short-term phase 3 study and a long-term phase 3 study showed that esketamine nasal spray in combination with a newly initiated oral antidepressant "provided statistically significant, clinically meaningful, rapid and sustained improvement of depressive symptoms in this difficult-to-treat population," the company said in a February 12 news release.

The most common side effects associated with the nasal spray include dissociation, dizziness, nausea, sedation, vertigo, decreased feeling or sensitivity, anxiety, lethargy, increased blood pressure, vomiting, and feeling drunk.

https://go.nature.com/2Hr57GJ

The marine worms that can sprout new heads — including brains

Lop off the heads of these ribbon worms, then watch.

Many species of marine ribbon worm have gained the power to regrow their heads — an unprecedented example of related animals independently mastering the trick of regeneration.

Eduardo Zattara at the Smithsonian Institution's National Museum of Natural History in Washington DC and his colleagues cut off the heads of individuals from 22 species of ribbon worm and observed that 5 species sprouted new heads.

The researchers also found published accounts of 3 other species with this ability.

A ribbon worm (Lineus sanguineus) is shown 4 days after its head was cut off (top left). By 15 days after decapitation (bottom right), its head has regrown. **Eduardo E. Zattara**

The team's analysis of the ribbon-worm family tree suggests that head replacement arose at least four times in separate worm lineages. The lineage of the species *Lineus sanguineus* evolved the ability to replace a missing head only 10 million to 15 million years ago, which is much more recently than other animals are known to have acquired the art of regeneration.

This means that *L. sanguineus* could provide a valuable model for understanding how regeneration evolves, the authors say.

Proc. R. Soc. B (2019)

http://bit.ly/2Uqx0T7

Dinosaurs were thriving before asteroid strike that wiped them out

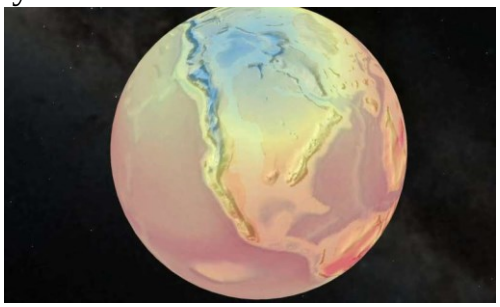
Dinosaurs were unaffected by long-term climate changes and flourished before their sudden demise by asteroid strike.

By Hayley Dunning, Imperial College London

Scientists largely agree that an asteroid impact, possibly coupled with intense volcanic activity, wiped out the dinosaurs at the end of the Cretaceous period 66 million years ago.

However, there is debate about whether dinosaurs were flourishing before this, or whether they had been in decline due to long-term changes in climate over millions of years.

Previously, researchers used the fossil record and some mathematical predictions to suggest dinosaurs may have already been in decline, with the number and diversity of species falling before the asteroid impact.



A global map showing the distribution of surface temperature over the Earth in the Late Cretaceous, .76 million years ago. Warmer colours represent higher temperatures, while colder colours indicate lower ones. **Alfio Alessandro Chiarenza/ BRIDGE University of Bristol/ GETECH**

Now, in a new analysis that models the changing environment and dinosaur species distribution in North America, researchers from Imperial College London, University College London and University of Bristol have shown that dinosaurs were likely not in decline before the meteorite.

Lead researcher Alessandro Chiarenza, a Ph.D. student in the Department of Earth Science and Engineering at Imperial, said: "Dinosaurs were likely not doomed to extinction until the end of the Cretaceous, when the asteroid hit, declaring the end of their reign and leaving the planet to animals like mammals, lizards and a minor group of surviving dinosaurs: birds.

"The results of our study suggest that dinosaurs as a whole were adaptable animals, capable of coping with the environmental changes and climatic fluctuations that happened during the last few million years of the Late Cretaceous. Climate change over prolonged time scales did not cause a long-term decline of dinosaurs through the last stages of this period."

The study, published today in *Nature Communications*, shows how the changing conditions for fossilisation means previous analyses have underestimated the number of species at the end of the Cretaceous.

The team focused their study on North America, where many Late Cretaceous dinosaurs are preserved, such as Tyrannosaurus rex and Triceratops. During this period, the continent was split in two by a large inland sea.

In the western half there was a steady supply of sediment from the newly forming Rocky Mountains, which created perfect conditions for fossilising dinosaurs once they died. The eastern half of the continent was instead characterised by conditions far less suitable for fossilisation.

This means that far more dinosaur fossils are found in the western half, and it is this fossil record that is often used to suggest dinosaurs were in decline for the few million years before the asteroid strike.

Co-author Dr. Philip Mannion, from University College London, commented: "Most of what we know about Late Cretaceous North American dinosaurs comes from an area smaller than one-third of the present-day continent, and yet we know that dinosaurs roamed all across North America, from Alaska to New Jersey and down to Mexico."

Instead of using this known record exclusively, the team employed 'ecological niche modelling'. This approach models which environmental conditions, such as temperature and rainfall, each species needs to survive.

The team then mapped where these conditions would occur both across the continent and over time. This allowed them to create a picture of where groups of dinosaur species could survive as conditions changed, rather than just where their fossils had been found.

The team found habitats that could support a range of dinosaur groups were actually more widespread at the end of the Cretaceous, but that these were in areas less likely to preserve fossils.

Furthermore, these potentially dinosaur-rich areas were smaller wherever they occurred, again reducing the likelihood of finding a fossil from each of these areas.

'Ecological niche modelling does not support climatically-driven dinosaur diversity decline before the Cretaceous/Paleogene mass extinction' by Alfio Alessandro Chiarenza, Philip D. Mannion, Daniel J. Lunt, Alex Farnsworth, Lewis A. Jones, Sarah-Jane Kelland & Peter A. Allison is published in Nature Communications.

More information: *Nature Communications (2019). DOI: 10.1038/s41467-019-08997-2*

http://bit.ly/2EWE1Ey

Low-carb diet tied to common heart rhythm disorder

Study suggests using caution when restricting carbohydrates for weight loss

WASHINGTON -- Low-carb diets are all the rage, but can cutting carbohydrates spell trouble for your heart? People getting a low proportion of their daily calories from carbohydrates such as grains, fruits and starchy vegetables are significantly more likely to develop atrial fibrillation (AFib), the most common heart rhythm disorder, according to a study being presented at the American College of Cardiology's 68th Annual Scientific Session.

The study, which analyzed the health records of nearly 14,000 people spanning more than two decades, is the first and largest to assess the relationship between carbohydrate intake and AFib. With AFib, a type of arrhythmia, the heart doesn't always beat or keep pace the way it should, which can lead to palpitations, dizziness and fatigue. People with AFib are five times more likely to have a stroke than people without the condition. It can also lead to heart failure.

Restricting carbohydrates has become a popular weight loss strategy in recent years. While there are many different low-carbohydrate diets including the ketogenic, paleo and Atkins diets, most emphasize proteins while limiting intake of sugars, grains, legumes, fruits and starchy vegetables.

"The long-term effect of carbohydrate restriction is still controversial, especially with regard to its influence on cardiovascular disease," said Xiaodong Zhuang, MD, PhD, a cardiologist at the hospital affiliated with Sun Yat-Sen University in Guangzhou, China, and the study's lead author. "Considering the potential influence on arrhythmia, our study suggests this popular weight control method should be recommended cautiously."

The findings complement previous studies, several of which have associated both low-carbohydrate and high-carbohydrate diets with an increased risk of death. However, while previous studies suggested the nature of the non-carbohydrate component of the diet influenced the overall pattern observed, the new study did not.

"Low carbohydrate diets were associated with increased risk of incident AFib regardless of the type of protein or fat used to replace the carbohydrate," Zhuang said.

Researchers drew data from Atherosclerosis Risk in Communities (ARIC), a study overseen by the National Institutes of Health that ran from 1985-2016. Of the nearly 14,000 people who did not have AFib when they enrolled in the study, researchers identified nearly 1,900 participants who were subsequently diagnosed with AFib during an average of 22 years of follow-up.

Study participants were asked to report their daily intake of 66 different food items in a questionnaire. The researchers used this information along with the Harvard Nutrient Database to estimate each participant's daily carbohydrate intake and the proportion of daily calories that came from carbohydrates. On average, carbohydrates comprised about half of calories consumed. The Dietary Guidelines for Americans recommend that carbohydrates make up 45 to 65 percent of total daily calorie intake.

Researchers then divided participants into three groups representing low, moderate and high carbohydrate intake, reflecting diets in which carbohydrates comprised less than 44.8 percent of daily calories, 44.8 to 52.4 percent of calories, and more than 52.4 percent of calories, respectively.

Participants reporting low carbohydrate intake were the most likely to develop AFib. These participants were 18 percent more likely to develop AFib than those with moderate carbohydrate intake and 16 percent more likely to develop AFib than those with high carbohydrate intake.

Several potential mechanisms could explain why restricting carbohydrates might lead to AFib, Zhuang said. One is that people eating a low-carbohydrate diet tend to eat fewer vegetables, fruits and grains--foods that are known to reduce inflammation. Without these foods people may experience more inflammation, which has been linked with AFib. Another possible explanation is that eating more protein and fat in lieu of carbohydrate-rich foods may lead to oxidative stress, which has also been associated with AFib. Finally, the effect could be related to an increased risk of other forms of cardiovascular disease.

Zhuang said that while the research shows an association, it cannot prove cause and effect. A randomized controlled trial would be needed to confirm the relationship between carbohydrate intake and AFib and assess the effect in a more ethnically diverse population. In addition, the study did not track participants with asymptomatic AFib or those who had AFib but were never admitted to a hospital, nor did it investigate different subtypes of AFib, so it is unknown whether patients were more likely to have occasional episodes of arrhythmia or persistent AFib. The study did not account for any changes in diet that participants may have experienced after completing the questionnaire.

The ARIC study is supported by the National Heart, Lung, and Blood Institute. Collaborating researchers also received support from the National Natural Science Foundation of China and Natural Science Foundation of Guangdong Province.

Zhuang will present the study, "U-shaped Relationship Between Carbohydrate Intake Proportion and Incident Atrial Fibrillation," on Saturday, March 16, at 10:00 a.m. CT in Poster Hall, Hall F.

http://bit.ly/2HnqzN0

Growing evidence: water as a potential treatment for inherited cause of kidney failure

People with polycystic kidney disease (PKD) could benefit from a moderate increase in water intake, according to new research.

A study from The Westmead Institute for Medical Research found that a moderate increase in water intake in rats with PKD led to a long-term reduction in kidney cyst growth and fibrosis.

This latest findings add to the growing body of evidence that supports water as a safe and effective treatment for PKD.

Polycystic kidney disease is the most common inherited cause of end-stage kidney disease. It is a chronic condition, in which fluid-filled cysts damage healthy tissue and kidney function.

Left untreated, it can cause complications, including high blood pressure, heart problems and, in severe cases, kidney failure.

More than 2,000 Australians with PKD currently receive dialysis or need a kidney transplant.

Lead researcher Dr Priyanka Sagar said that water may be a potential treatment for PKD, because it stops the hormone responsible for cyst growth. "Previous studies in animals haven't shown whether this benefit continues over time, and there is presently no evidence in humans," Dr Sagar said.

"Our research in rats showed that increased water intake reduces the long-term progression of cyst growth and kidney fibrosis when administered during the early stages of kidney disease.

"Significantly, we identified that only a moderate increase in water was needed to have this sustained benefit in rats."

The research also showed that increased water intake had secondary benefits for some complications associated with PKD.

"Interestingly, we found that increased water intake also reduced hypertension," Dr Sagar said. "PKD is linked to an increased risk of cardiovascular disease, so this is an important protective effect."

Currently, treatment options for PKD in humans are limited. Dr Sagar said that further studies are needed in humans to prove that water is an effective treatment for kidney cysts. "We're finding more evidence to support water as a viable treatment for PKD," she said. "However, further studies are needed to determine its effectiveness. "Water is cheap and accessible, so the idea that it could be used as a treatment for PKD in the future is very exciting," she concluded.

Drs. Annette Wong and Gopi Rangan (a kidney specialist) from Westmead Hospital and the Westmead Institute for Medical Research are currently leading a NHMRC-funded multi-centre clinical trial in Australia that will determine the effectiveness of increasing water intake in people with autosomal dominant polycystic kidney disease (ADPKD), and the final results of this study are expected in 2021.

The research paper was published in PLOS ONE:
https://journals.plos.org/plosone/article/authors?id=10.1371/journal.pone.0209186

http://bit.ly/2Ce2ghb

Baby T. Rex Was an Adorable Ball of Fluff

It may be hard to imagine towering Tyrannosaurus rex as tiny, but the toothy Cretaceous giant didn't spring from an egg fully grown.

By Mindy Weisberger, Senior Writer

Every T. rex was once a vulnerable, feather-covered youngster. **AMNH/R. Peterson, Copyright AMNH**

In fact, *T. rex* hatchlings were about the size of very skinny turkeys, with "arms" that were longer in proportion to their tiny bodies than in adults. And each baby *T. rex* was covered in a coat of downy feathers.

What's more, *T. rex*'s feathers likely grew along the animal's head and tail into adulthood, according to new reconstructions that represent the most accurate models of the dinosaur to date.

These and many more *T. rex* surprises abound in T. rex: The Ultimate Predator, a new exhibit opening March 11 at the American Museum of Natural History (AMNH) in New York City. While *T. rex* is one of the most iconic dinosaurs, the exhibition presents new discoveries that are transforming scientists' understanding of this colossal carnivore and its tyrannosaur cousins, all of which likely had feathers, too.

Most of the tyrannosaur species featured in the exhibit were unknown to science prior to 2000, Martin Schwabacher, an exhibition writer at the AMNH, told Live Science. Early tyrannosaurs first appeared about 167 million years ago, around 100 million years before *T. rex* ruled the Cretaceous. These early tyrannosaurs had relatively long arms, and were smaller and faster than the giant *T. rex*.

But even *T. rex* wasn't always enormous. The exhibit's minuscule and endearingly fluffy model of a *T. rex* hatchling underscores the dinosaur's dramatic growth, as it ballooned from a turkey-size juvenile to a gargantuan adult. By the time it was about 20 years old, a full-grown *T. rex* would stand about 12 to 13 feet (3.6 to 3.9 meters) tall at the hip, span 40 to 43 feet (12 to 13 m) from nose to tail and weigh approximately 6 to 9 tons (5,500 to 8,000 kilograms).

Most defenseless T. rex hatchlings never made it past age 1. **Copyright AMNH/D. Finnin**

During their rapid growth, juveniles would gain about 6 lbs. (3 kg) per day for 13 years, said paleontologist Mark Norell, curator of both the exhibit and the Division of Paleontology at the AMNH.

Though *T. rex* has long been known to have dramatically undersized "arms" for its body size, few of this species' front limbs have been recovered from the fossil record, Norell told Live Science. And based on the few fossil arms that paleontologists have recently discovered, the puny arms on the exhibit's adult *T. rex* model are even smaller than they've been portrayed in the past, Norell said.

However, that doesn't mean that *T. rex* arms were weak or useless. "They're not fragile; the bones are very robust, the joints are mobile and it looks like they were well-muscled," Schwabacher said. In *T. rex* hatchlings, the proportions of their arms were a much better match to their body size, which means that very young *T. rexes* may have been able to use their arms to grasp prey, as other small tyrannosaurs likely did.

A full-grown T. rex weighed about 6 to 9 tons (5,500 to 8,000 kilograms). And yes, it was probably feathered. **Illustration by Zhao Chuang, courtesy of PNSO**

Adult *T. rex* also may have used its arms and claws to slash at prey that it had already knocked down with its massive head and jaws, Schwabacher said. But with a bite force estimated at 7,800 pounds-force (34,500 newtons) — the strongest of any living animal and most extinct animals — *T. rex* probably didn't need to do much with its arms to subdue a meal.

"Its head was adapted to apply pressure until bones just exploded," Schwabacher said.

T. rex: The Ultimate Predator is on display at the AMNH from March 11, 2019, to Aug. 9, 2020.

Editor's note: This story was updated to reflect that T. rex's bite force was stronger than the bite force in most extinct animals (but not all).

http://bit.ly/2u0y4BC

Bone fractures increasing as seniors walk dogs to stay active

Fractures related to dog walks have more than doubled between 2004 and 2017 for older patients

PHILADELPHIA - While walking a dog provides older Americans with a valuable outlet for regular, physical activity, a Penn Medicine study has shown that fractures related to these walks have more than doubled between 2004 and 2017 in patients 65 and older. In this population, 78 percent of the fractures occurred in women, with hip and upper extremity breaks being the most common. This study was published today in JAMA Surgery.

The rise in injuries in this population is a result of two trends, the researchers say: increased pet ownership and a greater emphasis, in recent years, on physical activity at older ages.

"Dog walking, which has repeatedly demonstrated social, emotional and physical health benefits, is a popular and frequently recommended activity for many older Americans seeking new ways to stay active," said the study's lead author Kevin Pirruccio, a second-year medical student in the Perelman School of Medicine at the University of Pennsylvania.

"This study highlights that while there are undoubtedly pros to dog walking, patients' risks for falls must be factored into lifestyle recommendations in an effort to minimize such injuries."

The study team, which included senior author Jaimo Ahn, MD, PhD, an associate professor of Orthopaedic Surgery, and Yeo Myoung Yoon, a research assistant at Penn, reviewed all fractures in the 65-and-older population related to "pet products" in the National Electronic Injury Surveillance System database of the United States Consumer Product Safety Commission.

The entries the team found stretching across roughly 100 participating hospitals' emergency departments corresponded to 32,624 cases in the United States, overall.

Fracture injuries linked to walking leashed dogs were found to have increased significantly from 1,671 cases in 2004 to 4,396 in 2017--a 163 percent increase. Approximately half of the injuries were related to people's upper extremities; fractures of the wrist, upper arm, finger and shoulder were the most common in that category.

Specifically, seniors fractured their hip most often, accounting for 17 percent of the injuries in the database. This is particularly concerning as mortality rates related to hip fractures in the in patients over 65 are close to 30 percent.

Why hip injuries among older people can be so deadly has to do with the possibility of setting off a domino-effect of factors that relate to poorer health, such as a sudden lack of mobility and activity.

While the numbers are sobering, the researchers believe that their count of dog walking injuries may actually be low.

The study only examined reported fractures and those who went to an emergency room. Debilitating tendon or muscle damage and those who may refuse or seek out other avenues of care were not included in the study.

Ahn, Pirruccio, and Yoon aren't setting out to keep seniors from walking dogs or owning them. But they hope their study and others that build off of it provide grounds for deeper considerations about the risks everyone faces as they grow older.

"Everyday actions mean everyday consequences," Ahn said. "While it is important for medicine to sometimes focus on the rarer but devastating conditions such as cancer and heart attacks, we also have to remember that understanding and improving the little things in life can have a dramatic, positive effect."

http://bit.ly/2UwdCUS

Unvaccinated Oregon Boy Is Diagnosed with Tetanus, the State's 1st Child Case in 30 Years

While playing outside on a farm in Oregon, a 6-year-old boy fell down and cut his forehead.

By Yasemin Saplakoglu, Staff Writer

His parents cleaned and sutured his wound at home, and for a few days, everything seemed all right, according to a new report of his case. But six days after his fall, the boy began crying, clenching his jaw and having muscle spasms. His symptoms got worse, and when he started having trouble breathing, his parents called emergency services, who airlifted the boy to a hospital.

Tetanus is caused by the bacterium *Clostridium tetani*. Shutterstock

There, doctors diagnosed the boy with tetanus — making him the first documented case of the infection in Oregon in more than 30 years, according to the report, published today (March 7) by the Centers for Disease Control and Prevention (CDC).

Tetanus is an infection caused by the bacterium *Clostridium tetani*, but it is preventable thanks to the tetanus vaccine, the CDC says.

The boy in the case, however, had not received his tetanus vaccine, nor any of the other vaccines recommended for a child his age, according to the report.

A serious and expensive illness

When the boy arrived at the hospital, his jaw muscle was spasming, and though he wanted water, he couldn't open his mouth to drink. He was also experiencing a condition called opisthotonus, or an arching neck and back, which got progressively worse.

The boy was admitted to the intensive care unit (ICU), where he was given the tetanus vaccine as well as medication containing antibodies

to fight the bacteria. These antibodies had been taken from people who had been vaccinated against tetanus. The boy needed to be cared for in a darkened room with earplugs, because stimulation made his muscle spasms worse, the report said. He was also placed on a ventilator to help him breathe and given medications for his blood pressure and muscle spasms.

The boy remained in the ICU for 47 days, followed by several weeks of intermediate care and rehab, the report said. Finally, with a medical bill exceeding $800,000, the boy was able to return to his normal life, which included running and bicycling.

"Ubiquitous" bacteria

Despite recommendations by doctors to give the boy the second dose of tetanus vaccine along with other required vaccinations for children, the family declined, according to the report.

Dr. William Schaffner, an infectious-disease specialist at Vanderbilt University who was not involved with the case, said that the boy's infection was "a tragic event that [was] completely preventable."

And the parents' decision to not give him a second dose of the tetanus vaccine amounted to a "second tragedy," Schaffner told Live Science.

But not all is grim: Save for the occasional anti-vaxxer parents, most children do receive their tetanus shots. And thanks to the vaccine, cases of this infection have decreased by 95 percent and deaths by 99 percent since the 1940s.

The bacterium that causes tetanus is "ubiquitous, it's everywhere," Schaffner said. Though often associated with rusty nails, the bacteria don't really have to do with rust — people can be infected by any kind of deep, penetrating wound. Indeed, *C. tetani* is found everywhere in the environment, including in soil, dust and feces.

The only way to protect yourself is to get vaccinated, Schaffner said. What's more, a previous tetanus infection doesn't confer immunity against future infections. The vaccine works in part by combating toxins created by tetanus bacteria, rather than the bacteria themselves. The CDC recommends multiple doses of the tetanus vaccine (that also protects against other infections such as whooping cough) for children: one dose at 2, 4 and 6 months each; one at 15 to 18 months; and one at 4 to 6 years old. Pre-teens should also receive another version of that tetanus vaccine and people should receive tetanus booster shots once every 10 years.

Even if you're up to date on your tetanus shots, however, with any kind of intense penetration wound, you should seek medical care to clean and suture it, Schaffner said. And if you haven't had a booster shot in over five years, doctors will recommend you get one, he added.

https://wb.md/2JeFiw2

FDA Warns About Serious Adverse Events With Surgical Staplers

FDA is alerting clinicians about an increasing number of medical device reports associated with the use of surgical staplers

Megan Brooks

The US Food and Drug Administration (FDA) is alerting clinicians about an increasing number of medical device reports (MDRs) associated with the use of surgical staplers for internal use and implantable surgical staples and providing additional recommendations to help reduce risks associated with their use.

From January 1, 2011, to March 31, 2018, the FDA received more than 41,000 individual MDRs for surgical staplers and staples for internal use, including 366 deaths, more than 9000 serious injuries, and more than 32,000 malfunctions, the agency said in a March 8 letter to clinicians.

The most commonly reported problems include an opening of the staple line or malformation of staples, misfiring, difficulty in firing, failure of the stapler to fire the staple, and misapplied staples (eg, user applying staples to the wrong tissue or applying staples of the wrong size to the tissue).

Stapler and/or staple malfunctions or misuse may result in prolonged surgical procedures or unplanned, additional surgical interventions, which may lead to other complications such as bleeding, sepsis, tearing of internal tissues and organs, increased risk for cancer recurrence, and death, the FDA said.

The letter to healthcare providers reminds clinicians of the importance of reviewing labeling instructions and indications for use for surgical staplers and implantable staples, such as choosing the appropriate staple size for the patient's tissue type and thickness.

The letter also suggests considering alternative options if the patient's tissues are swollen, prone to bleeding, or necrotic and provides recommendations on how to recognize and manage device malfunction.

"The agency's analysis of adverse events associated with surgical staplers and implantable staples is ongoing, but we know these devices provide important benefits for patients undergoing surgery, so it's important for us to continue to educate providers about the devices' safety and risk," William Maisel, MD, MPH, chief medical officer in the FDA's Center for Devices and Radiological Health, said in a statement.

"We are asking providers to be aware of the new information and implement the recommendations we're outlining today to help improve the safe use of these devices. Improving the safety of surgical staplers and implantable staples is a top priority for the FDA, and we believe our forthcoming draft guidance to industry and planned advisory committee meeting will advance those efforts," Maisel said.

In the coming months, the FDA plans to issue a new draft guidance with labeling recommendations for manufacturers of surgical staplers and staples to help clinicians better understand the appropriate use and risks of these products.

The agency also plans to hold a public advisory committee meeting to discuss whether the current pathway for manufacturers to market surgical staplers for internal use is appropriate.

Specifically, they'll discuss whether reclassifying surgical staplers for internal use as Class II devices would be appropriate. Currently, surgical staplers for external and internal use are regulated as Class I medical devices, which do not require a premarket submission to the FDA.

Reclassifying surgical staplers for internal use as a Class II device would subject them to premarket notification and allow the FDA to establish mandatory special controls to help mitigate known risks of the device. Clinicians and healthcare facilities are encouraged to report adverse events related to these products to MedWatch, the FDA's Safety Information and Adverse Event Reporting program.

http://bit.ly/2HppLHr

50 is the new 40 for safe childbirth, according to Ben-Gurion U. researchers

It is as safe to give birth after age 50 as age 40 without endangering the mother or the baby

NEW YORK - Ben-Gurion University of the Negev (BGU) and Soroka University Medical Center researchers have determined that it is as safe to give birth after age 50 as age 40 without endangering the mother or the baby. The paper was recently presented at the Society for Maternal and Fetal Medicine 39th Annual Pregnancy Meeting in Las Vegas.

The researchers examined the complications of pregnancies among women over the age of 50 and the question of whether women who give birth at these ages are at increased risk for both themselves and the fetus compared with younger mothers.

The team included: Dr. Eyal Sheiner, director of the Department of Obstetrics and Gynecology at Soroka and vice dean for student affairs at BGU's Faculty of Health Sciences (FOHS); Dr. Gali Priante

and Dr. Erez Halevy of Soroka and the BGU FOHS, and Dr. Tamar Wainstock, of BGU's School of Public Health in FOHS.

The researchers found that thanks to medical and technological advancements - including extracellular fertilization and egg donation - the age at which a woman can give birth has gradually increased.

"It turns out that 50 is the new 40 when it comes to childbirth," according to Dr. Sheiner. "There is no doubt that medical teams will need to handle increasing numbers of birth for women over age 50."

The study included 242,771 deliveries at Soroka, of which 234,824 (96.7 percent) occurred in women younger than 40. The rest occurred in women from age 40 to 50 and older. It focused mainly on whether women found themselves during pregnancy and childbirth with complications such as premature births, gestational diabetes, hypertension, and cesarean sections. The study also examined if the newborn suffered from poor physical condition, mortality or distress during labor.

The researchers concluded that all complications were higher among women over 40 who gave birth to children compared with those who gave birth below that age. Remarkably, there was no escalation of complications in women over the age of 50, compared with women who gave birth between the ages of 40 and 50. Dr. Sheiner still advises to treat the pregnancies of women over the age of 40 as high-risk, and even more so, the pregnancies of women over 50. Special emphasis should be placed on tracking fasting glucose and pregnant blood pressure for early detection of complications.

http://bit.ly/2NXbeUo

Thyroid hormone helped our ancestors survive but left us susceptible

Our earliest mammalian ancestors may have lost the ability to regenerate heart tissue in exchange for endothermy

Although most victims survive the 735,000 heart attacks that occur annually in the U.S., their heart tissue is often irreparably damaged - unlike many other cells in the body, once injured, heart cells cannot regenerate. According to a new UC San Francisco study, the issue may date back to our earliest mammalian ancestors, which may have lost the ability to regenerate heart tissue in exchange for endothermy -- or as it's known colloquially, "warm-bloodedness" -- a Faustian evolutionary bargain that ushered in the age of mammals but left modern humans vulnerable to irreparable tissue damage after heart attack.

The Warm-Blooded Advantage

Early mammals were small, rodent-like creatures that emerged in a world dominated by cold-blooded animals. Rather than compete directly, early mammals evolved a novel strategy that enabled them to occupy new niches: endothermy. While cold-blooded animals, unable to regulate their own body temperature, were hostage to ever-changing weather conditions and relegated to temperate climates, warm-blooded mammals were able to spread to colder climes and to thrive nocturnally. But, as the new study shows, this came at a steep cost.

"Many of the lower vertebrates can regenerate body parts and organs, including the heart, but most mammals cannot. This feature was lost somewhere in the ectotherm-to-endotherm transition," said Guo Huang, PhD, investigator at UCSF's Cardiovascular Research Institute, assistant professor of physiology and senior author of the new study, published March 7 in the journal *Science*.

At first glance, there's no obvious connection between a mammal's ability to regulate its body temperature and its inability to repair heart damage. But the new study reveals that these seemingly disparate biological traits are inextricably linked -- by thyroid hormones.

Thyroid Hormones Halt Heart Cell Regeneration

The thyroid gland produces a pair of well-studied hormones that are known to regulate body temperature, metabolic rate and normal heart function. Because of their critical role in promoting heat generation

to maintain body temperature, these hormones have been posited to be the driving force behind the evolutionary transition from cold- to warm-bloodedness.

But Huang's study revealed that these hormones are also responsible for shutting off cardiac cell division, thus preventing heart tissue from repairing itself after an injury. This discovery represents the first demonstrated connection between thyroid hormones, cardiac development and repair, and the evolution of endothermy.

"Before our study, scientists knew that thyroid hormones were important for controlling heart rate and heart contractility. But the link with heart regenerative potential had never been shown before," Huang said.

Huang's team took a multi-species approach, comparing heart cell "ploidy" -- the number of copies of each chromosome pair in a cell -- across 41 different vertebrate species. Ploidy is closely linked to a cell's ability to divide and replicate. Virtually all actively dividing animal cells are diploid, containing only one pair of each chromosome, a copy inherited from mothers and another from fathers. By contrast, polyploid cells contain multiple copies of each pair and generally can't divide.

This comparative approach revealed a clear connection between ploidy and body temperature. Cold-blooded animals -- fish, amphibians and reptiles -- had heart cells that were largely diploid and responded to cardiac injury by ramping up cell division. Warm-blooded mammals had heart cells that were overwhelmingly polyploid, and lab experiments confirmed that these cells rarely divide in response to cardiac damage.

"This led us to hypothesize that the same thyroid hormones responsible for regulating body temperature might also be responsible for the diploid-to-polyploid transition and the arrest of cardiac cell division," Huang said.

The researchers confirmed their hunch in a series of lab experiments involving mice, a warm-blooded mammal in which heart cells normally cannot regenerate, and zebrafish, a cold-blooded animal noted for its ability to completely repair its heart, even if large chunks -- up to 20 percent -- are surgically amputated.

Mammals Gain, Fish Lose Heart Healing After Thyroid Hormone Levels Altered

In the womb, mice have diploid heart cells that regularly replicate to produce new cardiac tissue. But the heart cells of newborn mice undergo rapid polyploidization and lose the ability to divide -- events that coincide with a more than 50-fold increase in circulating thyroid hormones.

Experiments showed that these events were more than mere coincidence. When the researchers injected newborn mice with a drug that blocked thyroid hormone receptors and inspected their hearts two weeks later, they found four times as many dividing diploid heart muscle cells than mice that received no drug. Similar results were observed when they administered a different drug that impeded the production of thyroid hormones.

The researchers also produced genetically engineered mice whose heart cells lacked a functional receptor for thyroid hormone, which allowed their hearts to develop free from the influence of thyroid hormones. Unlike normal mice, these mutant mice were found to have significant numbers of actively dividing, diploid heart cells. Furthermore, when the scientists restricted blood flow to the heart -- a condition that usually causes permanent damage to cardiac tissue -- they observed a 10-fold increase in the number of dividing heart cells and 62 percent less scar tissue when compared with normal mice. Meanwhile, echocardiograms revealed an 11 percent improvement in heart function over normal mice after injury.

In stark contrast to mice and other mammals, adult zebrafish have relatively low levels of circulating thyroid hormone. This led Huang

to wonder whether increasing the levels of thyroid hormone could shut off the self-repair machinery that makes zebrafish hearts uncommonly resilient.

The researchers added thyroid hormone to the water in zebrafish tanks, then surgically amputated a portion of the heart and provided the fish with ample recovery time. Normally, zebrafish would be able to completely repair this kind of damage over the course of a few weeks. But fish that were reared in a high-hormone environment experienced a 45 percent reduction in heart cell division, a significant increase in polyploid heart cells and pronounced scarring of heart tissue after injury. Just as in mammals, thyroid hormones led to impaired cardiac regeneration in fish.

"Our results demonstrate an evolutionarily conserved function for thyroid hormone in regulating heart cell proliferation and suggest that loss of regenerative potential was a trade-off that allowed mammals to become warm-blooded," Huang said. "For early mammals, endothermy was more advantageous than retention of regenerative potential. But now, with medical improvements allowing us to live much longer, this loss of cardiac regeneration becomes more problematic and is a fundamental cause of heart disease."

Authors: *Additional authors on the paper are Kentaro Hirose, Alexander Y. Payumo, Stephen Cutie, Alison Hoang, Hao Zhang, Dominic Lunn, Rachel B. Bigley, Emily Wilson and Jeffrey E. Olgin of UCSF; Romain Guyot and Frederic Flamant of the University of Lyon; Hongyao Yu, Jiajia Wang and Guang Hu of the National Institute of Environmental Health Sciences; Megan Smith and Rochelle Buffenstein of Calico Life Sciences; Ellen Gillett and Frank Gru?tzner of the University of Adelaide; Sandra E. Muroy, Tobias Schmid and Michael M. Yartsev of UC Berkeley; Kenneth A. Field and DeeAnn M. Reeder of Bucknell University; Malcom Maden of the University of Florida; Michael J. Wolfgang of the Johns Hopkins University School of Medicine; Thomas S. Scanlan of the Oregon Health & Science University; and Luke I. Szweda of the University of Texas Southwestern Medical Center.*

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http://bit.ly/2J4ovMn

Mount Sinai researchers lead trial showing aspiration is equally effective as, and significantly cheaper than, traditional stent retriever approach for clot removal

Comparing direct aspiration first pass to the current standard of care, stent retriever first-line for mechanical clot removal (thrombectomy)

Sucking a clot directly out of the artery in patients experiencing a stroke is just as effective as, and significantly cheaper than, removing it by use of a stent, according to a study co-led by researchers at the Icahn School of Medicine at Mount Sinai and published in print March 9 in *The Lancet*.

The study, known as COMPASS, concerned large vessel occlusion stroke, the most devastating kind of ischemic stroke. It compared the direct aspiration first pass (ADAPT) approach to the current standard of care, stent retriever first-line (SRFL), for mechanical clot removal (thrombectomy) in patients suffering acute ischemic strokes.

"Our data strongly demonstrates that the two approaches have comparable clinical results, meaning that patients do just as well when you start with aspiration, or clot suction, as when you start with a stent retriever to trap and pull out the clot," says J Mocco, MD, MS, Vice Chair of Neurosurgery and Director of the Cerebrovascular Center for the Mount Sinai Health System and senior author of the study. "COMPASS is the first prospective randomized trial designed to compare both patient outcome and cost between these treatment approaches, and we found that patients do equally well with the aspiration approach, which is significantly cheaper."

Both techniques are initiated by inserting a guide catheter into the femoral artery in the groin and guiding it up into the brain under image guidance. The aspiration-first approach involves passing a specialized aspiration microcatheter through the guide catheter, moving it directly to the lesion, and then attaching it to an aspiration pump. Once attached to the suction system, the catheter is advanced into the end of the clot, suction is initiated, and the clot is either aspirated through the catheter or it becomes stuck at the catheter tip and is withdrawn back into the guide catheter.

The SRFL approach involves introducing a stent retriever, which resembles a tiny wire cage, through the guide catheter and moving it to the clot. The stent then opens up and traps the clot, and then both are removed through the guide catheter.

The COMPASS trial enrolled 270 patients into a prospective, randomized, open-label, blinded outcome assessment and core lab adjudicated trial to assess the clinical outcome of the patient, meaning how functional they were after treatment with either ADAPT using a large-diameter aspiration catheter (ACE68 ™) system, made by Penumbra Inc., or an SRFL approach. To compare clinical outcomes, researchers used the modified Rankin scale for neurologic activity (mRS), a standard measurement of the degree of disability or dependence in the daily activities of people who have suffered a stroke, which runs from 0 (no symptoms at all) to 6 (dead). The data showed that the ADAPT technique was non-inferior to stent retrievers for treatment of large vessel occlusions: 51.5 percent of patients treated with Penumbra's aspiration system achieved the primary endpoint of independence (mRS 0-2) at 90 days compared with 49.3 percent of patients treated with stent retrievers. Final revascularization rates were also similar for the two study groups: 91.7 percent of patients treated with aspiration achieved TICI compared to 90.4 percent with stent retrievers (p=0.83). Moreover, the percentage of patients achieving TICI 3 was 37.6 percent for the ADAPT arm and 27.2 percent for the stent retriever arm (p=0.09).

Secondary safety endpoints presented, including embolization in new territory (ENT) and symptomatic intracranial hemorrhage (sICH), were not statistically different between the two groups.

Using prespecified device-related procedural cost analyses, the COMPASS trial showed that the aspiration-first cohort had significantly lower device costs across all analysis methods. When using aggregate supply chain data as the primary source and list price as the secondary source, the aspiration-first group had a mean $4,541 reduction in the cost of devices used compared with the stent retriever first line group. When using list price as the primary source and aggregate supply chain data as the secondary source, the aspiration-first group had a mean $5,074 reduction in the cost of devices used. Furthermore, the reduction in median device costs was even greater ($6157.40 and $6,838, respectively) (p<0.0001 for all price comparisons).

A number of clinical trials published in 2015 demonstrated the superiority of endovascular thrombectomy (restoring blood flow to the brain by surgically removing the clot) over medical management (administration of clot-busting drugs) for treatment of ischemic strokes. However, the majority of stroke thrombectomy data to date has been based on the stent retriever approach, leading many to believe that stent retrievers represented the gold standard of thrombectomy devices, as reflected by recent American Heart Association/American Stroke Association guidelines.

"This study is very exciting because it shows that there are other ways to open the arteries that are just as effective and importantly, less expensive. Whether you approach the brain clot with suction or whether you approach it with trapping and pulling it out, patients do equally well," says Dr. Mocco. "Stroke is a horrible disease that is prevalent across the globe, so finding ways to provide these therapies

to patients who need it in a cost-effective manner is a great step forward in medicine."

Dr. Mocco designed the COMPASS trial in collaboration with leading doctors Aquilla Turk, DO, from the Medical University of South Carolina and Adnan Siddiqui, MD, PhD, from the University at Buffalo. The COMPASS trial was paid for by Penumbra but the trial was conducted independently by Dr. Mocco and his collaborators, who also handled all data analysis. The Mount Sinai Health System served as the international data coordinating center for the study.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30297-1/fulltext

http://bit.ly/2VMHlcq

Nature journals open their doors to sharing papers with ResearchGate

Full-text of scientific articles published since November 2017 will now be freely available through ResearchGate

By Rebecca Trager

The full-text of scientific articles published in more than 20 Nature journals since November 2017 will now be freely available through academic networking site ResearchGate. This is thanks to a new pilot programme that aims to make it easier for the website's users to read and download research on or off campus.

The pilot project builds on an agreement reached between ResearchGate and three publishers – the other two were Cambridge University Press and Thieme – back in April 2018 to support the sharing of scientific articles. As part of that arrangement, ResearchGate vowed to promptly remove copyright-infringing content from its site when notified by the publisher.

'This pilot unites Springer Nature's experience in publishing ground-breaking research with ResearchGate's 15 million scientist strong global network and its reach as the most visited website for science,' said ResearchGate's chief executive, Ijad Madisch. Besides *Nature*, *Nature Chemistry and Nature Chemical Biology* will also be available through ResearchGate.

Publishers including the American Chemical Society (ACS) and Elsevier have accused ResearchGate of illegally sharing millions of copyrighted articles, and sued the site for a second time in October. In the most recent legal complaint, ACS and Elsevier estimate that the social networking website has distributed more than 3100 of their research papers, and they claim they're entitled to $150,000 (£113,809) per infringement.

Meanwhile, the dispute between Springer Nature and the social networking site appears to be settled. 'We've been working with ResearchGate exploring how best we can serve the academic community for some time now,' said Susie Winter, who directs communications for Springer Nature, in a statement to *Chemistry World*. 'We believe that ResearchGate, as the largest scholarly collaboration network, is an important partner for us to ensure our authors' research reaches the widest possible audience.'

Not all publishers are enthusiastic about the pilot, however. The Coalition for Responsible Sharing (CRS) – a group launched in October 2017 whose membership now includes 17 scientific publishers, including the ACS and Elsevier – is warning that the new pilot programme does not address its 'fundamental concern' about ResearchGate making copyrighted content available on its site. CRS cites data showing that ResearchGate hosts as many as 4 million articles that violate copyright law, and the coalition estimates that many more are added every month.

http://bit.ly/2ST1Bap

Disorder left ancient human relative with teeth pocked like golf balls

Add this to your list of nightmare jobs: prehistoric dentist.

By Michael Price

Had the profession existed 1.8 million years ago, it would have encountered an ancient human relative with a disconcertingly

common dental disorder: weakened, pockmarked teeth resembling the surface of a golf ball.

The patient in question is *Paranthropus robustus*, a massive-jawed, thick-molared creature that looked a bit like a gorilla and feasted on tropical grasses, hard seeds and nuts, and fibrous fruits in southern Africa. Scientists have long suspected *P. robustus*'s tough, gritty diet contributed to the overall poor condition of the species's fossil teeth found over the years.

Ian Towle

Hoping to learn more, paleontologists compared hundreds of fossilized *P. robustus* teeth, pictured above, with those of other southern African hominins such as *Australopithecus sediba* and *A. africanus* that lived at roughly the same time, as well as with more recent hominins and living apes. The golf ball–like pitting was a common feature of *P. robustus* teeth, showing up in 47% of baby teeth and 14% of permanent teeth of the species, whereas it occurred only in about 7% and 4%, respectively, of the baby and permanent teeth of the other ancient hominins combined. These pits in the teeth enamel would have made them wear down quickly and break easily. However, these defects probably didn't come from *P. robustus*'s diet. The condition closely resembles a somewhat rare modern genetic disorder called amelogenesis imperfecta that affects about one in 1000 people worldwide, the researchers report this week in the *Journal of Human Evolution*. The disorder causes a breakdown in enamel-producing cells, leading to scattered pits and grooves in the teeth.

How did *P. robustus* develop this condition? In modern humans, the genes responsible also contribute to thick, dense enamel. It's possible, the researchers suggest, that the defect was a side effect of evolving thicker, denser teeth to cope with the species's rough diet.

http://bit.ly/2Ch81e2

Success of university programs to promote rural healthcare in Japan

Researchers confirm university programs encourage physicians to work in rural areas

An ambitious health economics study from a consortium of 5 Japanese universities has shown that different university programs to promote the equal geographic distribution of physicians increases the number of graduates practicing in rural areas in Japan. Graduates from these programs were on average 24% more likely to work in non-metropolitan areas than those not involved these programs.

Access to healthcare in rural or low-population areas is a problem that affects countries worldwide, not limited only to developing nations. Many developed nations have an aging population, which in countries like Japan and Germany, is putting pressure on their healthcare systems and services for both rural and urban populations. Ease of access to healthcare in rural communities is an important global challenge that must be tackled and is one of the priorities of the World Health Organization (WHO).

"I believe that here at Hiroshima University has a destiny to improve this problem," asserts Professor Matsumoto of the Department of Community-Based Medical System in Hiroshima University. "This sort of research is very important to me because I am part of Hiroshima University researchers [sic]".

Japan has an urgent problem concerning access to healthcare. This barrier to access has become a long-lasting social problem, due to the uneven distribution of doctors, says Matsumoto. Article 25 of the Constitution of Japan states that everybody has a right to be healthy regardless of the living area or income level. This article was drafted in 1945 by Tatsuo Morito, the founding President of Hiroshima University. "Unfortunately in the real-world the access is not at all equal," says Matsumoto.

Japan does not currently have any government policies to allocate doctors to areas experiencing shortages. Matsumoto recounts a story of how a rural town in northern Hiroshima did not have a local obstetrician for 13 years so there was no choice for pregnant women except to move to another area to give birth. "In Japan the poor access to healthcare is largely derived from the geographic barriers rather than economic barriers," concludes Matusmoto.

To help overcome these barriers to healthcare, current actions are targeting physicians early, implementing policies that focus on medical school students. Japan has admissions programs integrated in each University with a medical school, which either obliges or encourages medical school graduates to practice in rural areas. There are three types of programs: the regional quota program where a certain number of the incoming high-school students in a medical course must be from a local region, the scholarship program where the medical students benefit from a scholarship for 6 years in exchange for practicing in designated areas after graduation, and a combined quota and scholarship program. This combined program is unique to Japan, as is the scale of its implementation. Canada, Thailand and the US all have similar programs but none of this scale or as a combined regional quota with scholarship, says Matsumoto.

In this study, a project of the Japanese Council for Community Based Medical Education sent out surveys to 77 medical schools and 47 prefectures across Japan, targeting graduates who were admitted through the regional quota system and/or benefitted from scholarship admission programs. Location data about graduates was acquired from the Physician Census compiled by the Ministry of Health, resulting in the study examining almost 24,000 graduate physicians. "The proportion of those working in rural areas is the most important outcome of this study," states Matsumoto.

The result was satisfactory for Matsumoto. Not only were the graduates of the programs more likely to work in rural areas, the population density of those areas was vastly lower than 'usual' medical graduates. "We are recommending the government continue this system. Otherwise we don't have any other solution to solve the unequal distribution of doctors," says Matsumoto.

http://bit.ly/2tYb5qK

Found: A Medical Manual Linking Medieval Ireland to the Islamic World

Knowledge transcends borders.

by Noor Al-Samarrai

An exciting link between medieval Ireland and the Islamic world has been discovered on two sheets of calfskin vellum lodged into the binding of a book from the 1500s. The sheets hold a rare 15th-century Irish translation of an 11th-century Persian medical encyclopedia. For 500 years, they sat in a family home in Cornwall with no one the wiser to their origins.

The manuscript bound into the printed text. **Courtesy of Pádraig Ó Macháin**

"I suppose [the owners] just took a notion to photograph it with their phone and they sent the photograph to one of the universities in England, who sent it to another university, and eventually it got to me," says Pádraig Ó Macháin, who has spent his life with medieval Gaelic manuscripts and leads the modern Irish department at University College Cork. For him, identifying it as a medieval Irish medical text was a cinch, but he needed a little help to determine its source.

Ó Macháin, founder of Irish Script on Screen, Ireland's first deep digitization project, where the manuscript and many more old Irish texts can be seen, shared the fragment with Aoibheann Nic Dhonnchadha, a specialist in Irish medical texts at the Dublin

Institute for Advanced Studies. She identified it as a passage from the first book of the seminal five-volume *The Canon of Medicine*. Written by 11th-century Persian physician and polymath Ibn Sina, also known as Avicenna, the work is considered the foundational textbook of early modern medicine. While many references to Ibn Sina and his work pop up in old Irish medical texts, this is the only known evidence of a full translation of his encyclopedia.

He originally wrote in Arabic, and the Irish rendition is likely translated from a 13th-century Latin version by the prolific Gerard of Cremona. "This is one of the most influential medical books ever written," says Nic Dhonnchadha. "So the fact that it was being studied in Ireland in the 15th century was certainly a link to the Islamic world."

The unbound sheets, with a heading in Latin and the rest translated into Irish. **Irish Script on Screen**

The heading at the top right of the page is Ibn Sina's preface to his *Canon*, in Latin. It gives thanks to god and explains that one of his friends asked him to write a book about medicine (quite the favor!). The rest of the text is in Irish, peppered with transliterated Latin terminology. One sheet runs through the encyclopedia's contents, while the other details the anatomy of the jaw, teeth, nose, and throat. Using scraps of old manuscripts to bind newer books was a common practice as the world transitioned from handwritten to printed words, but it would have been unusual for such a precious text to have been taken apart on purpose. "These kinds of manuscripts would have been very valuable to the people who owned them," says Nic Dhonnchadha. "Anyone who owned it would have been unlikely to part with it." Many manuscripts were destroyed during England's encroachment upon Ireland, and the scholars believe that the *Canon* manuscript suffered such a fate. It's just a stroke of luck that this fragment was salvaged and used to bind a much-less-interesting administrative text.

Ó Macháin hopes the find can help overturn some misconceptions about Ireland at that time in history. "Ireland was very much pre-urban, and we remained pre-urban until the 17th century," he says, "but what people don't understand is that there were great schools of learning here, including medical schools." In these Irish medical schools, unlike those in England or continental Europe, students studied in Irish rather than Latin, creating a unique repository of medical knowledge in a vernacular language. Nic Dhonnchadha's upcoming full translation of the manuscript will reveal some key differences between the Latin version and its Irish counterpart.

"This is an example of learning in its purest form, it transcends all boundaries, it transcends cultures and religions, it unites us all in a way that other things divide us," Ó Macháin says. "That's very personally important to me because I think learning is without borders and that this is maybe an opportunity to express that and make people understand it."

http://bit.ly/2NVtjSU

To Conceive a Girl in Ancient Greece, Eat a Salad and Tie Your Right Testicle

Doctors wrote recipes to cure patients' ailments and determine the sex of their children.

by Reina Gattuso

Greek women had it tough. At any moment, their wombs could dislodge and wander through their bodies, strangling them—or so said Hippocratic doctors. Their medical texts, which emerged in the fifth century B.C. and were attributed to the physician Hippocrates and his followers, changed Greek science by suggesting that illness had natural, rather than exclusively divine, causes. While wandering

womb syndrome, which has been thoroughly discredited, is largely forgotten, one Hippocratic idea is likely familiar to modern parents: that what you eat can determine the sex of your child.

We don't know much about Hippocrates's life or contribution to the texts of the Hippocratic corpus, says Dr. Rebecca Fallas, a visiting research fellow in classical studies at the U.K.'s Open University who specializes in fertility in Ancient Greece. We do know, however, that Hippocratic texts were widely read in the centuries after they were written, and were compiled in the Great Library of Alexandria. Surviving texts show that Hippocratic doctors were, to put it lightly, very concerned with women's reproductive health. In fact, the majority of the 1,500 existing Hippocratic recipes come from gynecological treatises. Of these, the dietary prescriptions for choosing the sex of one's children reveal a complex set of beliefs around food, gender, and the human body.

Hippocratic doctors believed the body was ruled by four, or sometimes three, humors, classified according to heat and moisture. Phlegm was cold and wet. Blood was hot and wet. Yellow and black bile were dry and hot or cold, depending on the text. This system of heat and moisture underlied all aspects of patients' health, including fertility.

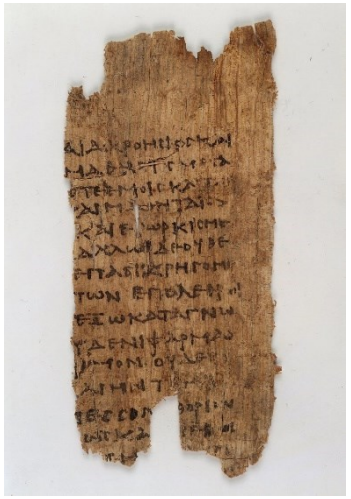
Quick quiz: According to Hippocratic medicine, is coriander hot and dry, or cold and wet? What about lettuce? If you said coriander is hot and dry, and lettuce cold and wet, you're right. But these classifications weren't descriptions of foods' literal moisture content and temperature. They were instead rooted in beliefs about how foods interact with bodily humors. Red wine, for example, was believed to heat and dry out the body, while white wine cooled and moistened it.

This delicate balance of humors was particularly important for women trying to conceive. With ancient couples facing high rates of infant mortality, producing healthy, viable children was a high-stakes affair. Boys and girls benefitted families in different ways: Boys promised future economic and political power, while girls offered the possibility of marriage alliances. While many scholars argue that Ancient Greeks valued boys over girls, there is evidence of women in holy shrines petitioning the gods for daughters.

As this system of medicine developed, Greek women had the option of skipping shrines and heading straight to a Hippocratic doctor. In the Hippocratic world, women were naturally weak, damp, and cold, while men were strong, dry, and hot. Doctors believed that conception resulted from a fight between "strong" male seed and "weak" female seed, with the winner determining the child's sex. Hippocratic doctors advised parents hoping for boys to consume hot, dry, and strong foods, such as red wine sprinkled with black cumin. To conceive a girl, Hippocratic doctors prescribed wet, cool, feminine foods, such as lettuce and white wine.

But if couples were really serious about sex selection, diet alone wouldn't cut it.

Hippocratic doctors believed that the left side of the womb nourished female children, and the right nourished males. To choose a child's sex, women had to conceive on the side of the womb corresponding to their preferred gender. So Hippocratic doctors advised couples who wanted girls to tie the male partner's right testicle with string, thus hopefully directing sperm toward the left side of the womb. The opposite was true for conceiving a boy. Scholars have no evidence of this method delivering anything besides sore nether regions.



The Hippocratic oath, written on papyrus circa 200. Wellcome Images/CC BY 4.0

While modern-day dads have left the testicle-tying behind, some Hippocratic beliefs do persist. Thanks to first-century Roman physician Galen and the work of Arab and Renaissance translators, says Fallas, “Hippocratic and Galenic medicine became the cornerstone of Western European medicine.” This includes the Hippocratic oath, the ethical pledge that doctors do no harm. And just like their ancient counterparts, contemporary parents continue looking for dietary prescriptions, be they from scientific studies or friends, to determine their children’s sex.

While Fallas says scholars can’t know for sure if this contemporary dietary advice descends directly from Hippocratic medicine, some folk wisdom, such as the belief that eating veggies will help couples conceive girls, resembles ancient beliefs. Modern doctors say most of this advice is quack. But for Fallas, the enduring appeal of diet-based interventions stems not from their efficacy, but from women’s desire to control their own health, at home, with ingredients they have on hand. As for the methods’ effectiveness? “Well,” says Fallas, “You’ve got a 50/50 chance of getting it right.”

http://bit.ly/2T0qqry

At what age do you feel 65?

New study reveals wide variations in how well or poorly people age; United States ranks 54th between Iran (53rd) and Antigua and Barbuda (55th)

SEATTLE - At what age do you feel 65?

A 30-year gap separates countries with the highest and lowest ages at which people experience the health problems of a 65-year-old, according to a new scientific study. Researchers found 76-year-olds in Japan and 46-year-olds in Papua New Guinea have the same level of age-related health problems as an "average" person aged 65.

"These disparate findings show that increased life expectancy at older ages can either be an opportunity or a threat to the overall welfare of populations, depending on the aging-related health problems the population experiences regardless of chronological age." said Dr. Angela Y. Chang, lead author and postdoctoral fellow at the Center for Health Trends and Forecasts at the University of Washington.

"Age-related health problems can lead to early retirement, a smaller workforce, and higher health spending. Government leaders and other stakeholders influencing health systems need to consider when people begin suffering the negative effects of aging."

These negative effects include impaired functions and loss of physical, mental, and cognitive abilities resulting from the 92 conditions analyzed, five of which are communicable and 81 non-communicable, along with six injuries.

The studies and additional information are available at http://www.healthdata.org Link to* The Lancet Public Health *study: https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(19)30019-2/fulltext

The study, published yesterday in the international medical journal *The Lancet Public Health*, is the first of its kind, according to Chang, whose center is housed at the UW's Institute for Health Metrics and Evaluation.

Where traditional metrics of aging examine increased longevity, this study explores both chronological age and the pace at which aging contributes to health deterioration.

The study uses estimates from the Global Burden of Disease study (GBD).

Researchers measured "age-related disease burden" by aggregating all disability-adjusted life years (DALYs), a measurement of loss of healthy life, related to the 92 diseases.

The findings cover 1990 to 2017 in 195 countries and territories.

For example, in 2017, people in Papua New Guinea had the world's highest rate of age-related health problems with more than 500

DALYs per 1,000 adults, four times that of people in Switzerland with just over 100 DALYs per 1,000 adults.

The rate in the United States was 161.5 DALYs per 1,000, giving it a ranking of 53rd, between Algeria at 52nd with 161.0 DALYs per 1,000 and Iran at 54th with 164.8 DALYs per 1,000.

Using global average 65-year-olds as a reference group, Chang and other researchers also estimated the ages at which the population in each country experienced the same related burden rate.

They found wide variation in how well or poorly people age.

Ranked first, Japanese 76-year-olds experience the same aging burden as 46-year-olds in Papua New Guinea, which ranked last across 195 countries and territories.

At 68.5 years, the United States ranked 54th, between Iran (69.0 years) and Antigua and Barbuda (68.4 years).

The study is entitled "Measuring population ageing: an analysis of the Global Burden of Disease Study 2017."

Additional findings include:

- ***Age-related disease burden rates decreased over time across all regions between 1990 and 2017, representing reductions in deaths and disease severity of age-related problems.***
- ***In 2017, people in 108 countries experienced earlier accumulation of problems associated with aging, whereas those in 87 countries experienced slower onset of aging.***
- ***Globally, the age-related diseases with the most deaths and DALYs were ischemic heart disease, brain hemorrhage, and chronic obstructive pulmonary disease (COPD).***

Countries with highest equivalent age to global 65-year-olds in 2017:

1. Japan: 76.1 years	*6. South Korea: 75.1*
2. Switzerland: 76.1	*7. Spain: 75.1*
3. France: 76.0	*8. Italy: 74.8*
4. Singapore: 76.0	*9. Puerto Rico: 74.6*
5. Kuwait: 75.3	*10. Peru: 74.3*

Countries with lowest equivalent age to global 65-year-olds in 2017:

1. Papua New Guinea: 45.6 years	*6. Central African Republic: 53.6*
2. Marshall Islands: 51.0	*7. Lesotho: 53.6*
3. Afghanistan: 51.6	*8. Kiribati: 54.2*
4. Vanuatu: 52.2	*9. Guinea-Bissau: 54.5*
5. Solomon Islands: 53.4	*10. Federated States of Micronesia: 55.0*

Countries with lowest age-related burden rate in 2017: (DALYs per 1,000 adults aged 25 or older)

1. Switzerland: 104.9	*6. Kuwait: 118.2*
2. Singapore: 108.3	*7. Spain: 119.2*
3. South Korea: 110.1	*8. France: 119.3*
4. Japan: 110.6	*9. Israel: 120.2*
5. Italy: 115.2	*10. Sweden: 122.1*

Countries with highest age-related burden rate in 2017: (DALYs per 1,000 adults aged 25 or older)

1. Papua New Guinea: 506.6	*6. Central African Republic: 364.6*
2. Marshall Islands: 396.6	*7. Lesotho: 360.5*
3. Vanuatu: 392.1	*8. Kiribati: 347.5*
4. Afghanistan: 380.2	*9. Guinea-Bissau: 343.4*
5. Solomon Islands: 368.0	*10. Eritrea: 325.7*

https://wb.md/2Ts4kwB

Chemo Is 'Invisible Threat' to Cancer Clinic Staff

Why Isn't Safety a Bigger Concern?

Nick Mulcahy

It's long been known that handling and administering chemotherapy is a health hazard for cancer clinic staff, especially nurses and pharmacists, owing to its potent toxicity. There is observational evidence that occupational exposure to chemotherapy is associated with conditions ranging from respiratory problems to miscarriage. However, getting health professionals in the United States to fully use protective gear is not easily achieved.

In a new randomized trial among 396 nurses at 12 American oncology clinics, not even a 2-year educational intervention increased the suboptimal baseline use of protective equipment. The study was published in the March edition of *Oncology Nursing Forum*.

But the study's lead author, Christopher Friese, PhD, RN, Rogel Cancer Center, University of Michigan, Ann Arbor, is undeterred. He wants chemotherapy exposure to be given its due attention.

"It's an invisible threat," said Friese in a press statement, referring to chemo exposure.

He explained that exposure through minor direct contacts and through vapors is not as obvious as a needlestick but is a "subtle" and "daily" threat to the health of nurses, pharmacists, and other staff.

Above all else, Friese wants to reduce this vulnerability. Innovation in devices and equipment could help, he told *Medscape Medical News*.

Currently, personal protection typically includes wearing two pairs of gloves during all handling and a thick, disposable gown made from a fabric of low permeability with back closure. Eye and face protection is also advised when splashing is a risk. A protective respirator is recommended for cleaning spills and for some forms of administration.

However, not using protective gear is common, as indicated by responses to an anonymous poll conducted at the 2016 Oncology Nursing Society annual meeting. More than one third (38%) of respondents reported not changing their gown or double-gloving because this equipment was not conveniently located. Other respondents skipped wearing the gear because it was too uncomfortable.

Unintentional chemo exposures are not uncommon. A 2011 survey, also led by Friese and reported by *Medscape Medical News,* found that the overall rate of exposure to the skin or eyes during a 1-year period among 402 nurses working in US outpatient settings was 16.9%.

A 2012 published record of a site visit at a Florida cancer clinic by inspectors from the National Institute for Occupational Safety and Health (NIOSH) reveals how housekeeping, clinic design, and even personal grooming might result in exposures.

The inspection was prompted by a confidential request from a clinic employee, who had reported upper respiratory symptoms, rash, diarrhea, migraine, and headaches among employees.

The NIOSH report includes a photo of a counter area where chemotherapy bags are stored in the open. Directly above the bags is a rack where personal protective equipment (masks and goggles) is hung on hooks, also in the open. In other words, protective gear was stored inches away from a potential source of toxins, with no barrier.

The report also details how easily an exposure can occur: "One employee was observed handling a chemotherapy drug and using her gloved hand to brush her hair away from her eyes."

Perhaps not surprisingly, various chemotherapies "were detected on surface wipe samples collected throughout the clinic, suggesting inadequate work practices and housekeeping," reads the report.

Are Nurses Neglecting Themselves or Being Neglected?

Alison Trinkoff, ScD, RN, of the University of Maryland School of Nursing, Baltimore, who has written about nurse safety, believes part of the problem with chemo exposures is that nurses may be neglecting themselves by not adhering more closely to safety practices.

"Nurses are generally very 'other' focused or patient focused and not so much focused on themselves," she told *Medscape Medical News*.

However, Trinkoff also strongly emphasized that, unlike dealing with infectious materials, taking precautions with chemo is "not generally something that is stressed in the workplace." In other words, systemic neglect is at work, she suggested.

Nurses are often in the dark about the health hazards of chemo exposure, said Samantha Toland, NP, RN, and Alison Simons, RN, of the School of Nursing and Midwifery, Birmingham City University, United Kingdom, who have studied oncology nurse health complaints. "Generally we do not think nurses are always fully aware of the risks to their health, certainly in the longer term," they told *Medscape Medical News* in a joint email. Perhaps more ominously, they added that nurses "may not attribute health issues to the fact that they have been handling chemotherapy agents."

The knowledge gap includes the mechanisms of chemotherapy's toxicity, the two lecturers say: "Nurses do not fully understand how or why this risk is posed — and that the drugs are in some cases carcinogenic, mutagenic and teratogenic."

However, on its news website, the Oncology Nursing Society suggests there is some understanding of the stakes. The society says it "commonly" receives questions in its clinical inbox (clinical@ons.org) about whether nurses who are pregnant, breastfeeding, or trying to conceive can safely administer or handle chemotherapy and other hazardous drugs.

Here is the Oncology Nursing Society's advice:

"Although consistent and thorough use of primary engineering controls and personal protective equipment when handling hazardous drugs minimizes risk of occupational exposure, it does not eliminate it (Polovich, 2011). Because of the increased susceptibility for harm, an added level of protection is needed for nurses who are pregnant, breastfeeding, or actively trying to conceive."

One of the reasons that some nurses are aware of reproductive risks linked to chemotherapy exposure is an often-cited 2012 study.

The authors, who were from NIOSH, retrospectively collected information about pregnancy outcomes and occupational exposures from 8461 participants of the Nurses' Health Study II.

Participants reported 6707 live births and 775 (10%) miscarriages (<20 weeks).

Antineoplastic drug exposure was associated with a twofold increased risk for miscarriage, particularly with miscarriage before the 12th week, and 3.5-fold increased risk among nulliparous women.

NIOSH has attempted to analyze and draw attention to chemotherapy exposure among nurses, said Thomas H. Connor, PhD, a recently retired research biologist at the agency, which is part of the Centers for Disease Control and Prevention, in an email to *Medscape Medical News.*

For example, he pointed to a 2004 NIOSH alert "published about hazardous drugs, including antineoplastic agents."

The alert includes a graphic introductory box: "Warning! Working with or near hazardous drugs [including chemotherapy] in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers."

Connor was also an author of a recent study that used data collected from more than 40,000 nurses participating in the Nurses' Health Study III (*Am J Nurs.* 2019;119:28-35).

Participants self-reported about the use of gloves and gowns and administration of antineoplastic drugs within the past month (among nonpregnant nurses) or within the first 20 weeks of pregnancy (among pregnant nurses).

More than a one third (36%) of the large study population had handled chemotherapy, the study found.

Notably, 12% of nonpregnant nurses and 9% of pregnant nurses indicated that they never wore gloves when administering antineoplastic drugs.

Furthermore, 42% of nonpregnant nurses and 38% of pregnant nurses reported never using a gown.

No Level I Evidence

About half of UK nurses experience symptoms related to chemotherapy exposure, suggests a 200-nurse survey conducted in 2017 by Birmingham's Toland and Simons.

The survey, which was anonymous, prompted nurses to remember whether adverse events occurred during or after the preparation and administration of chemo. Nearly half (46%) said they had experienced some ill effect.

Participants who reported that they had experienced an adverse event (n = 90) were most likely to identify headache (n = 57), dizziness (n = 30), or nausea (n = 27), alone or in combination. Participants also attributed hair loss (n = 18), miscarriage (n = 12), and fertility problems (n = 7) to exposure. Twenty-six respondents identified additional events. The two researchers pointed out that it makes sense that only some nurses experience symptoms because, as with patients, adverse events are not universal.

Despite this and other published reports, there is no level I evidence that chemotherapy exposure causes specific illness in nurses.

Michigan's Friese explained that there are few funding sources for large-scale occupational health studies. "Studying health effects in workers takes a long time and is costly," he said.

An alternative strategy, said Friese, is to establish a registry where workers can report hazardous drug exposures, including from chemotherapy, and report long-term health effects.

"There is a national registry for needlestick injuries, but no such registry exists for hazardous drugs," he said.

Toland and Simons believe the profession of nursing can do better — or at least as well as pharmacists, whom they credit as having strong guidelines and practices.

"We know that pharmacists would generally not carry out some of the tasks nurses do without the addition of more robust protective measures. Possibly if medics [physicians] handled chemotherapy, more research would have been carried out and measures adopted," they said.

In the United States, experts point out that NIOSH does not have the authority to ensure that hazardous drugs are being safely handled. However, the Occupational Safety and Health Administration (OSHA) could, but it does not have the resources to do so.

A Long History of Delayed Concern

The poisonous properties of cytotoxic drugs have been known since the 1940s, when they were first used in oncology and were described in a 1946 study of nitrogen mustard therapy for blood cancers.

However, it was not until 1979 — nearly 4 decades later — that the first article described an increase in mutagenicity in genetic material found in the urine of nurses handling cytotoxic drugs (*Lancet*.1979;1:1250–1).

"This was the first demonstration of the potential occupational risk involved in the manipulation of these medicines," write the authors a 2018 review article on the safe handling of cytotoxic agents.

More research subsequently pointed to the possible relationship between occupational exposure to cytotoxic drugs and increases of various health effects, say the review authors, led by Mari A. Bernabeu-Martínez, PhD, of Miguel Hernandez University, Elche, Spain.

Governments and major organizations finally acted on the information. In 1981, the Society of Hospital Pharmacists of Australia published the first guide for the safe management of cytotoxic medicines.

"This is an old problem," summarized Michigan's Friese, who wants further action to be taken in the United States.

"While there is a renewed conversation about this problem, we haven't seen approaches enacted to address it," he argued.

Recommendations for Action

Friese and his coinvestigators of the recent, failed randomized clinical trial, which attempted to increase use of protective gear among nurses, have three recommendations:

- ***First, support innovation in devices and equipment to reduce worker exposures.***
- ***Second, engage health system leaders in this problem to be sure they are fully implementing and supporting the recommendations by NIOSH, the Oncology Nursing Society, and the US Pharmacopeia.***
- ***Third, consider strategies to track exposures and health effects, such as the registry noted above.***

A lot of healthcare workers are affected, said Friese. NIOSH estimates that as many as 8 million may handle hazardous drugs.

Furthermore, "use of hazardous drugs has expanded beyond oncology settings," emphasized Friese.

"It's time...to reexamine the issue of hazardous drug exposure. Both leaders and frontline clinicians need to work together to make sure the people handling these drugs are doing so as safely as they can," he said.

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https://nyti.ms/2J6jrXU

Cancer Patients Are Getting Robotic Surgery. There's No Evidence It's Better.

High-tech surgical robots aren't an improvement over traditional operations, the F.D.A. warns. For some patients, the robots may be worse.

By Roni Caryn Rabin

Robotic surgery was never approved for mastectomy or any other cancer-related treatment, but that has hardly deterred doctors in the operating suite. The equipment is widely used to operate on patients with various malignancies, from breast cancer to prostate cancer.

Yet there have long been questions about how well doctors are trained on the machines, and whether the devices are better for patients than traditional methods.

Now the Food and Drug Administration has warned that there is no evidence cancer patients receiving robotic procedures live longer than those who have traditional procedures. And some research shows that patients with cervical cancer fare worse.

"We want doctors and patients to be aware of the lack of evidence of safety and effectiveness for these uses so they can make better informed decisions about their cancer treatment and care," said Dr. Terri Cornelison, assistant director for the health of women at the F.D.A.'s Center for Devices and Radiological Health.

Robotic systems have been on the market for more than 15 years, and have been used for cancer surgery for much of that time. The machine's tower, which is positioned over the patient, looks a bit like a multi-armed Star Wars droid. Three of its arms hold surgical devices, while a fourth holds a camera.

The robot's arms are controlled by a computer that replicates the movements of the operating surgeon, who manipulates the robot's controls while looking at a monitor that provides a magnified, high-definition image of the operating site.

The F.D.A. noted the findings of two studies published last year in the New England Journal of Medicine.

One of them was a clinical trial that was stopped early after investigators found that women with cervical cancer who had so-called minimally invasive hysterectomies, including robotically assisted procedures, experienced four times as many cancer recurrences and six times as many deaths, compared with patients who had the more traditional procedure.

The trial's findings were especially striking because the surgery, a radical hysterectomy, usually cures patients with cervical cancer, said Dr. Pedro T. Ramirez, lead author of the paper and director of

minimally invasive surgical research at M.D. Anderson Cancer Center in Houston.

A second study funded by the National Institutes of Health used a database to compare the outcomes of 2,461 women with cervical cancer who had different types of surgery. Four years after the operation, 9.1 percent of those who had minimally invasive surgery had died, compared with 5.3 percent of those who had open surgery.

Yet many physicians continue to recommend robotic surgery to patients, despite the evidence of harm. “Several surgeons have said to me, ‘I can’t find a flaw in your study, but I just can’t stop doing it,’” Dr. Ramirez said.

Dr. Ramirez’s own department stopped doing minimally invasive radical hysterectomies in October 2017, when the first study’s results were confirmed.

“My feeling is, this is about patient care,” he said. “It’s not about how much time you devoted to your training or your ego. It’s an issue of cancer, and having a high likelihood of cancer coming back if you have surgery through this approach.”

It is not clear why cervical cancer outcomes were worse following minimally invasive surgeries. Dr. Ramirez suggested that the instruments used to manipulate the cervix and uterus may cause cancer cells to spread.

Another possibility is that the carbon dioxide pumped into the abdomen during robotic and other minimally invasive procedures — it provides working and viewing space for the surgeon — may increase the likelihood of cancer cells implanting, Dr. Ramirez said.

The F.D.A.’s warning was not limited to cervical cancer: Robotic surgical devices are not authorized for prevention or treatment of any cancer, nor are they approved for mastectomy (removal of the breast), the agency said.

The agency also urged health care providers “to complete the appropriate training” needed for performing robotic surgery, and urged patients to ask doctors about their training and experience, as well as about their patients’ outcomes.

In 2000, the F.D.A. allowed the sale of one of the first robotic surgery systems, the da Vinci Surgical System, under a process called “premarket notification,” which is often used to bring medical devices on to the market without the rigorous safety and efficacy trials required for new drugs.

Under premarket notification, devices are “cleared” for use on the grounds that they are similar to devices already available. The da Vinci system is cleared for some urological and gynecological procedures, among others.

A similar robotic device, the Senhance Surgical System, was approved for gynecological and colorectal surgery, among other procedures.

But the efficacy of either system for cancer treatment has not been evaluated by the F.D.A. And none of the systems have been cleared for mastectomy, or removal of the breast, which has become a frequent use.

The F.D.A.’s approval was “based on evaluation of the device as a surgical tool and did not include evaluation of outcomes related to the treatment of cancer,” the agency said. The F.D.A. reviewed short-term data on outcomes, a spokeswoman said, not the long-term data important to cancer patients.

So why are these machines allowed in cancer surgery at all? According to a spokeswoman, the F.D.A. does not regulate the practice of medicine.

“If a medical provider determines it’s appropriate to use a product off-label, we don’t regulate that,” she said. “However, in this case, we were concerned about scientific journals and media reports referring to off-label uses.”

Many surgeons tout the benefits of robotic surgery, with its smaller incisions, saying the procedures bring shorter recovery times, less pain or blood loss and fewer scars and infections.

Those are important measures, said Dr. Ramirez. But “if you tell a patient you may stay in the hospital one or two days longer versus going home the same day, but there is a higher likelihood your cancer is going to come back, what are you going to choose as a patient? Of course, you’ll stay in the hospital.”

Proposals to conduct another clinical trial to test the cervical cancer outcomes would be unethical, Dr. Ramirez said, because results from the first study were clear.

Physicians who continue to use robotic and minimally invasive approaches for cancer treatment “in the face of the evidence may put themselves in legal jeopardy,” said Dr. Michael Carome, director of the health research group at Public Citizen, a consumer advocacy organization.

Patients may not have been the only ones caught off guard by the F.D.A.’s warning. Officials at Intuitive Surgical, maker of the da Vinci robotic system, believed their device was cleared for radical hysterectomies and removal of the prostate. The latter would only be done to treat cancer.

“We have reached out to the F.D.A. for clarification,” said Peper Long, a company spokeswoman.