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Opioids prescribed less in states where medical marijuana legal, studies find

Two new studies have found a correlation using data from programs used by millions of older, poor and disabled Americans

Jessica Glenza in New York

The number of opioid prescriptions for the elderly and the poor declined in states where medical marijuana is legal, two new studies have found.

In one study, researchers at the University of Georgia, Athens, used data from Medicare Part D, a government-run prescription drug program for people older than 65.

They found prescriptions filled for all opioids decreased by 2.11m daily doses a year when a state legalized medical marijuana, and by 3.7m daily doses a year when marijuana dispensaries opened. Forty-one million Americans use Medicare Part D. The study analyzed data between 2010 and 2015.

In a second study, researchers at the University of Kentucky examined opioid prescription data from Medicaid, a government-run program for the poor and disabled. More than 74 million Americans use Medicaid.

That analysis found state medical marijuana laws were associated with a 5.8% lower rate of opioid prescribing, and states with recreational marijuana laws were associated with a 6.3% lower rate of opioid prescribing. That study used data from 2011 to 2016.

Both studies were published in Journal of the American Medical Association Internal Medicine.

The findings are likely to bolster legal marijuana advocates, who have long contended legal marijuana could curb the opioid epidemic.

America's overdose crisis has claimed more lives each year since the early 2000s, when powerful opioid painkillers such as Oxycontin were aggressively marketed. In 2016, more than 64,000 people died of an overdose. In a JAMA opinion piece accompanying the research, Drs Kevin Hill from Harvard and Andrew Saxon from the veterans affairs health system wrote that the research supports "anecdotal evidence from patients who describe a decreased need for opioids to treat chronic pain after initiation of medical cannabis pharmacotherapy".

Marijuana's effect on opioid use remains contested. Researchers at the National Institute on Drug Abuse found illicit marijuana use was associated with increased illicit opioid use. That study used data from the National Epidemiologic Survey on Alcohol and Related Conditions, which has produced analyses skeptical of the benefits of liberalizing marijuana.

Meanwhile, a 2014 JAMA Internal Medicine study would seem to support the new findings. That study found states with medical marijuana laws had higher overdose rates, but that those rates declined in years after medical marijuana laws were implemented, with an average 24.8% decline.

The Trump administration made curbing the epidemic a major public health target. Most efforts focus on criminal prosecutions of "drug dealers", including emphasizing the death penalty and civil litigation.

The attorney general, Jeff Sessions, opposes efforts to liberalize marijuana access, and claimed marijuana fueled the overdose epidemic.

No new money has been allocated to the crisis since Trump took office.

Further, Republican proposals for cuts to Medicaid would have disproportionately affected people in addiction treatment. Experts believe serious efforts to curb the epidemic will cost billions and will need to address bottlenecks in mental health infrastructure.

Both studies have limitations. First, the opioid crisis has touched every state in America, but there are regional variations. And marijuana laws vary significantly.

People who rely on Medicaid or Medicare Part D are generally poor, disabled and elderly, meaning the findings may not apply to the population in general. Further, it is unclear whether people avoided opioids when medical marijuana was available.

"Many companies and states (via taxes) are profiting from the cannabis industry while failing to support research at the level necessary to advance the science," wrote Hill and Saxon.

"This situation has to change to get definitive answers on the possible role for cannabis in the opioid crisis, as well as the other potential harms and benefits of legalizing cannabis."

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Modeling future earthquake and tsunami risk in southeast Japan

UMass Amherst, Smith College, Japanese scientists report, validate new techniques

AMHERST, Mass. - Geoscience researchers at the University of Massachusetts Amherst, Smith College and the Japanese Agency for Marine-Earth Science and Technology this week unveiled new, GPS-based methods for modeling earthquake-induced tsunamis for southeast Japan along the Nankai Trough. A Nankai-induced tsunami is likely to hit there in the next few decades, says lead author Hannah Baranes at UMass Amherst, and has the potential to displace four times the number of people affected by the massive Tohoku tsunami of 2011.

She and her doctoral advisor Jonathan Woodruff, with Smith College professor Jack Loveless and Mamoru Hyodo at the Japanese agency report details in the current *Geophysical Research Letters*. Baranes says, "We hope our work will open the door for applying similar techniques elsewhere in the world."

As she explains, after the unexpectedly devastating 2011 quake and tsunami, Japan's government called for hazard-assessment research to define the nation's worst-case scenarios for earthquakes and tsunamis. Baranes notes, "The government guideline has focused attention on the Nankai Trough. It's a fault offshore of southern Japan that is predicted to generate a magnitude 8 to 9 earthquake within the next few decades."

The team's research, supported by the National Science Foundation and a NASA graduate fellowship, began with a study of coastal lake sediments in Japan to establish long-term records of tsunami flooding. Between 2012 and 2014, Baranes and Woodruff collected sediment cores from lakes, looking for marine sand layers washed onshore by past extreme coastal floods. "These sand deposits get trapped and preserved at the bottoms of coastal lakes," she says. "We can visit these sites hundreds or even thousands of years later and find geologic evidence for past major flood events."

Results from Lake Ryuuoo, a small lake on an island in the Bungo Channel, show a surprising sand layer washed into Lake Ryuuoo by seawater rushing over a 13-foot-high barrier beach. "We were able to date the layer to the early 1700s, which is consistent with the known Nankai Trough tsunami event of record from 1707," Baranes says.

She adds, "We were a bit puzzled. The Bungo Channel is tucked between two of Japan's main islands and is relatively sheltered from Nankai Trough-generated tsunamis. Given recent tsunamis in the region, a minimum 13-foot tsunami in the channel seemed very unlikely." Further, she points out, the Bungo Channel area today has much sensitive and critical infrastructure, including the only nuclear power plant on the island of Shikoku. This gave the researchers "particular concern" for tsunami hazard there, so they decided to investigate their original finding further using numerical modeling techniques.

As Baranes explains, an earthquake is caused by plates slipping past each other along faults in the earth's crust. That slip causes the earth's surface to deform, to uplift in some places and sink, or subside, in others. "When earthquake-induced uplift occurs on the sea floor, it displaces the entire column of water above it and generates the wave that we call a tsunami," she adds. "We can simulate that process with numerical models."

She and Woodruff tried using one of the most widely-cited models for the 1707 Nankai Trough earthquake to flood Lake Ryuuoo, but this only generated a six-foot tsunami that came nowhere near overtopping the 13-foot barrier beach.

"At that point, we were still stumped," says Baranes. "But it wasn't long before we had a stroke of good luck in learning that a leading expert on tectonic modeling in Japan, Jack Loveless, is a professor just down the road at Smith College." Loveless uses very precise GPS measurements

of earth surface motion to model the extent and spatial distribution of frictional locking that causes fault stress to build up between earthquakes.

With Loveless, the team created earthquake scenarios based on GPS estimates of present-day frictional locking along the Nankai Trough and for the first time rigorously tested methods for creating potential future earthquake scenarios from the GPS measurements. They tested various methods for creating a suite of GPS-based earthquake scenarios and simulated the resulting ground surface displacement and tsunami inundation.

Baranes reports that they found GPS measurements of present-day earth surface motion around the Nankai Trough yield an earthquake of a similar magnitude and extent as the 1707 event, and their simulated tsunami heights are consistent with historical accounts of the 1707 event. As for matching the Lake Ryuuoo geologic record, she adds, "Our model earthquake scenarios showed the Bungo Channel region subsiding seven feet and lowering Lake Ryuuoo's barrier beach from 13 to six feet, such that a tsunami with a feasible height for an inland region easily flooded the lake."

Woodruff, who conducted the study as part of a Fulbright fellowship, says, "Although our methodology was well received, our result for the Bungo Channel was met with a lot of skepticism. We needed to find an independent method for validating it." They enlisted Hyodo, who had previously published earthquake scenarios based on models of the Nankai Trough's physical characteristics. His physical model yielded the same focused subsidence in the Bungo Channel, Woodruff reports. Baranes adds, "His model was also consistent with our GPS-based model in terms of earthquake magnitude, ground surface displacement and tsunami inundation. This was a really neat result because in addition to providing an independent line of evidence for significant tsunami hazard in the Bungo Channel, we demonstrated a connection between the Nankai Trough's physical characteristics and GPS measurements of surface motion."

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400-year-old documents reveal evidence of Japanese opium production and winemaking

17th century lord ordered his people to produce not only wine but also opium for medical purposes

Research from the Eisei Bunko Research Center of Kumamoto University reveals that Tadatoshi Hosokawa, a 17th century lord of Kyusyu, Japan, ordered his people to produce not only wine but also opium for medical purposes.

The Eisei Bunko Research Center of Kumamoto University, Japan has confirmed that both wine and opium were made for medical use in Lord Hosokawa's territory of Kokura nearly 400 years ago **Prof. Tsuguharu Inaba**

Wine making appears in 15th and 16th century Japanese trade documents, diaries, catalogues, and other texts. Christian missionaries and trade merchants delivered wine to Japan from Western Europe, and it continued as a luxury import item for over a century. It was believed that large-scale Japanese wine brewing began in the 1870's. However, as reported in 2016 by Kumamoto University's Eisei Bunko Research Center, the wine produced by the Hosokawa family in the Kokura Region began more than 200 years earlier in 1627. The researchers also showed that Lord Hosokawa ordered his liegeman, Taroemon Ueda, to make wine from wild grapes and send it to Edo, the former name of Japan's capital city.

A detailed investigation by the Eisei Bunko Research Center has recently clarified that wine was only produced from 1627 to 1630, and that Lord Hosokawa ordered the wine be sent to Edo for each of those four years. During that time, winemaker Taroemon was promoted to vassal for his successful wine and medicinal sake making techniques. Researchers found that black soybeans were used in addition to wild

grapes in the wine making process. Black soybeans promote fermentation and it is believed that the addition of black soybean yeast helped ferment the wild grapes, which have a relatively low sugar content. In essence, Lord Hosokawa's wine was made by fermenting wild grapes, rather than by simply soaking wild grapes in alcohol.

Surprisingly, the researchers found that the Hosokawa family was also producing opium in 1629. It is thought that opium imported from Nagasaki was used for medicinal purposes, such as sedation, analgesia, cough suppression, and hypnosis. The winemaker Taroemon became responsible for opium production, which started in the spring and produced about 1.27 kg of opium by autumn. A description of opium imports was found in the historical record from the previous year (1628), as was a note from Lord Hosokawa which read, "I am dissatisfied with the opium ordered (from Nagasaki) so it shall be returned." It may be inferred that Lord Hosokawa desired a commodity of higher quality.

Evidence of wine imports to the Kokura region is older than the description of opium imports. In 1623, a letter written by Lord Hosokawa ordered the purchase of sweet wine from Nagasaki. Two years later, in 1625, he again ordered the purchase of sweet wine. In 1631, after the Hosokawa Family's winemaking period appears to have ended, there were further instructions to procure 3.6 liters of fine wine for medicinal use, with imports continuing until 1639.

In 1638, a sick Lord Hosokawa entered the Shimabara Rebellion (an uprising of mostly Catholics that resulted in the prohibition of Christianity) on the side of the central government. He commanded that wine be sent to Kumamoto, which became his territory in 1632, for medical use on the battlefield. In that same year, another regional lord with an affinity for wine requested some through Lord Hosokawa's son. Lord Hosokawa replied, "I have contacted Nagasaki, but since wine is known to be used when converting to Christianity, merchants have stopped trading it to avoid suspicion that they may be Christians." Lord Hosokawa then arranged to send wine that was already in his possession. From these transcripts, researchers uncovered that both lords and merchants recognized that wine had become a prohibited Christian drink.

In the following year, Lord Hosokawa appears to have made one last order to send wine to Edo. After making this request to a Nagasaki merchant, documents from the Hosokawa family concerning wine have not been found. For an ailing Lord Hosokawa, it is inferred that wine had great medicinal value, but as a lord famous for his loyalty to the central government he could not continue to produce or import the forbidden Christian potation. His suffering is evident in the documents from this time period.

These historical texts show that Taroemon and his company had innovative technologies for making western food and western watches, and that Lord Hosokawa, who promoted him to an important position, was highly interested in such items and technologies. After the Shimabara Rebellion was suppressed, the central government prohibited port entry from Portuguese ships, eliminated Christianity, and restricted trade with Western Europe to only the Netherlands, which promised not to propagate Christianity in Japan. This marked the beginning of Japanese isolationism.

The research performed here by Kumamoto University's Eisei Bunko Research Center clearly shows that Lord Hosokawa had a passion for importing and producing wine during the twenty years before Japan's isolation. This research was published in the first issue of the *Bulletin of the Eisei-Bunko Research Center* in March 2018.

https://go.nature.com/2JmuKY5

Cancer researchers push to relax rules for clinical trials

US government examines whether criteria for participating in drug studies unnecessarily exclude some people.

Heidi Ledford

Nearly 20% of publicly funded cancer clinical trials in the United States fail because investigators are unable to enrol enough participants. Yet patients and their physicians often grow frustrated when they encounter the sometimes insurmountable requirements to join a study.

Now, researchers are pruning the lengthy lists of eligibility criteria for trials, in the hope of nixing unnecessary rules that might be hindering research. On 16 April, representatives of the US Food and Drug Administration (FDA) will meet stakeholders in Washington DC to discuss how restrictive eligibility criteria for clinical trials could be limiting patients' ability to access experimental treatments — and the quality of the data generated by the studies. The agency plans to use the information it gathers to develop guidelines for drug makers.

"You can have the greatest ideas and the greatest science," says Stuart Lichtman, an oncologist at Memorial Sloan Kettering Cancer Center in New York City. "But if no one goes on the study, what good is it?"

Eligibility requirements are typically intended to protect either the participant or the study. Participants with some degree of liver failure, for example, might not be allowed to take part in a trial of a drug thought to pose a risk to that organ. Criteria might also exclude people with conditions that could confound the results of a study.

But some researchers say that a 'cut-and-paste' mentality has increased clinical-trial requirements over time, as scientists have used previous trial protocols as templates for their next studies. That may needlessly restrict participation in a trial.

Fenced off

David Gerber, a lung-cancer specialist at the University of Texas Southwestern Medical Center in Dallas, and his collaborators have found[1] that 80% of clinical trials sponsored by the US National Cancer Institute excluded people with previous cancer diagnoses. Yet in many cases, he says, the previous cancer might have been caught early and removed successfully before the person developed lung cancer.

"What really frustrates me are instances when, in my mind and in my heart, it really seemed that the patients should be eligible," says Gerber. "If I had the exact same treatment outside of a clinical trial, I would give it to them without a concern."

A joint project by the FDA, the American Society of Clinical Oncology (ASCO) in Alexandria, Virginia, and the advocacy group Friends of Cancer Research in Washington DC has found that five common criteria for cancer-trial eligibility often could be amended without harming participants or the integrity of the trial. The team published its results last October[2].

People with HIV, for example, were once excluded from trials because of their poor prognosis. Now, with treatment, they often live as long as people without the virus and should be included in many cancer trials, the group concluded.

The team also recommended that in some cases, researchers should ease restrictions on people with organ dysfunction. That could be particularly important in light of the ageing populations in some countries, including the United States, says Lichtman. The restrictions were put in place when cancer treatments were more broadly toxic, he notes, and might not be necessary for the more targeted drugs available today.

Youth movement

One recommendation that could generate some controversy, he says, is a push to lower the age of eligibility for many adult cancer trials from 18 to 12. This reflects an understanding of basic drug metabolism, says Edward Kim, an oncologist at Atrium Health in Charlotte, North Carolina, who chaired the ASCO effort. "There is nothing magical about 18," he says. "Your body pharmacologically metabolizes drugs the same way at age 12 as it does at age 18."

But some adult-cancer physicians might feel uncomfortable treating younger people, and often that treatment takes place in specialized children's hospitals, unlike adult clinical trials. Furthermore, most adolescent cancers are rare, and can differ from adult cancers — even when they start in the same organ. This means the change might have little impact on research overall, says paediatric oncologist Peter Adamson of the Children's Hospital of Philadelphia in Pennsylvania. But it could still help individual adolescents who might otherwise have been excluded from trials, he adds: "It's the right thing to do."

Kim and others are now working to see their changes implemented, and have submitted their suggestions to an influential programme that coordinates clinical development of new therapies at the US National Cancer Institute. Kim says he has been contacted by researchers at large pharmaceutical companies who are eager to make the changes in their upcoming trials. And Gerber, who has been asked to give talks on his analyses around the world, says that countries with aging populations — such as Japan and Italy — would do well to reevaluate their own clinical trial criteria.

The result, Kim says, could be data that are more relevant to the people whom he and his colleagues treat every day. “These patients have these characteristics and they’re going to be treated eventually by their doctors,” he says . “This is the real world.”

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http://bit.ly/2H3QBoH

Long-term caffeine worsens symptoms associated with Alzheimer's disease

Mice exposed to coffee develop Alzheimer's disease in a very close manner to the human patients with early-onset form of the disease

It is well known that memory problems are the hallmarks of Alzheimer's disease. However, this dementia is also characterised by neuropsychiatric symptoms, which may be strongly present already in the first stages of the disorder. Known as Behavioural and Psychological Symptoms of Dementia (BPSD), anxiety, apathy, depression, hallucinations, paranoid, sundowning, etc. are part of an array of symptoms which are manifested in different manners depending on the individual patient. They are considered the strongest source of distress for patients and caregivers.

Coffee or caffeine has recently been suggested as a strategy to prevent dementia, both in patients with Alzheimer's disease and in normal ageing processes, due to its action in blocking molecules - adenosine receptors - which may cause dysfunctions and diseases in old age. However, there is some evidence that once the cognitive but also the NPS symptoms are developed, caffeine may exert opposite effects.

To address these issues, the study was conducted with normal ageing mice and familial Alzheimer's models. "The mice develop Alzheimer's disease in a very close manner to the human patients with early-onset form of the disease. They not only exhibit the typical cognitive problems but also a number of BPSD-like symptoms, so it is a valuable model to address whether the benefits of caffeine will be able to compensate its putative negative effects", explains Raquel Baeta-Corral, first author of the research.

"We had previously demonstrated the importance of the adenosine A1 receptor as the cause of some of caffeine's adverse effects. Now, we simulated a long oral treatment with a very low dose of caffeine (0.3 mg/mL) equivalent to three cups for a human coffee-drinker to answer a question which is relevant for patients with Alzheimer's, but also for the ageing population in general, and that in humans would take years to be solved since we should wait until the patients were aged' - explains Dr Björn Johansson, researcher and physician at the Karolinska University Hospital. The research was conducted from the onset of the disease up to more advanced stages, as well as in healthy age-matched mice.

The results indicate that caffeine alters the behaviour of healthy mice and worsens the neuropsychiatric symptoms of mice with Alzheimer's disease. The researchers discovered significant effects in the majority of variables studies, especially in relation to neophobia, a fear of everything new, anxiety-related behaviours, and emotional and cognitive flexibility.

In mice with Alzheimer's disease, the increase in neophobia and anxiety-related behaviours exacerbates their BPSD-like profile. Learning and memory, strongly influenced by anxiety, got little benefit from caffeine.

"Our observations of adverse caffeine effects in an Alzheimer´s disease model together with previous clinical observations suggest that an exacerbation of BPSD-like symptoms may partly interfere with the beneficial cognitive effects of caffeine. These results are relevant when coffee-derived new potential treatments for dementia are to be devised and tested", says Dr Lydia Giménez-Llort, researcher from the INc-UAB Department of Psychiatry and Legal Medicine and lead researcher of the project.

The results of the study form part of the PhD thesis of Raquel Baeta-Corral, first author of the article, and are the product of a research led by Lydia Giménez-Llort, Director of the Medical Psychology Unit, Department of Psychiatry and Legal Medicine and researcher at the UAB Institute of Neuroscience, together with Dr Björn Johansson, Researcher at the Department of Molecular Medicine and Surgery, Karolinska Institutet and the Department of Geriatrics, Karolinska University Hospital, Sweden, under the framework of the Health Research Fund project of the Institute of Health Carlos III*.

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NIH Turned Down Investigators Who Provoked Ire From Alcohol Industry

An email exchange and an unusual meeting suggest a connection between an institute's pursuit of industry support and the rejection of a grant application.

By Shawna Williams | April 3, 2018

A research funding request to the National Institutes of Health (NIH) may have been quashed as part of an effort to woo industry sponsors of another large study, reports *STAT News*. The evidence includes an email exchange between the director of the National Institute of Alcohol Abuse and Alcoholism (NIAAA) and an alcohol company executive pledging not to fund the type of study that linked alcohol advertising to teen drinking.

The news report builds on earlier revelations by *Wired* and *The New York Times* that NIAAA scientists courted industry funders of a study on the health effects of moderate alcohol consumption by emphasizing the probability that the results would favor such consumption. *STAT* adds fresh evidence that conflicts of interest may have influenced decisions at the National Institutes of Health (NIH), the largest federal funder of biomedical research.

In the article published by *STAT* yesterday (April 2), Michael Siegel, a community health researcher at Boston University School of Public Health, gives an account of a 2015 meeting in which he and a coinvestigator on an NIAAA-funded study were summoned to the institute to discuss the work. In the meeting, George Koob, the NIAAA Director, "kept trying to downplay the importance of this research, insisting it was not advertising that made teenagers drink but peer pressure and parents. He was giving us the industry line," Siegel tells *STAT*. A new proposal by the coinvestigator to study social media activity by alcohol companies was rejected soon afterward, despite receiving high marks from reviewers.

As it turned out, months after assuming the NIAAA directorship in 2014, Koob had written an email to Samir Zakhari of the Distilled Spirits Council, *STAT* found, promising that research like Siegel's advertising project would not be funded again. Zakhari thanked Koob, responding in part, "This kind of research not only wastes precious research dollars but also damages NIAAA's stature within the NIH community." In an email to *STAT*, Koob stated his exchange with Zakhari "was to convey that I had no intention of supporting research that was not of the highest scientific quality."

In October 2017, *Wired* reported that for the first time, the alcohol industry was expected to partially sponsor an NIH study, in which thousands of participants would be randomly assigned to either have an alcoholic drink of their choice each day for six years (its cost reimbursed by the investigators), or to abstain. Their health outcomes and mortality rates would be tracked. At the time, five alcohol corporations had pitched in a total of $67 million for the project. Koob and Peggy Murray, who directs the institute's Global Alcohol Research

Program, had both appeared in an Anheuser-Busch InBev video promoting the company's sponsorship of research.

Then, last month, *The New York Times* reported that NIAAA had "waged a vigorous campaign to court the alcohol industry." One slide from the agency presented to an industry audience states, "A definitive clinical trial represents a unique opportunity to show that moderate alcohol consumption is safe and lowers risk of common diseases."

Siegel, who reviewed the presentation, told the *Times* that the study "is not public health research—it's marketing. . . . They're admitting the trial is designed to provide a justification for moderate drinking. That's not objective science."

http://bit.ly/2uY374v

Meet "Dracula," the Largest Pterosaur Found to Date

A reconstruction of the reptile, found in Transylvania, is on display in Germany

By Yasemin Saplakoglu

Between 240 and 66 million years ago, gigantic reptiles ruled the skies. Pterosaurs—close cousins of dinosaurs—may not have breathed fire, but with their strong limbs and light, hollow-boned skeletons, they were the first vertebrates to fly.

An artist's reconstruction of Dracula, the largest pterosaur found to date. **Frederik Spindler, Altmühltal Dinosaur Museum**

Unlike bats, which have three fingers embedded in their wings and one free digit for climbing, pterosaurs had one elongated finger that formed the front edge of each wing and three exposed digits for running and climbing. Some earlier species had tails that scientists believe were used to help maneuver, but these disappeared as the pterosaurs evolved into more graceful flyers.

In 2009 Romanian scientists discovered the bones of a new pterosaur species among a fairy-tale landscape of hills and rock structures near a small town called Sebes in Romania's Transylvania region. They nicknamed their find "Dracula."

Visitors can gauge the size of Dracula via a reconstruction at a new pterosaur exhibit at the Altmühltal Dinosaur Museum in Denkendorf, Germany. The scientists estimate the creature had a wingspan of 12 meters and stood 3.5 meters tall. **Axel Schmidt, Altmühltal Dinosaur Museum**

Using the fragments of bone as their guide, scientists reconstructed a model of the creature—which they say is the largest pterosaur found to date, reaching around 3.5 meters high with an estimated 12-meter wingspan. The reconstruction is now on display as part of a new pterosaur exhibit at the Altmühltal Dinosaur Museum in Denkendorf, Germany. The exhibit also separately showcases the original specimen's excavated bones.

The size of Dracula's neck is comparable to the width of a full-grown man, according to the museum's press release. Scientists think he must have weighed at least half a ton and was at the top of the food chain. **Axel Schmidt, Altmühltal Dinosaur Museum**

Researchers are not sure whether pterosaurs this size could actually fly. According to the exhibit's introductory information there is no conclusive evidence to the contrary, but Dracula has a wrist joint that differs greatly from that of other species that have been found, which could mean it was not meant for flight. But if it did fly, Dracula would have been quite a sight (and probably sound): a small-aircraft-sized animal circling the skies, throwing giant shadows over land-dwellers below.

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Study reveals a way to make prostate cancer cells run out of energy and die

Cancer cells lacking PTEN are particularly vulnerable to drugs that impair their energy-producing mitochondria

Cold Spring Harbor, NY - Scientists at Cold Spring Harbor Laboratory (CSHL) have discovered that cells lacking the tumor-suppressor protein PTEN--a feature of many cancers-- are particularly vulnerable to drugs that impair their energy-producing mitochondria. Such drugs induce them to literally eat themselves to death, the research shows.

Unlike normal cells, cells without PTEN seem driven to preserve their mitochondria at all costs, says the team leader, CSHL Professor Lloyd Trotman. He and colleagues have found that when such cells are treated with certain mitochondrial inhibitors, they consume vast quantities of glucose to fuel these efforts. As a result, they quickly run out of energy and die.

Some mitochondrial inhibitors, including the widely prescribed diabetes medication metformin - one of the most widely taken drugs in the world -- are already being evaluated in clinical trials for their ability to prevent or treat many types of cancer.

The new findings, reported today in *Cell Reports*, suggest that such drugs have the potential to eliminate cancer cells at doses that leave healthy cells intact. The timing is critical, however. When glucose levels are high, this window of opportunity is completely lost. "The hope is that carefully timed administration of these drugs can generate a much better window of selective killing," Trotman says.

Two related compounds, both derived from the root of the same plant, emerged from a screen performed by the team. Both killed cells missing PTEN and another tumor suppressor, p53. Loss of these together is common among men with advanced prostate cancer and is associated with highly metastatic disease. The two drugs had little effect on nearly identical cells with functional PTEN. One, rotenone, is a known mitochondrial inhibitor. In collaboration with Navdeep Chandel at Northwestern University, Trotman's lab established that the second compound, deguelin, works in much the same way.

Oddly, further experiments with deguelin revealed that it shuts down mitochondrial function just as well in cells with PTEN as it does in cells that lack it. So why did cells with PTEN tolerate the toxic compound so much better?

The answer has to do with how cells use glucose, say co-first authors of the paper, postdoctoral researchers Adam Naguib and Grinu Mathew. They found that cells without PTEN use glucose from their environment to generate the energy-rich molecule ATP, which they import into mitochondria to keep them intact. "That's the exact opposite of what mitochondria are supposed to be doing," Trotman points out. "Mitochondria are supposed to generate ATP for the rest of the cell." For these cells lacking PTEN, unless there is an endless supply of glucose, they quickly use up the sugar and die.

Eventually, any cell subjected to mitochondrial inhibitors will run out of energy and die. Cells without PTEN just get there much faster, Trotman says. That means it could be critical to administer mitochondrial inhibitors to cancer patients when their blood sugar is low, he says. That's counter to how metformin and related medications are currently tested in cancer, because the protocol used to manage diabetes calls for the drugs to be taken immediately after meals.

Funding: American Cancer Society, Pershing Square Sohn Foundation, U.S. Department of Defense, National Institutes of Health, American Cancer Society, Robertson Research Fund of CSHL, CSHL Cancer Center Support Grant from the NIH.

Citation: Naguib A. et al, "Mitochondrial complex I inhibitors expose a vulnerability for selective killing of Pten-null cells" appears online in Cell Reports April 3, 2018.

http://bit.ly/2H04N1O

Losing your nest egg can kill you

People have a 50 percent higher risk of death if they suffer a shocking financial loss

CHICAGO --- A sudden loss of net worth in middle or older age is associated with a significantly higher risk of death, reports a new Northwestern Medicine and University of Michigan study.

When people lose 75 percent or more of their total wealth during a two-year period, they are 50 percent more likely to die in the next 20 years, the study found.

"We found losing your life-savings has a profound effect on person's long-term health," said lead author Lindsay Pool, a research assistant professor of preventive medicine at Northwestern University Feinberg School of Medicine. "It's a very pervasive issue. It wasn't just a few individuals but more than 25 percent of Americans had a wealth shock over the 20 years of the study."

Though the rate of savings loss spiked during the Great Recession, middle- and older-age Americans consistently lost savings across the 20-year period, regardless of the larger economic climate.

The study, which will be published April 3 in JAMA, is the first to look at the long-term effects of a large financial loss.

"Our findings offer new evidence for a potentially important social determinant of health that so far has not been recognized: sudden loss of wealth in late middle or older age," said senior author Carlos Mendes de Leon, professor of epidemiology and global public health at University of Michigan's School of Public Health.

The study also examined a group of low-income people who didn't have any wealth accumulated and who are considered socially vulnerable in terms of their health. Their increased risk of mortality over 20 years was 67 percent. "The most surprising finding was that having wealth and losing it is almost as bad for your life expectancy as never having wealth," Pool said. The likely cause of the increased death risk may be twofold. "These people suffer a mental health toll because of the financial loss as well as pulling back from medical care because they can't afford it," Pool said.

The new study builds on prior research in the wake of the Great Recession from 2007 to the early 2010s. Those studies examined short-term health effects such as depression, blood pressure and other markers of stress that changed as peoples' financial circumstances took a nosedive.

The study was based on data from the Health and Retirement Study from the National Institute on Aging (NIA). Started in 1992, the longitudinal study follows a representative group of U.S. adults 50 years and older every two years. More than 8,000 participants were included in the Northwestern study.

"This shows clinicians need to have an awareness of their patients' financial circumstances," Pool said. "It's something they need to ask about to understand if their patients may be at an increased health risk."

Next, Pool and colleagues will investigate the mechanisms that lead to higher mortality after a big financial loss. "Why are people dying, and can we intervene at some point in a way that might reverse the course of that increased risk?" she said.

This work was supported by NIA grant T32AG027708. The Health and Retirement Study is sponsored by NIA grant U01AG009740 and is conducted by the University of Michigan. NIA is part of the National Institutes of Health.

http://bit.ly/2EpdPQU

New 'Nightmare' Bacteria Are Popping Up All Over the US

What's worse than "nightmare" bacteria that are resistant to nearly all antibiotics?

By Rachael Rettner, Senior Writer

New nightmare bacteria that have the potential to spread their resistance genes to germs in hospitals around the country.

Researchers say that last year, they identified more than 200 cases of these "nightmare" bacteria with new or rare antibiotic-resistance genes, according to a new report from the Centers for Disease Control and Prevention (CDC). These rare types of antibiotic-resistant bacteria popped up all over the country, in 27 states.

The good news is that researchers have come up with an aggressive strategy to identify, track and contain these germs, which appears to help stop their spread, according to the report.

"We are working to get in front of them before they do become common," Dr. Anne Schuchat, principal deputy director of the CDC, said at a news conference today (April 3). "We have data showing an

aggressive approach works" to halt the spread of these new threats, Schuchat said.

Nightmare bacteria

Antibiotic-resistant bacteria are, unfortunately, a common problem in medicine today — more than 2 million Americans get an antibiotic-resistant infection each year, and 23,000 die from these infections, according to the CDC. Antibiotic-resistant infections are a major concern for health care workers because they are difficult to treat.

One particularly concerning type of antibiotic-resistant bacteria is called carbapenem-resistant Enterobacteriaceae, or CRE, which has been dubbed "nightmare" bacteria. These bacteria are not only resistant to many antibiotics but are also highly lethal, killing up to 50 percent of infected patients, according to the CDC.

Doctors liken the spread of CRE and other antibiotic-resistant germs to a wildfire, which is difficult to contain once it spreads widely. Therefore, doctors are trying to stamp out new or unusual types of antibiotic resistance when they first appear — to extinguish the "spark" before it has a chance to grow and spread, Schuchat said.

To aid in these efforts, the CDC recently established the Antibiotic Resistance Laboratory Network (ARLN), a network of labs across the country that test patients' samples for highly resistant bacteria and track emerging antibiotic resistance.

In the first nine months of 2017, ARLN tested more than 5,700 samples of highly resistant bacteria, including CRE, from hospitals, nursing homes and other health care facilities around the country. Of the 1,400 CRE-positive samples tested, 221 samples (15 percent) had new or unusual types of antibiotic resistance, the report said.

"I was surprised by the numbers" of bacteria with unusual antibiotic resistance, Schuchat said. "This was more than I was expecting."

When researchers detected a case of unusual antibiotic resistance, they screened other patients in the facility to see if some had "silent" infections, meaning they were infected but weren't showing symptoms. They found that about 1 in 10 people screened had a silent infection, meaning that "unusual resistance may have spread and could have continued spreading if left undetected," Schuchat said.

Preventing spread

Fortunately, researchers were often able to stop the spread of these unusual antibiotic-resistant bacteria with an aggressive "containment" strategy. This strategy involves rapidly identifying antibiotic-resistant germs at a given facility, assessing the facility for gaps in infection control, screening other patients to see if any are "silent" carriers of the infection, coordinating a response with other facilities in the area that may transfer patients to and from the affected facility, and continuing these steps until transmission of the antibiotic-resistant bacteria is controlled.

This containment strategy can "help stop the spread of unusual types of antibiotic resistance that haven't yet spread widely," Schuchat said.

Using a mathematical model, the researchers estimated that implementing this strategy could prevent as many as 1,600 new CRE infections in three years, or a 76-percent reduction in cases.

Schuchat stressed that efforts to fight antibiotic resistance are ongoing. "We need to do more, and we need to do it faster and earlier with each new antibiotic-resistance threat," Schuchat said.

https://wb.md/2JrrfPV

The Anti-inflammatory Diet's Surprising Benefits in Children

Fighting Back Against Inflammation

Diane L. Barsky, MD April 03, 2018

Hello. I am Diane Barsky, attending physician in the Division of Gastroenterology, Hepatology, and Nutrition at the Children's Hospital of Philadelphia (CHOP). I have a special interest in nutrition for children, and today I'd like to talk to you about the anti-inflammatory diet.

Why should you consider an anti-inflammatory diet for your patients or for yourself? As you know, inflammation is a natural way the body reacts to protect us and help us heal. But sometimes chronic

inflammation goes awry. Those cycles of cytokines and anti-inflammatory mediators can continue to escalate; and, in turn, the body's immune response produces mediators that allow inflammation to occur in an ongoing and out-of-control manner. This chronic inflammation can increase our lifetime risk for obesity, type 2 diabetes, heart disease, and some forms of cancer as well as other autoimmune diseases.

Our goal is to maintain health, prevent the chronic inflammatory cycle if possible, or utilize the diet when it occurs. In doing so, we need to remember that food is not a replacement for medicine but a part of medicine for prevention and intervention.

The Basics of the Anti-inflammatory Diet

What is an anti-inflammatory diet? It's a diet based on two ancient healthy patterns of eating: the Asian diet and the Mediterranean diet. The combination of the two is thought to be one of the healthiest ways of eating on a daily basis. The Mediterranean diet has actually been studied for the past 30 years.

The anti-inflammatory diet encourages fresh foods and avoids processed foods, artificial flavors, high-fructose corn syrup, and trans fat. Instead, it incorporates healthy monounsaturated and polyunsaturated fats, which have a higher omega-3 to omega-6 fatty acid ratio. It includes a variety of sources of plant proteins that are high in fiber with a low glycemic index, such as beans and other legumes. It is lower in saturated animal fat and thus includes healthier fats. The emphasis is on fruits and vegetables that have important antioxidants as well as herbs, nuts, seeds, and green tea.

What are the mechanisms by which the anti-inflammatory diet works? The phytochemicals in this diet have key anticarcinogenic and anti-cardiovascular disease properties, promote important antioxidants (eg, polyphenols, flavonoids), and are high in oleic acid and polyunsaturated fatty acids and low in monounsaturated fatty acids, which promote the anti-inflammatory, antithrombotic prostaglandin pathway.

Because this diet is high in fiber and has a low glycemic index, there is a decreased risk for diabetes. The higher magnesium content reduces inflammation and improves cognitive ability. Spices that are rich in phytochemicals such as ginger, garlic, cayenne, black pepper, rosemary, and turmeric, are associated with maintaining a favorable microbiome. Other phytochemicals in these diets (eg, alpha linolenic acid, beta-carotene, curcumin) offer important anti-inflammatory mediators.

Benefits in a Pediatric Population

The Asian diet is relatively less studied than the Mediterranean diet. However, the ongoing China Project from Cornell University evaluated approximately 6500 people and demonstrated an association that the consumption of the Asian diet in rural China protected against many of the cancers we see in Western civilization.[1] There was also a decrease in the incidence of cardiovascular disease and significantly greater longevity. However, as soon as the rural Chinese moved into cities and acquired the Western diet, a much higher incidence of diabetes, breast cancer, colon cancer, and cardiovascular disease was reported.

The anti-inflammatory Mediterranean diet has been studied in pediatrics for the past 20 years. In that time, it has been associated with not only a reduction in the severity of asthma and allergies in children but a reduction in the recurrence of asthma and also in the prevention of chronic asthma.[2] A study in an Italian population found that the earlier in life subjects adhere to this diet, the more it reduced the risk for nonalcoholic steatohepatitis (NASH) and obesity in children.[3] The effect was also seen in children who already had NASH, who nonetheless had a reduction in the severity and even a regression the more adherent they were to the diet.

A recent study in *Pediatrics*[4] linked attention-deficit/hyperactivity disorder (ADHD) to the Mediterranean diet. It is not clear if those with ADHD are more likely to consume an unhealthy diet of fast food and processed foods, or if those following the Mediterranean diet have less of a risk for ADHD. That association should be monitored in future studies.

Two Regional Diets, Connected by Health

Traditional Mediterranean and Asian diets have many similarities. They are rich in vegetables, with a primary focus on legumes, fruits, and fresh foods. Both are moderately rich in fish and associated omega-3 fatty acids. They include some lean meats and eggs but avoid processed foods, artificial flavoring, high-fructose corn syrup, saturated fat, and trans fat. They're high in antioxidants that protect the body from many chronic diseases.

There is also a social component to these diets, with their focus on slower eating together with the extended family. It is a whole-foods approach, with minimal commercial processing and using more organic practices that minimize herbicides, insecticides, and toxic residues. It emphasizes the interconnection between the food, the people, and the land. Adherents know where their food is coming from, either through their own agriculture or through their local villages and neighbors.

The Mediterranean diet is composed of healthy fats with high monounsaturated fats, such as olives and olive oil, nuts, and seeds. It includes spices, eggs, and meat, but with a focus on white meat and soy proteins. It also advises the regular consumption of water.

The traditional Asian diet focuses on oily fish; miso soup; and fermented foods such as kimchi, pickles, and natto (fermented soybeans) that encourage and stimulate a favorable microbiome. This is associated with a lower incidence of irritable bowel disease.[5] The mushrooms consumed in the Asian diet (shiitake, enoki, and oyster) are actually now being studied in cancer centers in the United States because they've been linked to improvement in cancer risk and recurrence. The inclusion of herbs, medicinal garnishes, spices, turmeric, phenol, and green seaweed, just to name a few aspects of this diet, offer important antioxidants.

Conclusion

The anti-inflammatory diet is a combination of Mediterranean and Asian diets. It incorporates vegetables (4-6/day) and emphasizes fruit, fish, and plant proteins. It includes healthier fats (eg, canola oil, olive oil, seeds, nuts, avocados) that provide omega-3s, which promote a different prostaglandin pathway that is not proinflammatory. This diet highlights the intake of antioxidant-rich foods as well as beverages like green tea. Remember, it is not only about nutrition but a healthier lifestyle.

For those seeking an informational resource, CHOP offers a pediatric anti-inflammatory diet pyramid on its website.

With these diets, we are promoting a lifelong attitude of healthy eating, family togetherness, and physical activity. It's all-important in preventing chronic disease or managing inflammatory diseases in pediatrics. Thank you.

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http://bit.ly/2GHowA8

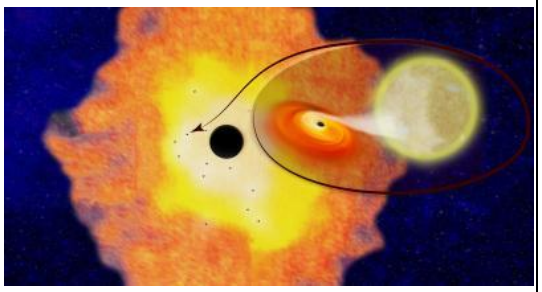
New study suggests tens of thousands of black holes exist in Milky Way's center

A dozen black holes gathered around the supermassive black hole in the center of the Milky Way Galaxy

A Columbia University-led team of astrophysicists has discovered a dozen black holes gathered around Sagittarius A* (Sgr A*), the supermassive black hole in the center of the Milky Way Galaxy. The finding is the first to support a decades-old prediction, opening up myriad opportunities to better understand the universe.

"Everything you'd ever want to learn about the way big black holes interact with little black holes, you can learn by studying this distribution," said Columbia Astrophysicist Chuck Hailey, co-director of the Columbia Astrophysics Lab and lead author on the study.

"The Milky Way is really the only galaxy we have where we can study how supermassive black holes interact with little ones because we simply can't see their interactions in other galaxies. In a sense, this is the only laboratory we have to study this phenomenon." The study appears in the April 5 issue of Nature.



Columbia astrophysicists have discovered 12 black hole-low mass binaries orbiting Sgr A* at the center of the Milky Way galaxy. Their existence suggests there are likely about 10,000 black holes within just three light years of the Galactic Center. **Columbia University**

For more than two decades, researchers have searched unsuccessfully for evidence to support a theory that thousands of black holes surround supermassive black holes (SMBHs) at the center of large galaxies.

"There are only about five dozen known black holes in the entire galaxy -- 100,000 light years wide -- and there are supposed to be 10,000 to 20,000 of these things in a region just six light years wide that no one has been able to find," Hailey said, adding that extensive fruitless searches have been made for black holes around Sgr A*, the closest SMBH to Earth and therefore the easiest to study. "There hasn't been much credible evidence."

He explained that Sgr A* is surrounded by a halo of gas and dust that provides the perfect breeding ground for the birth of massive stars, which live, die and could turn into black holes there. Additionally, black holes from outside the halo are believed to fall under the influence of the SMBH as they lose their energy, causing them to be pulled into the vicinity of the SMBH, where they are held captive by its force.

While most of the trapped black holes remain isolated, some capture and bind to a passing star, forming a stellar binary. Researchers believe there is a heavy concentration of these isolated and mated black holes in the Galactic Center, forming a density cusp which gets more crowded as distance to the SMBH decreases.

In the past, failed attempts to find evidence of such a cusp have focused on looking for the bright burst of X-ray glow that sometimes occurs in black hole binaries

"It's an obvious way to want to look for black holes," Hailey said, "but the Galactic Center is so far away from Earth that those bursts are only strong and bright enough to see about once every 100 to 1,000 years."

To detect black hole binaries then, Hailey and his colleagues realized they would need to look for the fainter, but steadier X-rays emitted when the binaries are in an inactive state.

"It would be so easy if black hole binaries routinely gave off big bursts like neutron star binaries do, but they don't, so we had to come up with another way to look for them," Hailey said. "Isolated, unmated black holes are just black -- they don't do anything. So looking for isolated black holes is not a smart way to find them either. But when black holes mate with a low mass star, the marriage emits X-ray bursts that are weaker, but consistent and detectable. If we could find black holes that are coupled with low mass stars and we know what fraction of black holes will mate with low mass stars, we could scientifically infer the population of isolated black holes out there."

Hailey and colleagues turned to archival data from the Chandra X-ray Observatory to test their technique. They searched for X-ray signatures of black hole-low mass binaries in their inactive state and were able to find 12 within three light years, of Sgr A*. The researchers then analyzed the properties and spatial distribution of the identified binary systems and extrapolated from their observations that there must be anywhere from 300 to 500 black hole-low mass binaries and about 10,000 isolated black holes in the area surrounding Sgr A*.

"This finding confirms a major theory and the implications are many," Hailey said. "It is going to significantly advance gravitational wave research because knowing the number of black holes in the center of a typical galaxy can help in better predicting how many gravitational wave events may be associated with them. All the information astrophysicists need is at the center of the galaxy."

Hailey's co-authors on the paper include: Kaya Mori, Michael E. Berkowitz, and Benjamin J. Hord, all of Columbia University; Franz E. Bauer, of the Instituto de Astrofísica, Facultad de Física, Pontificia, Universidad Católica de Chile, Millennium Institute of Astrophysics, Vicuña Mackenna, and the Space Science Institute; and Jaesub Hong, of Harvard-Smithsonian Center for Astrophysics.

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Ancient origins of viruses discovered

New study transforms understanding of virus origins and evolution

Research published today in Nature has found that many of the viruses infecting us today have ancient evolutionary histories that date back to the first vertebrates and perhaps the first animals in existence.

The study, a collaboration between the University of Sydney, the China Center for Disease Control and Prevention and the Shanghai Public Health Clinical Centre, looked for RNA viruses in 186 vertebrate species previously ignored when it came to viral infections.

The researchers discovered 214 novel RNA viruses (where the genomic material is RNA rather than DNA) in apparently healthy reptiles, amphibians, lungfish, ray-finned fish, cartilaginous fish and jawless fish.

"This study reveals some groups of virus have been in existence for the entire evolutionary history of the vertebrates - it transforms our understanding of virus evolution," said Professor Eddie Holmes, of the Marie Bashir Institute for Infectious Diseases & Biosecurity at the University of Sydney.

"For the first time we can definitely show that RNA viruses are many millions of years old, and have been in existence since the first vertebrates existed.

"Fish, in particular, carry an amazing diversity of viruses, and virtually every type of virus family detected in mammals is now found in fish. We even found relatives of both Ebola and influenza viruses in fish."

However, Professor Holmes was also quick to emphasise that these fish viruses do not pose a risk to human health and should be viewed as a natural part of virus biodiversity.

"This study emphasises just how big the universe of viruses - the virosphere - really is. Viruses are everywhere. "It is clear that there are still many millions more viruses still to be discovered," he said.

The newly discovered viruses appeared in every family or genus of RNA virus associated with vertebrate infection, including those containing human pathogens such as influenza virus.

Because the evolutionary histories of the viruses generally matched those of their vertebrates, the researchers were able to conclude that these viruses had long evolutionary histories.

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Tourniquet practice adopted from the military saves lives and limbs in civilians

National Stop the Bleed campaign to train the public to use tourniquets immediately after a severe bleeding injury validated by Texas Tourniquet Study Group

CHICAGO - Civilian trauma medicine has adopted many methods and techniques that have been developed and tested on the battlefield. One such technique, the use of tourniquets to stanch early bleeding in arms and legs, has been shown to improve a trauma victim's chance of survival. Although the use of tourniquets in civilians had been previously studied, its survival benefit had remained unclear. However, new study results published as an "article in press" on the website of the *Journal of the American College of Surgeons* demonstrate that the use of tourniquets improves survival in civilian trauma victims. These

findings are very timely as the first ever National Stop the Bleed Day was just observed across the U.S. on March 31.

"This is the first time that we were actually able to prove the survival benefit of using the tourniquet in the civilian population," said lead study author and trauma surgeon Pedro G. R. Teixeira, MD, FACS, of the University of Texas at Austin, Dell Medical School.

While tourniquets may seem like a simple way to stop serious bleeding, their use had fallen out of favor in both civilian and military medicine in the 20th Century. "During the Korean and the World Wars, there was a lot of concern about tourniquet use and they got a bad reputation, but much of the problem was that tourniquets were left in place too long, cutting circulation to the extremity for many, many hours," Dr. Teixeira said. Since then, trauma surgeons have become more sophisticated about tourniquet use.

"What we learned from more recent conflicts in the Middle East is that when tourniquets are applied early and removed in a timely fashion and the definitive repair is performed, also in a timely fashion, they actually have a significant role in preventing death from severe blood loss from an extremity injury," Dr. Teixeira said.

For the study, the Texas Tourniquet Study Group evaluated 1,026 patients with vascular injuries of the arms or legs admitted to 11 urban Level I trauma centers--the highest level for trauma centers--in Texas from 2011 to 2016. A prehospital tourniquet was used in 17.6 percent of the cases, although tourniquet use varied widely among individual centers, ranging from 62 percent to 1.4 percent.

Overall, 9.6 percent of the study patients had amputations, but more than one-third of them--35.7 percent--had received a tourniquet. Among the amputation patients, those who received a tourniquet had significantly lower mortality rates than those who did not--2.9 percent vs. 7.9 percent (adjusted p=0.015). The non-tourniquet group had almost six times greater odds of death (odds ratio 5.86, 95 percent confidence interval, range 1.41 to 24.47).

Dr. Teixeira explained that the types of civilian settings in which tourniquets can be used are automobile and motorcycle accidents, pedestrian struck by a vehicle, stab wounds, and gunshot wounds. "All these types of mechanisms that have a major hemorrhage coming from either an arm or a leg are amendable to having a tourniquet placed to stop that bleeding and allow that patient to survive long enough to reach a trauma center and get taken care of," Dr. Teixeira said.

Tourniquets work best when they are applied as early as possible at the site of the injury. "The ideal person to apply that tourniquet is the person who can do it the quickest immediately after the wound is identified," said Dr. Teixeira. "That scenario is the highest chance for the patient to survive."

The study noted efforts to increase the use of tourniquets in the civilian population, most notably the American College of Surgeons forming the Joint Committee to Create a National Policy to Enhance Survivability From Mass Casualty Shooting Events as a response to recent mass shootings. Their recommendations became known as the "Hartford Consensus." In 2015, the White House issued a call to action called the Stop the Bleed campaign to train bystanders to help in a bleeding emergency. Tourniquet use is a key component of that call to action.

"The idea is that the same way that we have defibrillators in public spaces for patients that have a cardiac arrest, we would have bleeding control kits in public spaces too, allowing for tourniquet application by someone who has had minimal training for a patient that has an injury resulting in bleeding from a limb," Dr. Teixeira said.

He acknowledged that there is a cost involved in having tourniquets available for general use, but the study may help justify that cost. "Being able to demonstrate that tourniquets actually do the job they're supposed to do is important and supports the recommendations by the Stop the Bleed campaign, contributing to reducing mortality from bleeding on the streets of America and elsewhere," Dr. Teixeira said.

The study results were first presented in September 2017 at the 76th annual meeting of the American Association for the Surgery of Trauma and Clinical Congress of Acute Care Surgery in Baltimore.

The study involved 18 coauthors comprising the Texas Tourniquet Study Group.

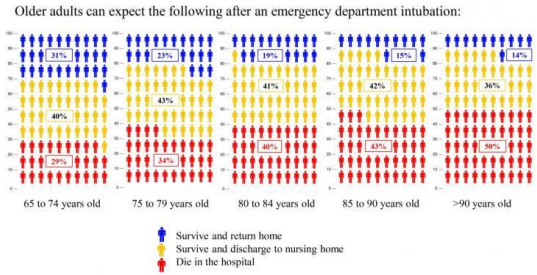
Citation: Civilian Prehospital Tourniquet Use is Associated with Improved Survival in Patients with Peripheral Vascular Injuries. Journal of the American College of Surgeons. Available at: http://www.journalacs.org/article/S1072-7515(18)30101-7/abstract.

http://bit.ly/2GBG3Oh

One in 3 older patients die following emergency department intubation

Nationwide analysis reveals large number of patients 65 and older died in the hospital or were discharged to a nursing home following emergency intubation

Intubation in the emergency department is common and can prevent a patient from dying from a reversible condition. While the benefits of such intubation for young and otherwise healthy patients are clear, it is less obvious whether the benefits of intubation outweigh the risks in older patients.



The researchers found that in-hospital mortality following intubation was worse for patients over 90 than any other group, with 50 percent of those patients dying in the hospital following intubation, and 14 percent of these patients being discharged home. However, the outcomes were not drastically better for patients on the younger side of the study, with 29 percent patients between 65 and 74 dying in hospital following emergency intubation, and only 31 percent of these patients being discharged home. **Kei Ouchi, Brigham and Women's Hospital**

A new study by researchers at Brigham and Women's Hospital investigated the outcomes for patients aged 65 and older after emergency department intubation across a variety of conditions and disease. Their results are published in *Journal of the American Geriatrics Society*.

"A surprisingly large number of older patients who underwent intubation in the emergency department either died in the hospital or were discharged to a nursing home," said lead author Kei Ouchi, MD, MPH, of the Department of Emergency Medicine at BWH. "On average, one-third of patients over 65 who received intubation in the emergency department died in the hospital."

The retrospective study examined the outcomes of more than 41,000 adults aged 65 and older who were intubated in the emergency departments from 262 hospitals across the U.S. between 2008 and 2015. The study found that, overall, 33 percent of these patients died in the hospital after receiving intubation, 24 percent were discharged home, and 41 percent were discharged to a location other than home, such as a nursing home.

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"It's important that older patients, their families and their care team are aware of this information and can use it to make informed, shared decisions about whether the patient should receive emergency intubation should such intubation be needed," said Ouchi. "It is difficult to make informed decisions on whether to provide intubation in older patients in an emergency situation because this is a very stressful and emotional time. Older patients, their families, and care providers are encouraged to make this decision before emergency situations requiring emergency department admission and intubation arise.

There was no conflict of interest or sponsor for any of the authors of the study.

Paper cited: Kei Ouchi, MD, MPH et al., "Prognosis After Emergency Department Intubation to Inform Shared Decision-Making". Journal of the American Geriatrics Society *DOI: https://doi.org/10.1111/jgs.15361*

http://bit.ly/2uNdPui

Could Boeing's 'Starliner' Spacecraft Be a Next Step for Reaching the Moon and Beyond?

Automated spacecraft designed to transport people into low Earth orbit could be have its first voyage as early as this summer

By Mindy Weisberger, Senior Writer

WASHINGTON — Picture this: A team of space travelers blasts off from Earth in a fully automated shuttle that carries them to an outpost orbiting around the moon, where they will embark on a voyage to Mars.

An artist's rendition shows Boeing's CST-100 Starliner heading for a rendezvous with the International Space Station. **Boeing**

Though it sounds like science fiction, this fantastic journey may be closer than you think: An automated spacecraft designed to transport people into low Earth orbit could be ready for its maiden (uncrewed) voyage as early as this summer.

The new spacecraft, called the Crew Space Transportation (CST)-100 Starliner, is being developed in partnership with NASA by a private company generally associated with commercial airplanes: Boeing. The Starliner is capable of carrying up to seven passengers as far as the International Space Station (ISS) in low Earth orbit.

But that milestone will be just the first step toward eventually flying travelers to the moon and then Mars, experts here at the Future Con panel "Intergalactic to Planetary: Science Fiction to Science Fact" told audience members on March 30.

Starliner is intended to be the world's first commercial space vehicle, a reusable capsule designed for land-based returns. It will also be fully autonomous, to reduce training time for its crews, according to the project website.

Next stop: Mars

Starliner will initially carry astronauts and science experiments to the ISS, panelist and Boeing representative Tony Castilleja Jr. told the audience. The spacecraft's automated flight system requires only one astronaut to fly it, using tablets and touch screens to interact with the mostly self-piloting vehicle, said panelist Jim May, a Boeing software engineer.

Starliner, scheduled to launch by the end of 2018, can carry up to seven passengers, or a mix of human passengers and cargo **Boeing**

Once Starliner has ferried people as far as the ISS, humans would be one step closer to establishing an orbiting base near the moon — the final outpost before the long journey to Mars, Castilleja said. That outpost could help launch missions that would first explore Mars from orbit and then eventually send researchers to the Red Planet's surface for the first stages of colonization, Castilleja said.

Starliner will also bring experiments to the ISS that aim to improve life in space, refining methods for growing fresh vegetables and 3D printing tools and equipment parts, Alexandra Deal, a materials and process engineer for Boeing, told the panel audience.

Fly me to the moon

Engineers are also developing plans to build that proposed orbiting moon base, known as the Lunar Orbital Platform-Gateway (LOPG), or just "the Gateway," said panelist David Pederson, a Boeing systems engineer for LOPG.

"We want to take what we've learned from the ISS and apply it to living near the moon," he said.

Astronauts will use the Gateway as a testing ground for a more distant target: Mars. On the Gateway, scientists can develop techniques for insulating crews from intense radiation that does not reach low Earth

orbit and the ISS. Working from the Gateway — about a five-day journey from Earth — will also be critical in learning to be "Earth independent," as Mars travelers would have to be, Pederson told the panel.

Eventually, the Gateway could serve as a hub for Mars missions — as a fueling station and depot for ferrying Mars travelers to and from Earth and the moon, and as the launch site for flights to the Red Planet, Pederson said.

Starliner's first mission — an uncrewed test flight, launched by the Atlas V rocket — is scheduled to take place as soon as August 2018, according to NASA.

http://bit.ly/2Ixx9h3

Found the oldest Neanderthal wooden tools in the Iberian Peninsula

Archaeological excavations at the Aranbaltza site in the Basque Country coast (Northern Spain) have revealed several episodes of Neandertal occupations with preserved wooden remains.

The fieldwork is led by Joseba Rios-Garaizar, archaeologist from the Spanish Centro Nacional de Investigación sobre la Evolución Humana (CENIEH). In 2015, the excavation revealed two very well preserved wooden tools, one of which is a 15 cm-long digging stick. The report has been published in the journal *PLOS ONE*.

Centro Nacional de Investigación sobre la Evolución Humana

The detailed analysis of this tool and the luminescence dating of the sediment that bears the wooden remains indicate that the objects were deposited around 90,000 years ago, and thus were made by Neandertals. The Micro-CT analysis and a close examination of the surface have shown that a yew trunk was cut longitudinally into two halves. One of this halves was scraped with a stone tool and treated with fire to harden it and to facilitate the scraping to obtain a pointed morphology. Use-wear analysis revealed that it was used for digging in search of food, flint, or simply to make holes in the ground.

The preservation of wooden tools associated with Neandertals is very rare because wood degrades very quickly. Only in very specific environments, like the waterlogged sediments from Aranbaltza, it has been possible to find evidence of wooden technology. As it was suggested by indirect evidence, this type of technology was relevant in Neandertal daily life.

In the Iberian Peninsula wooden tools associated to Neandertals have been found only in the travertine from Abric Romaní (Catalonia), and in the rest of Europe only four sites (Clacton on Sea, Schöningen, Lehringen and Poggeti Vechi) have provided wooden tools associated to Neandertals or pre-Neandertals. Therefore, findings like the one from Aranbaltza are crucial to investigate the Neandertal technology and use of wood.

The archaeological project at Aranbaltza started in 2013 to investigate the last Neandertals from Western Europe, who were responsible of the Chatelperronian culture. The ongoing excavations have revealed different Neandertal occupation events spanning from 100,000 to 44,000 years. This makes of Aranbaltza an exceptional site to investigate Neandertal evolution and behavioral variability.

More information: *Joseba Rios-Garaizar et al. A Middle Palaeolithic wooden digging stick from Aranbaltza III, Spain, PLOS ONE (2018). DOI: 10.1371/journal.pone.0195044*

http://bit.ly/2HfEXVq

The time it takes to learn a new language depends on what you want to do with it

If you go by the ads for some language learning apps, you can "have a conversation in a new language in three weeks."

April 4, 2018 by Ingrid Piller, The Conversation

But the experience of most Australians when trying to learn a new language is more likely to resemble that of our prime minister who, a few years ago, wrote: "Learning any language at school is… difficult

because there simply aren't enough hours in the school calendar for most students to achieve any real facility – as many Australians have discovered when they tried out their schoolboy or schoolgirl French on their first visit to Paris!"

The time it takes to learn a language depends on what you mean by "learning a language." If your definition is being able to order a café au lait or ask for directions to "les toilettes, s'il vous plait" on your next trip to Paris, three weeks is perfectly realistic.

But if you need to study using another language, perform your job with it and negotiate all your relationships through that language – the answer changes dramatically. You'll be looking at six years and more, where *more* may well mean *never*.

Doing things with words

Language proficiency is therefore best thought of as the ability to do things with words. The things a tourist needs to do with words are vastly different from the things a migrant needs to do.

Not only do different people need to do different things with language but their proficiency is usually assessed differently. A tourist will be considered highly fluent if they can have an everyday conversation. But the same level of proficiency would be considered too low if they wanted to take up university study where a more mentally challenging use of language is necessary to succeed.

The problem isn't just that the goal of "knowing a language" is variable but also that the pathway towards that goal is different for everyone. How much time and effort a person will require to get to a similar point on the spectrum depends on a wide range of linguistic and non-linguistic factors.

Similarities and differences

An important language factor is similarity. Similar languages are easier to learn than vastly different languages. From the perspective of English, Afrikaans and Dutch are quite similar while Arabic and Chinese are very different.

Does this mean we should all be learning Afrikaans instead of Chinese? Obviously not. And this is where non-linguistic factors come in. Many Australians are likely to be more motivated to learn Chinese than Afrikaans. They may find there are better Chinese learning resources (classes, textbooks, qualified teachers) within reach. And they may have more opportunities to practise Chinese than Afrikaans.

All this may align in a way that makes Chinese easier to learn than Afrikaans, despite the obvious difficulties of contending with the tones and the script.

Individual learner differences also play a role in making language learning more or less difficult, such as age. Adolescence and young adulthood are particularly good times to learn a new language. At that age, the brain is still quite malleable as in the younger years. But adolescent and young adult learners have better strategies and problem-solving skills than younger learners.

Education, including good study skills and socioeconomic factors, also play a role. Being able to afford private tuition, for instance, will have an impact on learning a language.

It's an investment

English speakers can actually find it more difficult to learn another language precisely because they speak English. This is because the world has relatively low expectations of English speakers when it comes to their talent for foreign language learning.

At the same time, there is no shortage of enthusiastic English language learners keen to make good use of practising with native speakers. These dynamics are likely to make it harder for an English speaker to learn Korean than for a Korean speaker to learn English – although the linguistic challenge involved is theoretically the same in both directions.

Learning a language requires a considerable investment of time, effort and commitment. But it's well worth it because another language opens a door to another life.

http://bit.ly/2Jq8koM

'Coffee filter' helps make new cancer drug Z-endoxifen 1,000 times cheaper

Thorough analysis of synthesis reveals much cheaper purification route

Making drugs cheaper doesn't always require pricey investments. A joint initiative by researchers from Eindhoven University of Technology (TU/e), the Dutch company Syncom BV and the Antoni van Leeuwenhoek hospital proves just that. What started out as a Bachelor project at TU/e laid the foundation for a much cheaper production of the promising cancer drug Z-endoxifen.

Lech-Gustav Milroy of Eindhoven University of Technology demonstrating the simple paper filter separation method he used to replace expensive HPLC separation. In the background you can see the previously used HPLC equipment. **Credit: Bart van Overbeeke/TU Eindhoven.**

Tamoxifen is known world-wide as a blockbuster chemotherapeutic drug for the treatment of breast cancer, but it is not always effective. Before it can exert its healing effect, the patient's body must first convert it into the active component Z-endoxifen. Unfortunately, the conversion depends on the patient's genes, which can lead to a variable therapeutic response in patients. By not administering Tamoxifen but Z-endoxifen directly, this genetic dependence is circumvented and the medicine therefore becomes more effective and less toxic due to lower dosing. This has also been demonstrated by clinical trials in the US.

The application of Z-endoxifen had quite a hurdle to overcome: the drug's production was only feasible in small amounts, which led to the exorbitant price of about ten thousand euros per gram. Researchers from TU/e and Syncom have now overcome this hurdle with an improved method to produce Z-endoxifen. During a Bachelor project attentive researchers from TU/e recognized that the HPLC (high-pressure liquid chromatography) purification method used was not at all necessary. Especially on a larger scale HPLC can be particularly expensive.

The existing production method yields two variants (Z- and E-stereo isomers) of endoxifen in a 70:30 ratio, of which the latter is undesired. HPLC was necessary to remove the unwanted 30%. The researchers from Eindhoven made the seredipitous discovery that the ratio one step earlier in the process could be increased to 95:5 in favour of the preferred Z-isomer. At this purity a chemical process known as trituration is possible, which enables removal of the remaining 5% unwanted E-isomer by paper filter, not unlike filtering coffee granules from your morning coffee. The Dutch company Syncom showed this to be the case, and took the project to the next level by scaling up the production and rendering the synthesis more robust using a tailored protective group on the molecule. Finally, Prof Jos Beijnen's group in Amsterdam proved that this new approach did indeed produce pure Z-endoxifen and that the alternative method of purification is effective.

For the next phase of clinical trials of Z-endoxifen, it is important that researchers are able to obtain sufficient quantities of the potential drug at a sufficiently low price. The retail price of pure Z-endoxifen is estimated to be approximately 75,000 euros per gram. By comparison, the invention from Eindhoven makes it possible to produce dozens of grams or even kilos of high purity at the same time, a lot easier, and at a cost of production that is 1,000 times lower. The big breakthrough means that if medical research groups want to do research into the effects of the drug, they are no longer dependent on expensive producers, but they can now produce the drug themselves and at a much lower cost.

Former bachelor student Daphne van Scheppingen worked on the synthesis of Z-endoxifen under the supervision of assistant professor Dr Lech-Gustav Milroy, in 2011. The aim of Van Scheppingen's project was to synthesize 30-50 milligrams of Z-endoxifen for a collaboration

with the research group of Prof Jos Beijnen of the Antoni van Leeuwenhoek hospital. At that time, the drug was still in pre-clinical development and still had to undergo clinical testing. Van Scheppingen and Milroy made the discovery through careful inspection of the final steps in an already existing synthesis route. These steps include the purification of a mixture of the synthesis products into the pure substance, and involved a much cheaper and simpler alternative purification method. Since the clinical testing had not yet been completed, the scientific interest in Z-endoxifen was still small. Since the the publication of the clinical trial data, the project has received a new impulse and the work has quickly been published. Bartjan Koning and Jan Koek of Syncom have scaled up the synthesis significantly to dozens of grams. This opens the doors to more research into the activity and selectivity of the cancer medication.

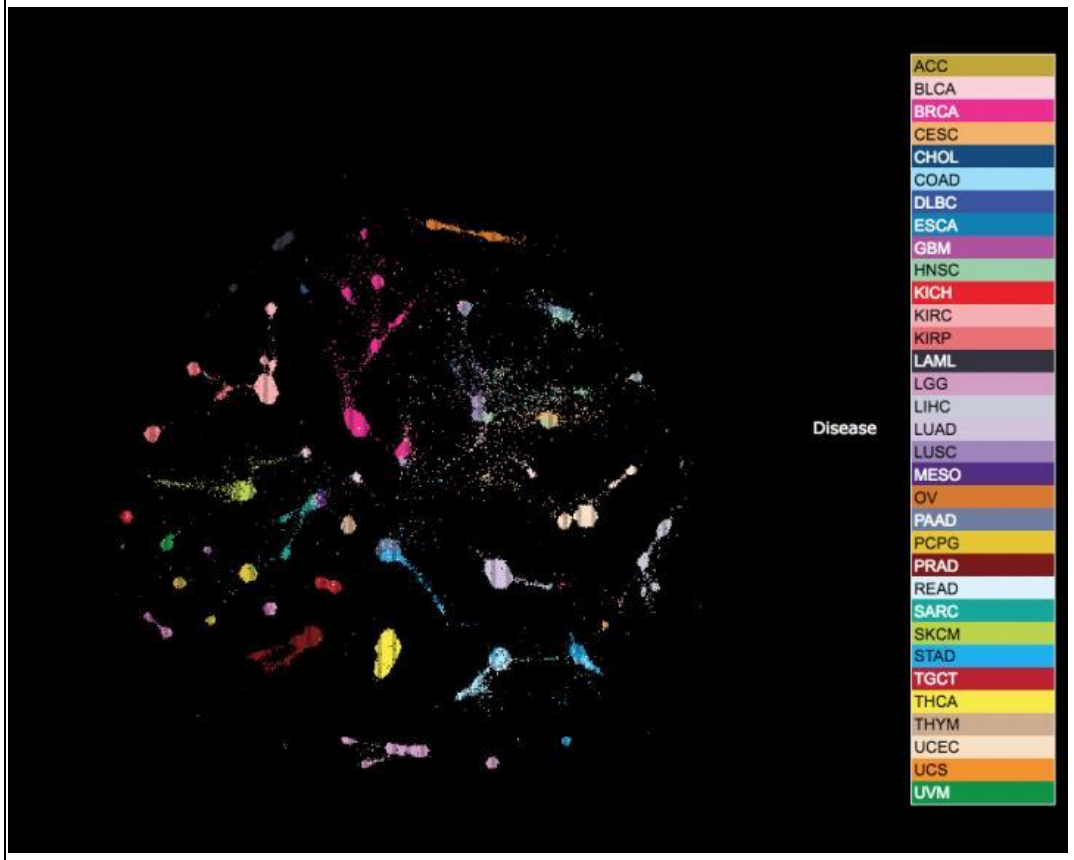
In order to make the drug available to patients, the newly discovered production method must be scaled up even further to industrial production (kilograms). The researchers expect that this will require approximately one year of R&D. More research is also needed on the effects of the drug, the so-called Phase II and III, which typically last between 1 and 6 years.

http://bit.ly/2GKTOGb

New 'Pan-Cancer' analysis reveals the common roots of different cancers

In the largest study of its kind, cancer researchers analyzed and classified over 10,000 tumors from 33 cancer types to trace connections between different cancers

Typically cancers are classified by where they originate in the body--think breast cancer, stomach cancer, and so on. But a collaboration called the Pan-Cancer Initiative, launched in 2012 at a meeting in Santa Cruz, California, sought to study cancers from a new angle--a molecular one. Preliminary analyses showed cancers that start in different organs actually share commonalities at the molecular level, whereas cancers that originate from the same tissue can have very different genomic profiles.



The UCSC Tumor Map helps researchers visualize the dominant patterns found in the TCGA data, such as the cell of origin, molecular histology, 'stemness' or differentiation status, specific altered genetic pathways, and the immune system component of the tumors. **UC Santa Cruz Genomics Institute**

Now, the Pan-Cancer Initiative has released the results of a much larger analysis of genomic and molecular data characterizing 33 different types of cancer from more than 10,000 patients. Called the Pan-Cancer Atlas, it is the most comprehensive cross-cancer analysis to date and is the final output of The Cancer Genome Atlas (TCGA) program, a joint effort of the National Cancer Institute (NCI) and the National Human

Genome Research Institute (NHGRI). The results appear in 27 papers published April 5 in Cell, Cancer Cell, Cell Reports, and Immunity.

"Insights about how one type of cancer relates to another form of the disease can have real clinical implications," said Josh Stuart, Baskin Professor of Biomolecular Engineering at UC Santa Cruz and an organizer of the Pan-Cancer Initiative. "In some cases, we can borrow clinical practices from better-known diseases and apply them to cancers for which treatment options are less well defined."

Stuart's main collaborators on the pan-cancer analyses have been Christopher Benz, professor of cancer and developmental therapeutics at the Buck Institute for Research on Aging and a clinical oncologist at UC San Francisco, and Christina Yau, assistant adjunct professor of surgery at UCSF and a senior scientist at the Buck Institute. Stuart and Benz are co-directors of the UCSC-Buck Institute Genome Data Analysis Center, one of seven national centers in the TCGA Research Network.

Working with an international team of researchers, they performed a comprehensive molecular analysis of the complete set of TCGA tumor data. The results showed that, based on their cellular and genetic makeup and independent of their anatomic site of origin, all 33 tumor types could be re-classified into 28 different molecular types, or "clusters." Nearly two-thirds of these clusters were considered heterogeneous as they contained up to 25 different histological tumor types that, traditionally, would all be treated differently. These molecular analyses and clustering results, now also linked to multiple clinical outcome endpoints, are available to clinicians and researchers worldwide via a single TCGA portal.

"This comprehensive body of final TCGA Pan-Cancer Atlas analyses will provide a new foundation for future cancer research efforts and clinical trials," Benz said. "It will also incentivize clinical oncologists to get newly diagnosed and recurrent tumors genomically characterized. Patients will have the best shot at successful treatment if their tumors can first be classified according to their genomic and molecular makeup."

The first wave of cross-tumor comparisons was completed in September 2013, when Stuart and his colleagues in the Pan-Cancer Initiative analyzed 12 types of tumors profiled by TCGA. While most tumors did end up being grouped by their tissue of origin, there were some common DNA, RNA, and protein signals that cut across those groupings. "It became clear, when we found similarities between different types of cancer, people wanted to do a more comprehensive comparison," Stuart said.

In 2014, he coauthored another pan-cancer paper in which the researchers sorted the tumors into subtypes, or clusters, using a statistical analysis of tumor molecular data. While a majority of the cancer subtypes matched their tissue-of-origin, some of the clusters consisted of tumors that originated in different parts of the body. The 2014 study indicated that one in 10 cancer patients would be classified differently using the new molecular classifications, and those differences could have ramifications for what types of treatment options or clinical trials should be made available to those patients.

As co-leader of the Pan-Cancer working group for TCGA and the International Cancer Genomics Consortium, Stuart has played an integral role in ensuring the research compiled by the collaboration was organized under one common umbrella and overseen by a single steering committee.

Stuart helped organize the 27 Pan-Cancer Atlas papers published April 5 in Cell Press journals. He said the Pan-Cancer Initiative's work so far resembles a giant tree, with roots representing different means of classifying tumors, and sub-roots branching off each of the main roots. This organizational structure provided the basis for "themed working groups," rather than groups based on organ or tissue type.

Stuart and Benz are senior authors of one of the papers, published in *Cell* and led by Peter Laird of Van Andel Research Institute, which provides a roadmap for other researchers seeking to delve into the

findings of the various working groups. "It's a survey of what kinds of overarching systems underlie the data. It's less about clinical implications, and more about the patterns we've found," Stuart said. The first authors of the paper include Yau and Christopher Wong, a staff scientist in Stuart's lab at the UC Santa Cruz Genomics Institute.

Stuart said he is confident that once scientists start scrutinizing the data, clinical implications won't be far behind. "Obviously, finding actionable pieces of logic from these root maps is the holy grail," he said. "The milestone we hit with this paper is finally being able to stand back and look at the big picture."

The UCSC Tumor Map, an interactive browser developed by Yulia Newton and Adam Novak to help researchers visualize the data, displays patient samples on a Google Maps interface. Wong used the browser to compile a set of 10 panels in the *Cell* paper illustrating the dominant patterns found in the data. These include the cell of origin, molecular histology, "stemness" or differentiation status, specific altered genetic pathways, and the immune system component of the tumors.

"Looking at these Tumor Maps is like looking at the Earth from orbit for the first time," Stuart said. "We now see cancer's complete picture and it fills me with hope that we can understand its finite, not infinite, complexity."

UC Santa Cruz has a legacy of creating browsers for the biological community, starting with the highly popular UCSC Genome Browser. "We are thrilled to make this rich data available to the public through this new portal," Stuart said.

Benz said the new TCGA data hold particular promise for expanding treatments designed to enlist the immune system to beat cancer, including approved immunotherapies now showing near-miraculous results against a limited number of classical cancer types. Remarkably, the study shows that one of the most heterogeneous of the observed 28 molecular clusters was composed of 25 different classical tumor types and exhibited very strong features linked to activation of the patient's immune response.

"This finding supports the growing notion that specific immunotherapies approved by the FDA for one cancer type would likely benefit patients with various other cancer types, if these other types could be molecularly identified," Benz said.

Drugs approved for other diseases could also be effective against some of the newly classified cancer types. "A couple of our newly defined cancer clusters also show activation of a molecular pathway (JAK/Stat) that's commonly upregulated in rheumatoid arthritis," said Yau, who provided bioinformatics expertise for much of TCGA's work over the past decade. "Perhaps we can repurpose drugs used to treat that non-malignant chronic disease, as researchers will now have the molecular rationale to explore this novel treatment strategy."

Even though TCGA is done--the database won't be added to or changed--this same kind of comprehensive and collaborative multi-platform genomic analysis continues nationwide under new NCI sponsorship. Stuart, Benz, and Yau continue to work together as part of their bioinformatic analysis center for the newly constituted Genomic Data Analysis Network which, among other challenges, is tasked with determining clinically measurable biomarkers that would make it easier and more cost effective to identify a priori those same tumor molecular subsets identified by the TCGA network's multi-platform analysis.

"It's time to re-write the textbooks on cancer, and it's time to break down the silos in clinical oncology that make it difficult for patients to take advantage of this paradigm shift in cancer classification," said Benz.

http://bit.ly/2Jnkejf

New point-of-care test quickly detects Lyme neuroborreliosis

A new research-based point-of-care test has been developed in Finland for detecting the Lyme neuroborreliosis spread by ticks.

The test makes rapid initiation of antibiotic treatment possible for patients with borreliosis, which reduces the post-treatment symptoms

related to the disease. At the same time, unnecessary antibiotic treatments can be avoided.

The diagnosis of Lyme neuroborreliosis, a tick-borne infection of the nervous system, relies on infection symptoms, cerebrospinal fluid tests, and detection of the antibody production by the activated immune response.

A Finnish company, Reagena, has developed a new point-of-care test to accompany these methods. The test speeds up the diagnostics and helps to target antibiotic treatment appropriately.

The idea for the test was developed by Assistant Professor in Bacteriology, Specialist in Clinical Microbiology Jukka Hytönen from the University of Turku, Finland, whose research group also validated the test.

The new point-of-care test measures CXCL13 concentration in cerebrospinal fluid, since a high CXCL13 concentration is almost exclusively related to untreated neuroborreliosis. Therefore, the CXCL13 chemokine concentration in the cerebrospinal fluid is a new, important biomarker in the diagnostics of neuroborreliosis.

The CXCL13 concentration increases more rapidly in early neuroborreliosis than the antibody concentration in the cerebrospinal fluid, and on the other hand, it declines rapidly after the initiation of antibiotic treatment.

- We have demonstrated that this point-of-care test is extremely efficient. As a result, we suggest that the diagnostic practice for neuroborreliosis in Finland would be reorganised so that the CXCL13 concentration would be measured immediately after the lumbar puncture for cerebrospinal fluid. In the current practice, the concentration results may take up to a week, whereas the new point-of-care test provides quick results, says Hytönen.

With the new test, antibiotic treatment can be targeted to those patients with a high probability of neuroborreliosis.

According to Hytönen, it is important to note that a rapidly initiated treatment reduces the post-treatment symptoms related to neuroborreliosis. At the same time, unnecessary treatment initiated just in case can be avoided, which is essential in order to minimise the negative effects related to antibiotics and to prevent the development of antibiotic resistance of bacteria.

Doctors Often Initiate Antibiotic Treatments without Laboratory Results

The clinical pictures of borreliosis vary from local skin infection to infections of the central nervous system, joints or the heart. A typical red rash, the so called erythema migrans lesion, developing and spreading around the tick bite should always be treated with antibiotics without laboratory tests.

- If the rash does not develop or is not diagnosed in the early stages of borreliosis, for example due to its location, the infection may spread to other organs from the skin.

Symptoms of the disseminated disease include various neurological symptoms, such as facial nerve paralysis and different types of pain in the limbs and body, notes Hytönen.

The diagnosis of Lyme neuroborreliosis is always clinical-based, meaning it is based on the symptoms experienced by the patient and the doctor's findings, but laboratory tests are necessary to support the diagnostics.

At the moment, the most important laboratory test in the diagnostics of neuroborreliosis is the assay of Borrelia-specific antibodies from the patient's blood and cerebrospinal fluid.

- The antibodies are produced as part of the human immune response against the Borrelia bacteria.

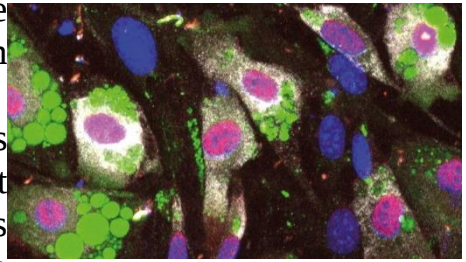
However, even at its fastest, receiving the results with this method lasts several days, and the doctor treating a patient needs to often make the decision about starting antibiotic treatment without the results, says Hytönen.

The research article is available online:
https://www.sciencedirect.com/science/article/pii/S0732889318300725

https://go.nature.com/2Hh7fPm

Why fat piles on when the body's daily cycles are in disarray

Timing of hormone fluctuations influences fat cells' development.



Changes in the patterns of hormone production might cause weight gain when circadian rhythms are disrupted.

Hormones called glucocorticoids stimulate the production of mature fat cells. In humans, glucocorticoid levels naturally rise in the morning and fall in the evening, but stress can also elevate them.

Precursor cells (blue) mature into adipose cells full of fat (green) with help from hormones, whose levels surge and fall over a day. **Z. Bahrami-Nejad et al/Cell Metab.**

To study how glucocorticoid levels relate to weight gain, Mary Teruel at Stanford University in California and her colleagues injected mice with glucocorticoids at varying times of day, but fed all mice the same amount of food. Mice given the hormone late in their wakeful phase gained weight. But mice injected just after they'd woken up — when their glucocorticoid levels were already naturally high — did not.

The results suggest that high glucocorticoid levels at unusual times of day could contribute to weight gain. This could help to explain why stress and disrupted sleep cycles are linked to rising weight.

Cell Metab. (2018)

http://bit.ly/2EsjFRu

Elon Musk Worries That AI Research Will Create an 'Immortal Dictator'

Imagine your least-favorite world leader. (Take as much time as you need.)

By Brandon Specktor, Senior Writer | April 6, 2018 01:33pm ET

Now, imagine if that person wasn't a human, but a network of millions of computers around the world. This digi-dictator has instant access to every scrap of recorded information about every person who's ever lived. It can make millions of calculations in a fraction of a second, controls the world's economy and weapons systems with godlike autonomy and — scariest of all — can never, ever die.

In a new documentary, Elon Musk warns that an 'immortal' digital dictator could forever trap humanity in its grasp unless we start regulating technology ASAP. **Max Whittaker/Getty**

This unkillable digital dictator, according to Tesla and SpaceX founder Elon Musk, is one of the darker scenarios awaiting humankind's future if artificial-intelligence research continues without serious regulation.

"We are rapidly headed toward digital superintelligence that far exceeds any human, I think it's pretty obvious," Musk said in a new AI documentary called "Do You Trust This Computer?" directed by Chris Paine (who interviewed Musk previously for the documentary "Who Killed The Electric Car?"). "If one company or a small group of people manages to develop godlike digital super-intelligence, they could take over the world."

Humans have tried to take over the world before. However, an authoritarian AI would have one terrible advantage over like-minded humans, Musk said.

"At least when there's an evil dictator, that human is going to die," Musk added. "But for an AI there would be no death. It would live forever, and then you'd have an immortal dictator, from which we could never escape."

And, this hypothetical AI-dictator wouldn't even have to be evil to pose a threat to humans, Musk added. All it has to be is determined.

"If AI has a goal and humanity just happens to be in the way, it will destroy humanity as a matter of course without even thinking about it. No hard feelings," Musk said. "It's just like, if we're building a road, and an anthill happens to be in the way. We don't hate ants, we're just building a road. So, goodbye, anthill."

Those who follow news from the Musk-verse will not be surprised by his opinions in the new documentary; the tech mogul has long been a vocal critic of unchecked artificial intelligence. In 2014, Musk called AI humanity's "biggest existential threat," and in 2015, he joined a handful of other tech luminaries and researchers, including Stephen Hawking, to urge the United Nations to ban killer robots. He has said unregulated AI poses "vastly more risk than North Korea" and proposed starting some sort of federal oversight program to monitor the technology's growth.

"Public risks require public oversight," he tweeted. "Getting rid of the FAA [wouldn't] make flying safer. They're there for good reason."

"Do You Trust This Computer?" focuses on the growing public health and safety concerns linked to the rise of AI, and contains interviews with many other tech moguls, researchers and Erica the creepy news-casting robot. The documentary is available to watch for free here until Sunday (April 8).

http://bit.ly/2H5Tp4I

How a Stranded Nurse Saved His Own Life During a Heart Attack

What do you do if you're in the middle of nowhere and you have a heart attack?

By Rafi Letzter, Staff Writer | April 6, 2018 04:05pm ET

If you're a nurse alone in Western Australia, apparently the answer is, save your own life, damn it.

A case report published March 8 in The New England Journal of Medicine tells the harrowing tale of a nurse who did just that. The unnamed 44-year-old man was the only nurse on duty at a small post more than 620 miles (1,000 kilometers) from Perth and about 90 miles (150 km) from the next nearest medical facility.

All by himself, he attached the leads of an electrocardiogram to his chest and sent the results by email to an emergency physician. The results showed that he had a "complete heart block, right bundle-branch block, hyperacute T waves in the inferior leads, and reciprocal ST-segment depression in the anterolateral leads," the researchers wrote in the paper.

In other words, much of his heart had stopped responding properly to nerve impulses telling it to beat, and other parts of the heart were beating poorly. It was a significant, life-threatening heart attack.

Nursing skills kicking into action, he inserted needles into the blood vessels on the insides of both his elbows and administered a cocktail of drugs designed to get his blood flowing, his heart beating and his pain within a manageable threshold. It included everything from aspirin to nitroglycerin to opioids.

He also attached "his own defibrillator pads" and got ready to dose himself with adrenaline and other drugs designed to kick a heart back into rhythm.

Eventually, Australia's Royal Flying Doctor Service arrived and airlifted him to a hospital in Perth. There, doctors found a severe blockage in his mid-right coronary artery, and he underwent surgery. Forty-eight hours later, he was released.

http://bit.ly/2IDQOMj

Military-Funded Study Successfully Tests 'Prosthetic Memory' Brain Implants

If a computer chip lived inside your brain and monitored your every memory, could it learn to remember for you?

By Brandon Specktor, Senior Writer | April 6, 2018 07:45am ET

The concept may sound like science fiction, but according to a new paper in the Journal of Neural Engineering, technology like this may be a reality before long. In a military-funded pilot study, scientists successfully tested what they call a "prosthetic memory" — a neural implant that can learn to recognize your brain activity when you correctly recall new information, and later replicate that activity with electrical signals to give your short-term memory a boost.

In a small test of 15 patients at Wake Forest Baptist Medical Center, this prosthetic memory system helped the patients improve their short-term memory by an average of 35 percent. According to lead study

author Robert Hampson, a professor of physiology, pharmacology and neurology at Wake Forest School of Medicine in North Carolina, this degree of short-term memory improvement is "huge."

"In one sense, we were not surprised to find that this worked," Hampson said in a video that accompanied the paper. "We had a long history of animal studies in which we were testing this concept in other species — in animals in the laboratory — and we were having success. What surprised us was how successful it was."

Making memories

In the study, which was funded by the U.S. Defense Advancement Research Projects Agency (DARPA), Hampson and his colleagues tested the prosthetic system on 15 patients enrolled for epilepsy treatments at Wake Forest Baptist Medical Center. The patients were taking part in a brain-mapping procedure to treat their seizures, and already had electrodes surgically implanted in various parts of their brains, including the hippocampus — the part of the brain involved in the formation of new memories.

When the patients weren't otherwise occupied with their medical care, they volunteered to test the prosthetic memory system with Hampson and his team.

"We [had] the patient play a computer game that [involved] memory, and we [recorded] the activity of the brain cells — the neurons — in the hippocampus," Hampson said.

The game was a basic memory challenge that involved identifying which of several images had been shown on a previous screen. The delay between seeing an image and having to recall it varied throughout the trials, at first lasting about 2 minutes, and eventually lasting up to 75 minutes. As the patients played, the researchers monitored their brain activity through the electrode implants. As patients answered more questions correctly, the researchers compiled an increasingly clear picture of what each patient's mental activity looked like when their short-term memory was hard at work.

During later trials, the researchers used these personalized memory codes to help stimulate specific parts of each patient's brain. When patients received this mental stimulation, their recall improved.

"When we tested patients by stimulating their hippocampus with a pattern that was derived from their own neural activity… we were able to improve their short-term memory by quite a bit," Hampson said.

According to the study, patients' correct responses increased by an average of 37 percent during the 2-minute trial and 35 percent in the 75-minute trial when their brains were stimulated — figures that Hampson called "a substantial improvement."

Given the study's small sample size, and the fact that each patient already had existing electrode implants to treat an unrelated condition, significantly more research is required before commercial prosthetic memory implants like these can become a reality. The next step, Hampson said, is to try to replicate the results in a sample of people who don't have epilepsy or existing neural implants.

"That is going to require some decisions by the doctors, by the patients and by the researchers as to when we put electrodes in and who we're going to help," Hampson said. "But our target is to help people who have had a traumatic brain injury, who have had a stroke, people who have memory loss due to aging, Alzheimer's or any number of other diseases that can affect the memory."

http://bit.ly/2qqGbsf

A paleontologist who teaches anatomy is good for medicine and science

Some students are surprised to learn that their gross anatomy professor is a paleontologist—that's a scientist who studies fossils, right?

April 6, 2018 by Kristian J. Carlson, University of Southern California

My research is actually focused on the origins and evolution of humans today, during the period from about 6 million years ago to present day. Teaching anatomy at the Keck School of Medicine of USC has benefits in both directions: I bring the history of the human body's development

to how (and why) it works as it does today. And lecturing future physicians on a campus with three hospitals benefits my science research into our past.

Science and medicine have in common that we don't only want to know what happens, we want to know why. In anatomy class, for example, I teach students that shoulder dislocations are a common injury they will see in patients. Falls or sports injuries are often causal factors. But why is the shoulder so vulnerable to dislocation in the first place?

Kristian J. Carlson, seen here holding a human femur bone, is a biological anthropologist who teaches anatomy at the Keck School of Medicine of USC.
USC Photo/Gus Ruelas

Paleontologists theorize that it's because over the last several millions of years, the way in which we use our upper limbs has changed dramatically. Humans who evolved manipulatory capabilities—those who could make and use tools—survived better than our ancestors who did not. At the same time, since we don't use our arms to move around like chimpanzees, our upper limbs, especially shoulders, have evolved away from being more mobile as they were in our ancestors millions of years ago.

In the present day, by examining living patients whose types and levels of activities vary, we've learned that human bones reinforce themselves differently based on what stresses are placed on them. So we can look back at the arm and leg bones of our ancestors from millions of years ago and tell by their patterns of bone development—bones usually reinforce their walls along directions in which they are stressed over time—if the owner of these bones spent their time moving in meandering paths through trees or if they had come out of the trees and lived most of their lives walking through less three-dimensional surroundings. These insights offer crucial information about how our ancestors interacted with their environment.

How basic science and clinical medicine overlap

Another way that basic science research and clinical medicine overlap is that neither field seeks a single, know-it-all answer for what's happening or why. We develop hypotheses, which over time may be supported or not through careful testing. A good scientist and a good physician have that in common: Neither would claim to have the definitive and final answers for anything, but both would base inferences on what is known at the time. This can be frustrating and confusing for patients who seek a guaranteed diagnosis and a foolproof treatment, or students who want definitive answers about the past.

But it's better for both that we're always learning and always willing to have our minds changed by new evidence. Today's athletes, for example, are pushing past boundaries once thought impossible in speed, distance, strength and stamina. How does that affect their bodies, and how do their bodies adapt to these record-breaking physical demands?

I'd love to work with world-class USC athletes to better understand how their bodies structurally reflect their training—when they're not injured. It could benefit medicine by leading to ways to combat reduced bone strength, either resulting from age-related processes or from osteoporosis. And it could advance science by teaching us more sedentary types about how we came to have the bodies we do, at a pace slightly faster than waiting for evolution to run its course.

http://bit.ly/2IARW3n

Scientists discover hybrid swarm in global mega-pest

CSIRO scientists have confirmed the hybridisation of two of the world's major pest species, into a new and improved mega-pest.

One of the pests, the cotton bollworm, is widespread in Africa, Asia and Europe and causes damage to over 100 crops, including corn, cotton, tomato and soybean.

The damage and controlling the pest costs billions of dollars a year.

It is extremely mobile and has developed resistance to all pesticides used against it.

The other pest, the corn earworm, is a native of the Americas and has comparatively limited resistance and host range.

However, the combination of the two, in a novel hybrid with unlimited geographical boundaries is cause for major concern.

Globalisation and increased movement between countries and continents means movement of agricultural pests is becoming more common. Global trade means global pests. **CSIRO**

Australia's Commonwealth Scientific and Industrial Research Organisation (CSIRO) researchers in a paper published in the *Proceedings of the National Academy of Sciences* provides clear evidence of the hybridisation of the two moths in Brazil.

"A hybrid such as this could go completely undetected should it invade another country," Research Director leading CSIRO's Biosecurity Risk Evaluation and Preparedness Program Dr Paul De Barro said.

"It is critical that we look beyond our own backyard to help fortify Australia's defense and response to biosecurity threats.

"As Australia's national science agency, we are constantly looking for new ways to protect the nation and technology like genome sequencing, is helping to tip the scales in our favour."

While a combination of insecticides currently controls these pests well in Australia, it is important to study the pests themselves for sustainable long-term management world-wide.

The scientists confirmed that among the group of caterpillars studied, every individual was a hybrid.

"No two hybrids were the same suggesting a 'hybrid swarm' where multiple versions of different hybrids can be present within one population," fellow CSIRO Scientist Dr Tom Walsh said.

The bollworm, commonly found in Australia, attacks more crops and develops much more resistance to pesticides than the earworm.

A concerning finding among the Brazilian hybrids was that one was 51 per cent earworm but included a known resistance gene from the bollworm.

Lead author of the paper Dr Craig Anderson, a former CSIRO scientist now based at The University of Edinburgh, believes the hybrid study has wide-ranging implications for the agricultural community across the Americas.

"On top of the impact already felt in South America, recent estimates that 65 per cent of the USA's agricultural output is at risk of being affected by the bollworm demonstrates that this work has the potential to instigate changes to research priorities that will have direct ramifications for the people of America, through the food on their tables and the clothes on their backs," Dr Anderson said.

More information: *Craig J. Anderson et al. Hybridization and gene flow in the mega-pest lineage of moth,Helicoverpa, Proceedings of the National Academy of Sciences (2018).* *DOI: 10.1073/pnas.1718831115*

http://bit.ly/2IAIoW6

Hot-air dryers suck in nasty bathroom bacteria and shoot them at your hands

Air filters can help, but healthcare and research centers may want to stick with towels.

Beth Mole - 4/7/2018, 3:28 AM

Washing your grubby mitts is one of the all-time best ways to cut your chances of getting sick and spreading harmful germs to others. But using the hot-air dryers common in bathrooms can undo that handy hygienic work.

Hot-air dryers suck in bacteria and hardy bacterial spores loitering in the bathroom—perhaps launched into the air by whooshing toilet flushes—and fire them directly at your freshly cleaned hands, according to a study published in the April issue of *Applied and Environmental Microbiology*. The authors of the study, led by researchers at the University of Connecticut, found that adding HEPA filters to the dryers can reduce germ-spewing four-fold. However, the data hints that places

like infectious disease research facilities and healthcare settings may just want to ditch the dryers and turn to trusty towels.

Indeed, in the wake of the blustery study—which took place in research facility bathrooms around UConn—"paper towel dispensers have recently been added to all 36 bathrooms in basic science research areas in the UConn School of Medicine surveyed in the current study," the authors note.

The research findings largely square with other data showing that hot-air dryers and jet dryers can launch and disperse germs *from* hands into the air and onto surfaces—essentially setting off a very dirty bathroom bomb. But the new study clearly demonstrates that the less powerful hot-air dryers can also bathe hands with germs already swirling in the wash room.

The researchers speculated that "one reason hand dryers may disperse so many bacteria is the large amount of air that passes through hand dryers, 19,000 linear feet/min at the nozzle. The convection generated by high airflow below the hand dryer nozzles could also draw in room air."

Commode commotion

The researchers landed on that speculation by first placing plates of gelled bacteria food (agar media plates) in some of UConn's bathrooms—either for two minutes without hot-air dryers blowing or blasting them with dryer air for 30 seconds while they were 12 inches from the nozzle. If bacteria landed on the plates, they'd begin to grow tiny, domed colonies, which researchers can then count.

In the still bathrooms, the researchers caught an average of zero to one bacterial landings per plate. When they left the plates open for 18 hours, that average leapt to six colonies per plate. But in the line of fire from the blowers for 30 seconds, the plates collected averages from 18 to 60, with a range as high as 254 depending on the bathroom.

The researchers concluded that those launched germs were originating from around the bathroom—not the air dryer nozzles themselves. They deduced this because the bacterial splatter could be replicated by placing tiny, sterile fans around the bathrooms (after accounting for rates of air flow and exposure times). Retrofitting the dryers with HEPA filters reduced the germ count about four-fold.

A unique ripple in the study was that the bathrooms were in the vicinity of a lab studying the harmless spore-forming bacterium *Bacillus subtilis* strain PS533. Though *B. subtilis* is a common environmental bug, this lab strain has a distinctive resistance to the antibiotic kanamycin. The researchers could easily pick it out of their bathroom samples by simply growing collected toilet germs in the presence of kanamycin—the survivors were likely PS533 and confirmed by further testing. The researchers ended up finding PS533 milling about in all the bathrooms tested—even the ones in different buildings from the lab.

Brutal blowout

Perhaps most concerning, the researchers found that the air dryers were spreading the spores of PS533. They tested this by exposing their potty germ collections to heat—which will kill growing bacteria and germinated spores but not the spores themselves—then seeing if any spores grew. They did. The researchers then found that the hand dryers were spewing spores onto the surfaces of the bathroom.

PS533 "was almost certainly dispersed throughout bathrooms in the research areas as spores, which would easily survive desiccation in room air, as well as the elevated temperatures in hand dryer air; however, growing or stationary-phase bacteria would not be nearly so hardy as spores," the authors note. "However, the facile dispersion of one bacterial strain throughout a research facility should probably be a concern to risk assessors and risk managers when dispersion of potentially pathogenic bacteria is considered."

In a final test, the researchers did a cursory look at some of the other bacteria the dryers were blowing around. They found that with or without a HEPA filter, the blowers stirred up potential pathogens, including *Staphylococcus aureus*.

The findings should be a wake-up call to managers of research and clinical settings. The authors note that *Clostridium difficile*—a

devastating and intractable diarrheal plague—also forms spores, and researchers have found that a flushing toilet can easily launch it into the air.

"This suggests another means of *C. difficile* transmission and one that may not be interrupted by either hand washing or traditional surface decontamination methods," the authors conclude. "The role of this potential mode of *C. difficile* transmission is worthy of future study."

Applied and Environmental Microbiology, *2018. DOI: 10.1128/AEM.00044-18 (About DOIs).*

http://bit.ly/2qklV9l

8 Reasons You Should Be Eating More Ginseng

Studies indicate that ginseng may improve brain function, boost the immune system and reduce the risk of certain cancers.

By Arlene Semeco / Authority Nutrition

Ginseng has been used in traditional Chinese medicine for centuries. This slow-growing, short plant with fleshy roots can be classified three ways, depending on how long it is grown: fresh, white or red.

Fresh ginseng is harvested before 4 years, while white ginseng is harvested between 4–6 years and red ginseng is harvested after 6 or more years. There are many types of this herb, but the most popular are American ginseng (*Panax quinquefolius*) and Asian ginseng (*Panax ginseng*).

***American wild ginseng root (Panax quinquefolius)* John Carl Jacobs/Wikimedia Commons**

American and Asian ginseng vary in their concentration of active compounds and effects on the body. It is believed that American ginseng works as a relaxing agent, whereas the Asian variety has an invigorating effect (1, 2).

Ginseng contains two significant compounds: ginsenosides and gintonin. These compounds complement one another to provide health benefits (3). Here are 8 evidence-based health benefits of ginseng.

1. Potent Antioxidant That May Reduce Inflammation

Ginseng has beneficial antioxidant and anti-inflammatory properties (4). Some test-tube studies have shown that ginseng extracts and ginsenoside compounds could inhibit inflammation and increase antioxidant capacity in cells (5, 6).

The results are promising in humans, as well.

One study investigated the effects of having 18 young male athletes take 2 grams of Korean red ginseng extract three times per day for seven days. The men then had levels of certain inflammatory markers tested after performing an exercise test. These levels were significantly lower than in the placebo group, lasting for up to 72 hours after testing (7).

Another study followed people with skin inflammation. It found improvements in inflammation and antioxidative activity after treatment with Korean red ginseng extract (8).

Lastly, a larger study followed 71 postmenopausal women who took 3 grams of red ginseng or a placebo daily for 12 weeks. Antioxidant activity and oxidative stress markers were then measured. Researchers concluded that red ginseng may help reduce oxidative stress by increasing antioxidant enzyme activities (9).

SUMMARY: Ginseng has been shown to help reduce inflammatory markers and help protect against oxidative stress.

2. May Benefit Brain Function

Ginseng could help improve brain functions like memory, behavior and mood (10, 11). Some test-tube and animal studies show that components in ginseng, like ginsenosides and compound K, could protect the brain against damage caused by free radicals (12, 13, 14).

One study followed 30 healthy people who consumed 200 mg of *Panax ginseng* daily for four weeks. At the end of the study, they showed improvement in mental health, social functioning and mood.

However, these benefits stopped being significant after 8 weeks, suggesting that ginseng effects might decrease with extended use (15).

Another study examined how single doses of either 200 or 400 mg of *Panax ginseng* affected mental performance, mental fatigue and

blood sugar levels in 30 healthy adults before and after a 10-minute mental test.

The 200-mg dose, as opposed to the 400-mg dose, was more effective at improving mental performance and fatigue during the test (16). It is possible that ginseng assisted the uptake of blood sugar by cells, which could have enhanced performance and reduced mental fatigue. Yet it is not clear why the lower dose was more effective than the higher one.

A third study found that taking 400 mg of *Panax ginseng* daily for eight days improved calmness and math skills (17).

What's more, other studies found positive effects on brain function and behavior in people with Alzheimer's disease (18, 19, 20).

SUMMARY: Ginseng has been shown to benefit mental functions, feelings of calmness and mood in both healthy people and those with Alzheimer's disease.

3. Could Improve Erectile Dysfunction

Research has shown that ginseng may be a useful alternative for the treatment of erectile dysfunction (ED) in men (21, 22). It seems that compounds in it may protect against oxidative stress in blood vessels and tissues in the penis and help restore normal function (23, 24).

Additionally, studies have shown that ginseng may promote the production of nitric oxide, a compound that improves muscle relaxation in the penis and increases blood circulation (24, 25).

One study found that men treated with Korean red ginseng had a 60% improvement in ED symptoms, compared to 30% improvement produced by a medication used to treat ED (26).

Moreover, another study showed that 86 men with ED had significant improvements in erectile function and overall satisfaction after taking 1,000 mg of aged ginseng extract for 8 weeks (27). However, more studies are needed to draw definite conclusions about the effects of ginseng on ED (24).

SUMMARY: Ginseng may improve symptoms of erectile dysfunction by decreasing oxidative stress in tissues and enhancing blood flow in penile muscles.

4. May Boost the Immune System

Ginseng may strengthen the immune system.

Some studies exploring its effects on the immune system have focused on cancer patients undergoing surgery or chemotherapy treatment.

One study followed 39 people with stomach cancer after surgical procedures, treating them with 5,400 mg of ginseng daily for two years. Interestingly, these people had significant improvements in immune functions and a lower recurrence of symptoms (28).

Another study examined the effect of red ginseng extract on immune system markers in people with advanced stomach cancer undergoing post-surgery chemotherapy. After three months, those taking red ginseng extract had better immune system markers than those in the control or placebo group (29).

Furthermore, a study suggested that people who take ginseng could have up to a 35% higher chance of living disease-free for five years after curative surgery and up to a 38% higher survival rate compared to those not taking it (30). It seems that ginseng extract could enhance the effect of vaccinations against diseases like influenza, as well (31).

Even though these studies show improvements in immune system markers in people with cancer, more research is needed to demonstrate the efficacy of ginseng in boosting resistance to infections in healthy people (32).

SUMMARY: Ginseng may strengthen the immune system in people with cancer and even enhance the effects of certain vaccinations.

5. May Have Potential Benefits Against Cancer

Ginseng may be helpful in reducing the risk of certain cancers (33).

Ginsenosides in this herb have been shown to help reduce inflammation and provide antioxidant protection (34, 35). The cell cycle is the process by which cells normally grow and divide. Ginsenosides could benefit this cycle by preventing abnormal cell production and growth (34, 35).

A review of several studies indicated that people who took ginseng had a 16% lower risk of developing cancer (35).

Moreover, an observational study suggested that people taking ginseng could be less likely to develop certain types of cancer, such as lip, mouth, esophagus, stomach, colon, liver and lung cancer, than those who do not take it (36).

Ginseng may also help improve the health of patients undergoing chemotherapy, reduce side effects and enhance the effect of some treatment drugs (34). While studies on the role of ginseng in cancer prevention show some benefits, they remain inconclusive (37).

SUMMARY: Ginsenosides in ginseng seem to regulate inflammation, provide antioxidant protection and maintain the health of cells, which could help decrease the risk of certain kinds of cancer. Nevertheless, more research is needed.

6. May Fight Tiredness and Increase Energy Levels

Ginseng has been shown to help fight fatigue and promote energy.

Various animal studies have linked some components in ginseng, like polysaccharides and oligopeptides, with lower oxidative stress and higher energy production in cells, which could help fight fatigue (38, 39, 40).

One four-week study explored the effects of giving 1 or 2 grams of *Panax ginseng* or a placebo to 90 people with chronic fatigue. Those given *Panax ginseng* experienced less physical and mental fatigue, as well as reductions in oxidative stress, than those taking the placebo (41).

Another study gave 364 cancer survivors experiencing fatigue 2,000 mg of American ginseng or a placebo. After eight weeks, those in the ginseng group had significantly lower fatigue levels than those in the placebo group (42). Furthermore, a review of over 155 studies suggested that ginseng supplements may not only help reduce fatigue but also enhance physical activity (43).

SUMMARY: Ginseng may help fight fatigue and enhance physical activity by lowering oxidative damage and increasing energy production in cells.

7. Could Lower Blood Sugar

Ginseng seems to be beneficial in the control of blood glucose in people both with and without diabetes (44, 45). American and Asian ginseng have been shown to improve pancreatic cell function, boost insulin production and enhance the uptake of blood sugar in tissues (44).

Moreover, studies show that ginseng extracts help by providing antioxidant protection that reduce free radicals in the cells of those with diabetes (44).

One study assessed the effects of 6 grams of Korean red ginseng, along with the usual anti-diabetic medication or diet, in 19 people with type 2 diabetes. Interestingly, they were able to maintain good blood sugar control throughout the 12-week study. They also had an 11% decrease in blood sugar levels, a 38% decrease in fasting insulin and a 33% increase in insulin sensitivity (46).

Another study showed that American ginseng helped improve blood sugar levels in 10 healthy people after they performed a sugary drink test (47). It seems that fermented red ginseng could be even more effective at blood sugar control. Fermented ginseng is produced with the help of live bacteria that transform the ginsenosides into a more easily absorbed and potent form (48).

In fact, a study demonstrated that taking 2.7 grams of fermented red ginseng daily was effective at lowering blood sugar and increasing insulin levels after a test meal, compared to a placebo (49).

SUMMARY: Ginseng, particularly fermented red ginseng, may help increase insulin production, enhance blood sugar uptake in cells and provide antioxidant protection.

8. Easy to Add to Your Diet

Ginseng root can be consumed in many ways. It can be eaten raw or you can lightly steam it to soften it. It can also be stewed in water to make a tea. To do this, just add hot water to freshly sliced ginseng and let it steep for several minutes.

Ginseng can be added to various recipes like soups and stir-frys, too. And the extract can be found in powder, tablet, capsule and oil forms.

How much you should take depends on the condition you want to improve. Overall, daily doses of 1–2 grams of raw ginseng root or 200–400 mg of extract are suggested. It's best to start with lower doses and increase over time. Look for a standard ginseng extract that contains 2–3% total ginsenosides, and consume it before meals to increase absorption and get the full benefits.

SUMMARY: Ginseng can be eaten raw, made into tea or added to various dishes. It can also be consumed as a powder, capsule or oil.

Safety and Potential Side Effects

According to research, ginseng appears to be safe and should not produce any serious adverse effects. However, people taking diabetes medications should monitor their blood sugar levels closely when using ginseng to ensure these levels do not go too low. Additionally, ginseng may reduce the effectiveness of anticoagulant drugs.

For these reasons, talk to your doctor before supplementing with it.

Note that due to the lack of safety studies, ginseng is not recommended for children or women who are pregnant or breastfeeding.

Lastly, there is evidence suggesting that the extended use of ginseng could decrease its effectiveness in the body. To maximize its benefits, you should take ginseng in 2–3-week cycles with a one or two week break in between (14).

SUMMARY: While ginseng appears to be safe, people taking certain medications should pay attention to possible drug interactions.

The Bottom Line

Ginseng is an herbal supplement that has been used for centuries in Chinese medicine. It is commonly touted for its antioxidant and anti-inflammatory effects. It could also help regulate blood sugar levels and have benefits for some cancers. What's more, ginseng may strengthen the immune system, enhance brain function, fight fatigue and improve symptoms of erectile dysfunction.

Ginseng can be consumed raw or lightly steamed. It can also easily be added to your diet via its extract, capsule or powder form.

Whether you want to improve a certain condition or simply give your health a boost, ginseng is definitely worth a try.

http://bit.ly/2HhHtdP

Life as a chemical reaction

Science has created life for 100 years – but where can it lead us?

By Philip Ball 8 April 2018

'It's alive!' That famous cry of Colin Clive playing Henry Frankenstein – never voiced by Mary Shelley's protagonist Victor 200 years ago, but emblematic of James Whale's movie version in 1931 – might just as well have issued from the lips of German marine biologist Jacques Loeb at the end of the 19th century, who was attributed with the creation of life. Here's Loeb in classic mad-scientist mode speaking to *McClure's* magazine in 1902: 'I wanted to take life in my hands and play with it, I wanted to handle it in my laboratory as I would any other chemical reaction – to start it, stop it, vary it, study it under every condition, to direct it at my will!'

Cue Clive's wide-eyed stare. The *Boston Herald* announced Loeb's achievements in 1899 with the claim that 'lower animals [have been] produced by chemical means'. *Scientific American* was explicit about the comparison with Shelley's anti-hero, titling a 1909 article on Loeb 'The achievements of the scientific Frankenstein.' There was a hubristic whiff of impiety in *Cosmopolitan*'s description of his work when it spoke of 'prying into nature's secrets'.

What on earth had Loeb done to warrant this? Not much. Working at the marine biology labs in Woods Hole, US, he had shown that the development of sea urchin eggs could be triggered by the chemical action of simple salts such as sodium and magnesium chlorides, rather than by fertilisation with sperm. This was artificially-induced parthenogenesis.

The immaculate misconception

Without a doubt it was a striking discovery. As historian Philip Pauly puts it, the result 'represented an attack on the privileged status of natural modes of reproduction'. You could say that it replaced biology

with chemistry, thereby encouraging the idea that the former could be reduced to the latter. We might find that an unexceptional notion in the era of molecular biology, but at the end of the 19th century it was far from clear how, or if, the two subjects intersected.

For Loeb the discovery vindicated his idea that life could be understood – and manipulated – using engineering principles, a view he outlined in his 1912 book *The mechanistic conception of life*. Others were skeptical, even satirical. The zoologist Camille Viguier joked that Loeb's sea-urchin progeny were 'chemical citizens, the son of madame Sea-Urchin and monsieur Magnesium Chloride'. Others remarked that this propensity of salt might deter 'maiden ladies' from bathing in the sea. The *Boston Herald* could not resist suggesting (without cause) that Loeb's process 'may apply to human species', adding that thereby the 'Immaculate Conception [is] explained.'

Silly hyperbole? Skip forward to 2003, and here's a headline in *New Scientist*: '"Virgin birth" method promises ethical stem cells'. The article discusses research[1] demonstrating that parthenogenesis can be induced in human eggs by a simple chemical stimulus using the compound called calcium ionophore. The resulting embryos, lacking the genes from sperm that promote full development, can't grow beyond the blastocyst stage that they reach in a few days. But that's far enough to produce embryonic stem cells that can be harvested for research and medicine – without the ethical quandaries presented by taking stem cells from human embryos discarded in IVF.

The method had already been known to work in other animals, including mice and monkeys, but it had hitherto failed in humans. Some vertebrates, such as certain lizards, reproduce naturally by parthenogenesis – but not mammals.

Fertile ideas

There's more, though, because chemical parthenogenesis might have a real role in research on assisted reproduction.[2] Sure, you can never get a baby this way, but the knowledge gained from studying early-stage embryogenesis could feed back into improvements in treatments for infertility.

Can't you make parthenogenic babies, though? While eggs chemically triggered to develop don't have what it takes to make a viable embryo, it's a different story if the egg has been given the chromosomes of a cell from a more mature organism, through the technique of somatic-cell nuclear transfer used in cloning. This was how Chinese scientists in Shanghai recently managed to clone macaque monkeys[3] – the first cloning of primates. After nuclear transfer, the researchers used a chemical stimulus to trigger growth of the embryos that developed to full term and produced live births.

Surprisingly simple chemistry can induce other profound changes in cells too. Small molecules, identified by screening, have been used to switch differentiated cells directly from one tissue type to another – cardiac fibroblasts to muscle, say – both outside and inside the body.[4] Such cell reprogramming is more typically done using protein transcription factors to 'persuade' the cells to adopt a new identity – but synthetic molecules can work too.

All this reinforces the claim in a 1912 *Cosmopolitan* article inspired by Loeb's work: 'Life is a chemical reaction.' But that idea unsettled some readers as much as did the materialism hinted at in *Frankenstein*. The same question was left hanging in both cases, as the article went on, a little crudely, to say: 'If man can lump together sand and salt and by pouring water on them create life, what becomes of the soul?'

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