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Polio-like Virus in Children Causing Concern Around US

Acute flaccid myelitis (AFM), a rare condition that causes a polio-like paralysis, has been circulating across the United States.

Roxanne Nelson BSN, RN

As of September 30, there have been 38 confirmed cases reported to the Centers for Disease Control and Prevention (CDC), which have occurred in 16 states, but the numbers appear to be growing.

In Washington state, six children have now presented with a sudden onset of paralysis of one or more of their limbs. The latest case was reported to the Washington State Department of Health on Thursday, October 11, and came out of Skagit County, which lies north of Seattle. All reported cases are in counties in Western Washington.

Also on Thursday, hospital officials from Oishei Children's Hospital in Buffalo, New York, have confirmed that physicians are treating a 3-year-old patient with a "highly suspected" case of AFM. The child and his family have been "in and out of the hospital the past two weeks and now, the boy is unable to walk," WKBW in Buffalo reports.

While the hospital has completed its own testing for AFM, samples have been sent to the CDC for further evaluation.

Affected states include California, Colorado, Florida, Illinois, Massachusetts, New York, Pennsylvania, Rhode Island, Texas, Virginia, and Washington.

True Numbers Hard to Determine

From August 2014 through August 2018, the CDC has been notified of 362 cases of the illness, mostly in children. But even though the official number of cases is 38 for 2018 (as of September 30), it may not reflect the actual number that will eventually be confirmed.

For example, Minnesota has reported six cases; three children are being treated in Pittsburgh; two are being treated in Chicago; and eight cases have been reported in Texas, one in Rhode Island, and 14 in Colorado.

However, the 38 cases reported by the CDC do not include all of the 14 cases announced by Colorado, as some were confirmed after September 30. It also doesn't include those from Minnesota, as they have also not yet been confirmed. In addition, nine cases have been reported in children in northern Illinois, but they too have not been confirmed by the CDC.

The CDC began actively investigating AFM in August 2014, when it noticed an increase in reports of people across the country presenting with AFM but without a discernible cause. In 2014, a total of 120 cases were reported, spread out over 34 states.

The number dropped the following year to 22 cases reported in 17 states, but that dramatically jumped to 149 in 2016, reported in 39 states and the District of Columbia. The following year, the number decreased again to 33 cases in 16 states.

The underlying cause of many of this year's cases has not yet been identified. The sharp increase in AFM cases in 2014 coincided with an outbreak of severe respiratory illnesses caused by enterovirus D68 (EV-D68). However, EV-D68 was not detected in all individuals with confirmed AFM. During 2015, the CDC did not receive any reports of large EV-D68 outbreaks, with local laboratories reporting only limited EV-D68 detections. The following year, a few localized clusters were reported.

Different Enterovirus Seen in Colorado

While EV-68 has been associated with this syndrome, in Colorado far more cases have been linked to infection with enterovirus A71 (EV-A71). According to the Colorado Department of Public Health and Environment (CDPHE), there have been 41 cases of EV-A71 infections tied to neurologic illnesses in young children this year. Of those cases, 14 have involved AFM, and 11 of the AFM cases have

tested positive for EV-A71. Only one child tested positive for EV-D68, and two were EV-negative.

"We have been conducting surveillance in Colorado for enteroviruses for a number of years, which may be the reason that we have observed some of these trends," Rachel Herlihy MD, MPH, state epidemiologist at CDPHE, told *Medscape Medical News*. "Back in 2003 and 2005, we did detect cases of EV-A71, which were identified by the children's hospital."

Those were cases that did involve neurologic illness in children, she explained. "In 2014, Colorado, along with other parts of the country, had a much wider outbreak of EV-D68 that was associated with AFM. We had 11 cases that year in Colorado. So this year it's different from what we had in 2014, but the same as what we had in 2003 and 2005."

The clinical course and presentation with EV-A71 is also quite different from that of EV-D68, Herlihy said. "Children with A71 do not present with a respiratory illness, and instead, they may have a rash, diarrhea, or a fever. D68 is associated with a respiratory illness that may be followed by AFM."

In Washington state, all of the children presented with symptoms indicative of a respiratory illness the week before they developed symptoms of AFM. Four children also had a fever of at least 100.4 degrees, but these symptoms do not precede all individuals who develop AFM. These differences make the problem harder to categorize around the country.

"I don't think we know which enterovirus is causing the cases — it may be D68 in other parts of the country, but again, we are not seeing that in Colorado," Herlihy said.

Any virus can cause neurological symptoms, the CDC says, and several have been linked with the paralyzing condition. To date, no specific pathogen has been consistently detected in the cerebral spinal fluid of affected patients.

The agency also points out that much remains unknown about AFM, such as what prompted the increase in cases that began in 2014. It also remains unclear as to which individuals are at a higher risk of developing AFM, or the reasons why they may be at higher risk.

"There can be diagnostic challenges with enteroviruses," Herilhy said. "Cerebral spinal fluid is often not positive for enteroviruses, and our recommendation is that providers collect specimens from alternative sites. We are seeing more positive cultures and less false negatives when specimens are collected from three sites — [cerebrospinal fluid], throat and rectal swabs."

http://bit.ly/2yqbk0r

The FDA Found Hundreds of Supplement Brands Tainted with Rx Drugs. Most Weren't Recalled.

More than 750 supplement brands have been found to be tainted with drugs

By Rachael Rettner, Senior Writer | October 12, 2018 11:33am ET

Dietary supplements aren't regulated like pharmaceutical drugs, so that means they shouldn't contain pharmaceutical drugs. Yet over the last decade, more than 750 supplement brands have been found to be tainted with drugs — sometimes containing two or more hidden drug ingredients, a new study finds.

What's more, although the Food and Drug Administration (FDA) identified these tainted supplements, less than half of these products were recalled.

That means that these products — which are essentially "unapproved drugs" — remain on the market, where they have the potential to cause serious health problems, the researchers, from the California Department of Public Health, wrote in the study, published today (Oct. 12) in the journal JAMA Network Open.

Now, medical experts are calling on the FDA to take more urgent action to remove these tainted supplements from the market.

"The agency's failure to aggressively use all available tools to remove pharmaceutically adulterated supplements from commerce leaves consumers' health at risk," Dr. Pieter Cohen, a general internist at Cambridge Health Alliance in Somerville, Massachusetts, wrote in a commentary accompanying the study. Cohen was not involved with the research.

Drugs in supplements

In the study, researchers analyzed data from an FDA database on dietary supplements tainted with pharmaceuticals that had been identified by the agency from 2007 to 2016. During this period, 776 dietary supplements were found to contain drugs. Of these, most (86 percent) were marketed for sexual enhancement or weight loss, and 12 percent were marked for muscle building.

About 1 in 5 products (20 percent) were found to contain more than one hidden drug ingredient, the study found.

The most common drugs found in supplements were sildenafil (the active ingredient in Viagra) for sex supplements, sibutramine (a banned weight-loss drug) for weight-loss supplements, and synthetic steroids or steroid-like ingredients for muscle-building supplements, the researchers said. Overall, fewer than half (46 percent) of the adulterated supplement brands were recalled.

Previous research by Cohen and colleagues has found that supplements continue to be sold in stores even after they are recalled. But "the shocking finding in the current study is that … over half the [supplement] brands that contain drugs never even were recalled in the first place," Cohen told Live Science. And "all of the ones that are not recalled will remain on the market."

It's unclear exactly why these products weren't recalled. It may be that the FDA wasn't able to reach the companies that made the tainted products to get them to issue a voluntary recall. Or the FDA may have contacted these companies, but they refused to voluntarily recall their products.

When a company refuses to voluntarily recall its products, the FDA has a number of tools it can use to get the product off the market: the agency can send a warning letter to the company, visit the factory for an inspection or issue a mandatory recall. But the study found that the FDA rarely employed such tools; out of the 146 companies involved in the making of the tainted supplements, the FDA issued just seven warning letters; and did not issue any mandatory recalls.

"There's just no way to interpret this other than the FDA is simply not doing its job," Cohen said.

What can be done

Supplements spiked with drugs pose a number of health risk to consumers — the drugs might interact with other medications that a person is taking; or they may be unsafe for people with certain health conditions. For example, sibutramine can increase blood pressure or heart rate, which could be risky for people with a history of stroke or heart disease.

A 2015 study found that dietary supplements are tied to 23,000 emergency room visits and 2,000 hospitalizations in the U.S. each year.

To get tainted supplements off the market, the FDA first has to try to get the companies to issue a voluntary recall every time the agency finds evidence of drugs in a supplement, Cohen said. If the company refuses to recall the product, the agency should follow up with aggressive actions to make sure the product is not available to consumers. "The FDA has to dedicate appropriate resources to getting the job done," Cohen said.

Another strategy could be to get Congress to change dietary-supplement regulations so that companies are required to register supplements with the FDA before they can sell them. That way, each supplement would have a registration code to identify it, which would allow the FDA to know exactly what supplements are being sold in the country. And if the supplement was found to be tainted,

the agency could "deactivate" the code so consumers could not purchase it, Cohen said.

But in the meantime, there are steps consumers can take to protect themselves from tainted supplements. Cohen advises consumers to speak with their doctor before they start taking a supplement. If people choose to start taking supplements without medical advice, Cohen recommends "single-ingredient" supplements rather than supplements with mixtures of ingredients, and to avoid supplement that promise health benefits like weight loss.

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

Climate change is about to make your beer more expensive

Extreme weather events are expected to reduce global barley production.

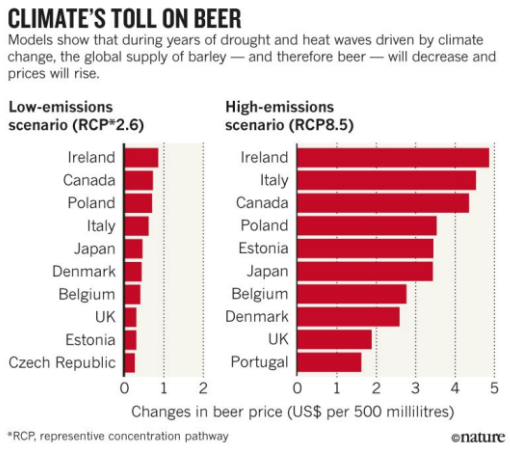
Matthew Warren

Extreme weather caused by climate change can have devastating effects — and it turns out that not even beer is safe.

More frequent droughts and heat waves in the twenty-first century will reduce global production of barley, finds a study published on 15 October in *Nature Plants*[1]. In turn, it finds, this will decrease the supply of beer and drive up prices, even under best-case-scenario models of climate change.

Many studies have explored how climate change will affect the production of staple foods such as wheat and rice, and some researchers have also looked at how luxury goods such as wine could be affected. But nobody has considered how beer will fare, says Dabo Guan, a climate-change economist at the University of East Anglia in Norwich, UK.

Guan and his colleagues combined a series of climate and economic models to predict how extreme weather produced by climate change is likely to affect barley crops (*Hordeum vulgare*) — and how this in turn will influence beer supply and pricing (see 'Climate's toll on beer').



Source: Xie, W. et al. Nature Plants **https://doi.org/10.1038/s41477-018-0263-1 (2018).**

Beer production might seem like a trivial consideration when it comes to climate change. But Guan hopes that highlighting a single luxury product will get people thinking about the broad implications of global warming.

"'What I'm trying to emphasize here is that climate change will impact people's lifestyle," he says — even those of people in industrialized countries, who may be shielded from the worst effects of climate change on food supply.

Guan hopes that helping people understand how climate change could affect their daily lives will motivate them to take action against climate change. If people "want to drink beer when we watch football, then we have to do something", he says.

Brewing storms

The team began by examining the chances of major droughts and heat waves in barley-growing regions on all six inhabited continents between 2010 and 2099. They considered four possible futures, from the best-case scenario, which sees relatively low levels of greenhouse-gas emissions during the twenty-first century, to the worst-case situation, in which emissions are high.

In each of these cases, the researchers found that the likelihood of extreme weather in barley-growing regions around the world increased compared with the number of similar events recorded in the late-twentieth and early twenty-first centuries. In the best-case

scenario, this chance increased by a modest 4%, but the worst case saw a rise of 31%.

The researchers then simulated the effect of these droughts and heat waves on barley production by using software to model crop growth and yield on the basis of weather and other variables.

They found that, globally, this extreme weather would reduce barley yield by between 3% and 17%. Some countries fared better than others: tropical areas such as Central and South America were hit badly, but crop yields actually increased in certain temperate areas, including northern China and the United States. Some areas of those countries saw yield increases of up to 90% — but this was not enough to offset the global decrease.

Finally, Guan and his colleagues fed these changes in barley yield into an existing economic model that can account for changes in supply and demand in the global market. This enabled them to look at how reduced barley production would affect pricing and consumption of beer in countries, as well as trade between nations.

In the worst-case scenario, the reduced barley supply worldwide would result in a 16% decrease in global beer consumption in the years of extreme-weather events. Prices would, on average, double.

Cutting back

As the world's largest overall consumer of beer, China would show the biggest national drop in beer consumption, drinking 4.34 billion fewer litres of beer each year. Even the United States — a rare case of a country actually producing more barley after climate change — would also see a decrease in national beer consumption, as it would be exporting more barley than it ever has before.

Meanwhile Ireland would see the biggest absolute price increase of the countries studied, with the price of beer going up by almost US$5 per 500 millilitre bottle, tripling the cost. That's because changes in price are partly influenced by consumers' willingness to pay — and Ireland is the world's largest consumer of beer on a per person basis.

Other countries like the Czech Republic have cheaper beer to begin with, but could see a huge relative rise in price of more than 600%.

Even under the best-case scenario, globally, the model predicted a 4% reduction in beer consumption and a 15% increase in price.

Klaus Hubacek, an ecological economist at the University of Maryland in College Park, says the study does a good job of combining climate, agriculture and economic models. He wonders how other alcohol crops might be affected, and whether beer drinkers might switch to cider or other alcoholic drinks.

But worries about beer pale in comparison to projections how climate change could harm food security generally, says David Reay, a climate-change scientist at the University of Edinburgh, UK.

"The effect on beer is going to be the least of our worries," he says, especially in the worst-case climate scenarios. Reay worries that this message could be diluted in studies such as Guan's, which concentrate only on luxury items.

"I think in that kind of future, I probably will need a beer, because it will be pretty bad," Reay says.

*Nature **562**, 319-320 (2018) doi: 10.1038/d41586-018-07015-7*

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Endurance exercise training has beneficial effects on gut microbiota composition

According to recent research, endurance exercise training beneficially modifies gut microbiota composition.

After six weeks of training, potentially inflammation causing microbes (Proteobacteria) decreased and microbes that are linked to enhanced metabolism (Akkermansia) increased.

Even though there was no significant drop in the weight of the subjects, exercise had other beneficial health effects, says Academy of Finland research fellow Satu Pekkala from the Faculty of Sport and Health Sciences of the University of Jyväskylä.

"We found that phospholipids and cholesterol in VLDL particles decreased in response to exercise. These changes are beneficial for cardiometabolic health because VLDL transports lipids from the liver to peripheral tissues, converts into 'bad' LDL cholesterol in the circulation, and thus has detrimental cardiovascular effects."

Exercise training also decreased Vascular adhesion protein-1 activity, which can have beneficial anti-inflammatory effects especially on vasculature, though the underlying mechanisms could not be determined in this study.

Whether Akkermansia mediates the health benefits of exercise is under further investigation

A few other cross-sectional studies have shown that microbes belonging to the *Akkermansia* genus are more abundant among physically active subjects than they are among inactive ones. *Akkermansia* has been a target of intense research recently, and some researchers believe that it may prevent obesity and diabetes.

"However, more studies are needed to prove that *Akkermansia* might mediate some of the health benefits of exercise," Pekkala says.

In addition to the composition of the gut microbiota, changes in their genes, that is, in their functionality, were studied.

"The abundance of the functional genes did not change much, which was perhaps to be expected because the diet did not change during training," Pekkala points out. "If the training period had been longer, greater effects probably would have been seen."

The research team made an exercise intervention for overweight women, which was completed by 17 subjects. Over a six-week period, previously sedentary women participated in three training sessions per week with a bicycle ergometer. The training intensity was controlled with heart rate. During the study, other lifestyle factors, including diet, were not changed in order to ensure that the effects of exercise could be observed. The research was carried out as a collaboration between the Faculty of Sport and Health Sciences of the University of Jyväskylä, University of Turku and the Spanish nonprofit research and healthcare organization FISABIO.

Original publication 3.10.2018: Munukka, E., Ahtiainen, J., Puigbo, P., Jalkanen, S., Pahkala, K., Keskitalo, A., Kujala, U., Pietilä, S., Hollmén, M., Elo, L., D'Auria, G., Pekkala, S. (2018). Six-Week Endurance Exercise Alters Gut Metagenome That Is not Reflected in Systemic Metabolism in Over-weight Women. Frontiers in Microbiology, *9, 2323. doi:10.3389/fmicb.2018.02323 Open access: https://doi.org/10.3389/fmicb.2018.02323*

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Mammals cannot evolve fast enough to escape current extinction crisis

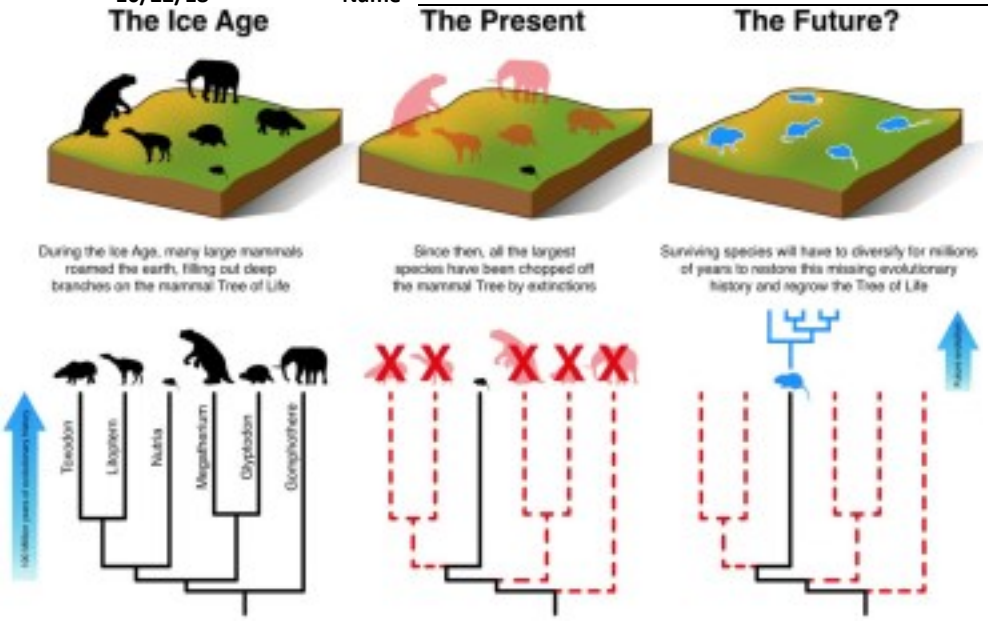
Humans are exterminating animal species so fast that evolution can't keep up

Humans are exterminating animal species so fast that evolution can't keep up; Unless conservation efforts are improved, so many mammal species will die out during the next 50 years that nature will need 3-5 million years to recover, a new study shows

We humans are exterminating animal and plant species so quickly that nature's built-in defence mechanism, evolution, cannot keep up. An Aarhus-led research team calculated that if current conservation efforts are not improved, so many mammal species will become extinct during the next five decades that nature will need 3-5 million years to recover.

There have been five upheavals over the past 450 million years when the environment on our planet has changed so dramatically that the majority of Earth's plant and animal species became extinct. After each mass extinction, evolution has slowly filled in the gaps with new species.

The sixth mass extinction is happening now, but this time the extinctions are not being caused by natural disasters; they are the work of humans. A team of researchers from Aarhus University and the University of Gothenburg has calculated that the extinctions are moving too rapidly for evolution to keep up.



An illustration of how the smaller mammals will have to evolve and diversify over the next 3-5 million years to make up for the loss of the large mammals.
Matt Davis, Aarhus University

If mammals diversify at their normal rates, it will still take them 5-7 million years to restore biodiversity to its level before modern humans evolved, and 3-5 million years just to reach current biodiversity levels, according to the analysis, which was published recently in the prestigious scientific journal, *PNAS*.

Some species are more distinct than others

The researchers used their extensive database of mammals, which includes not only species that still exist, but also the hundreds of species that lived in the recent past and became extinct as Homo sapiens spread across the globe. This meant that the researchers could study the full impact of our species on other mammals.

However, not all species have the same significance. Some extinct animals, such as the Australian leopard-like marsupial lion Thylacoleo, or the strange South American Macrauchenia (imagine a lama with an elephant trunk) were evolutionary distinct lineages and had only few close relatives. When these animals became extinct, they took whole branches of the evolutionary tree of life with them. We not only lost these species, we also lost the unique ecological functions and the millions of years of evolutionary history they represented.

"Large mammals, or megafauna, such as giant sloths and sabre-toothed tigers, which became extinct about 10,000 years ago, were highly evolutionarily distinct. Since they had few close relatives, their extinctions meant that entire branches of Earth's evolutionary tree were chopped off" says palaeontologist Matt Davis from Aarhus University, who led the study. And he adds:

"There are hundreds of species of shrew, so they can weather a few extinctions. There were only four species of sabre-toothed tiger; they all went extinct."

Long waits for replacement rhinos

Regenerating 2.5 billion years of evolutionary history is hard enough, but today's mammals are also facing increasing rates of extinction. Critically endangered species such as the black rhino are at high risk of becoming extinct within the next 50 years. Asian elephants, one of only two surviving species of a once mighty mammalian order that included mammoths and mastodons, have less than a 33 percent chance of surviving past this century.

The researchers incorporated these expected extinctions in their calculations of lost evolutionary history and asked themselves: Can existing mammals naturally regenerate this lost biodiversity?

Using powerful computers, advanced evolutionary simulations and comprehensive data about evolutionary relationships and body sizes of existing and extinct mammals, the researchers were able to quantify how much evolutionary time would be lost from past and potential future extinctions as well as how long recovery would take. The researchers came up with a best-case scenario of the future, where humans have stopped destroying habitats and eradicating

species, reducing extinction rates to the low background levels seen in fossils. However, even with this overly optimistic scenario, it will take mammals 3-5 million years just to diversify enough to regenerate the branches of the evolutionary tree that they are expected to lose over the next 50 years. It will take more than 5 million years to regenerate what was lost from giant Ice Age species.

Prioritizing conservation work

"Although we once lived in a world of giants: giant beavers, giant armadillos, giant deer, etc., we now live in a world that is becoming increasingly impoverished of large wild mammalian species. The few remaining giants, such as rhinos and elephants, are in danger of being wiped out very rapidly," says Professor Jens-Christian Svenning from Aarhus University, who heads a large research program on megafauna, which includes the study.

The research team doesn't have only bad news, however. Their data and methods could be used to quickly identify endangered, evolutionarily distinct species, so that we can prioritise conservation efforts, and focus on avoiding the most serious extinctions.

As Matt Davis says: "It is much easier to save biodiversity now than to re-evolve it later."

http://bit.ly/2Pbl9sH

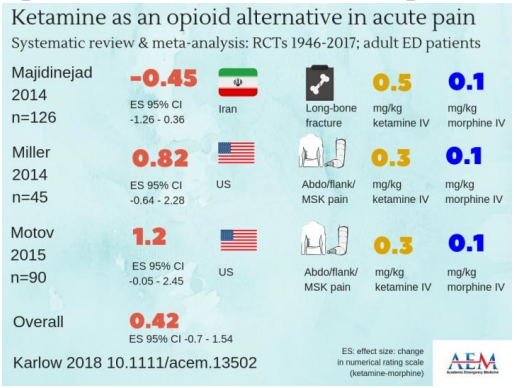
Ketamine is a safe, effective alternative to opioids in treating acute pain in the ED

Intravenous, low-dose ketamine is as effective as intravenous morphine in the control of acute pain in adults

DES PLAINES, IL -- Intravenous, low-dose ketamine (LDK) is as effective as intravenous morphine in the control of acute pain in adults in the emergency department (ED). That is the finding of a study to be published in the October 2018 issue of Academic Emergency Medicine (AEM), a journal of the Society for Academic Emergency Medicine (SAEM). The results indicate that ketamine can be considered as an alternative to opioids for ED short-term pain control.

The lead author of the study is Nicholas Karlow, MPHS, a medical student at the Washington University School of Medicine in St. Louis, Missouri. The findings of the study are discussed in the featured episode of SGEM Hop (Skeptics Guide to EM Hot Off the Press).

The systematic review and meta-analysis by Karlow, et al. maintains that there is a role for opioids in the treatment of pain in the ED, but suggest that as physicians continue to face pressure to reduce opioid use, it is important to establish that alternatives such as ketamine are comparable in providing patients with appropriate analgesia in a similar time frame.



Systematic review and meta-analysis: Randomized controlled trials 1946-2017; adult emergency department patients. **Kirsty Challen, B.SC., MBCHB, MRES, PH.D., Lancashire Teaching Hospitals, United Kingdom.**

The study further suggests that for patients with opioid use disorders or substance use disorders that require a potent analgesic in the emergency department, ketamine may be a favorable option compared to an opioid.

Moving forward, the authors suggest that observational studies assessing adverse events should use similar outcome measures and time frames, and that researchers should explore patient and physician satisfaction with ketamine analgesia and side effects compared to other opioid alternatives for acute pain.

"Karlow and colleagues provide persuasive evidence that emergency physicians can reasonably expect sub-dissociative ketamine to be as effective as morphine for patients with acute abdominal or

musculoskeletal pain. Minor ketamine adverse effects will likely prevent this therapy from becoming routinely first line, but low dose ketamine represents a good alternative choice for selected patients," commented Steven M. Green, MD, professor of emergency medicine and residency director at Loma Linda University, California.

Dr. Green's principal research interest has been on procedural sedation and analgesia, with numerous studies of ketamine dating back to 1990 and more recent works relating to sedation's optimal practice, politics, and future. He is a deputy editor at Annals of Emergency Medicine journal.

http://bit.ly/2Aif5WW

New research shows drinking No 1 Rosemary Water improves memory by up to 15 percent

Tests conducted at Northumbria University show drinking concentrated No 1 Rosemary Water improves cognitive performance

LONDON - New research published in the Journal of Psychopharmacology, has shown that drinking a concentrated rosemary extract drink, No 1 Rosemary Water, can boost cognitive and memory performance by up to 15%.

The research conducted by Dr Mark Moss at Northumbria University, is the first piece to be published on the benefit of drinking rosemary extract. The experiment used concentrated rosemary shots from No1 Rosemary Water, the only commercially available drink that combines rosemary extract with spring water and no other additives. The newly published research builds on Dr Moss' earlier trials showing the benefits of rosemary aroma in boosting memory function*.

About the trial - key findings

Dr Mark Moss and the team conducted a series of tests to measure cognitive performance, focusing on memory. These tests were designed to assess the participants' capability to retain and manipulate information. Across a number of tests, the group drinking No1 Rosemary Water saw an improvement in their ability to recall information and complete their cognitive tasks.

The test participants were each given 250ml of concentrated No1 Rosemary Water. 20 minutes after ingesting the shots, the experimental group performed the tasks while having their brain blood flow measured to assess how efficiently the body was extracting energy compared to the control group.

Those drinking No1 Rosemary Water shots saw an average increase of 15% in performance as well as an increase in the levels of deoxygenated red blood cells flowing through their brain. The researchers believe this indicates that the brain is extracting the energy it requires to perform the task more efficiently.

Bullets of findings:

Long-term and working memory tasks - 15% average improvement in a series of selected memory tasks in experimental group compared to placebo group. The current study therefore supports the body of evidence that rosemary has the potential for enhancing some memory-based aspects of cognitive functioning.

Brain blood flow - statistically significant increased levels of deoxygenated blood in the brain compared to placebo group. The study is the first evidence of a cerebrovascular benefit from the ingestion of rosemary and suggests improved extraction of oxygen in the control group during cognitive tasks.

Dr Mark Moss believes this study adds to the accumulation of studies already carried out suggesting that "rosemary offers a number of interesting possible health promoting applications, from antioxidant and anti-microbial to hepatoprotective and antitumorigenic activity." In particular, the team believe the presence of 1,8-cineole and rosmarinic acid, both found in No1 Rosemary Water, may be important in delivering improved cognitive performance.

He went on; "The results of this research show there are statistically reliable improvements in memory function thanks to the ingestion of No1 Rosemary Water. In fact, I'd say that the shots act like a turbo charger for the brain."

No1 Rosemary Water is developed using a unique and secret combination of extraction processes. The team use only fresh rosemary (not dried) and the herb is cold brewed to ensure that all the active compounds found in nature are extracted. This is not a flavour or essence.

History of rosemary

Throughout history, rosemary has been famous for its medicinal properties and its ability to improve memory.

From the alchemists of the past to modern day practitioners of aromatherapy, there is widespread acknowledgement of its power and benefits.

Rosemary has in fact, been associated with memory enhancement since ancient times. Ancient Greek students wore garlands of rosemary in exams and it has been referred to in literature of all kinds, as the herb of remembrance for hundreds of years.

Shakespeare's Hamlet, Act 4: Scene 5: "There's rosemary, that's for remembrance. Pray you, love, remember."

Today, science may finally be able to prove them right.

Read the article here: http://journals.sagepub.com/doi/full/10.1177/0269881118798339

http://bit.ly/2NMvaYt

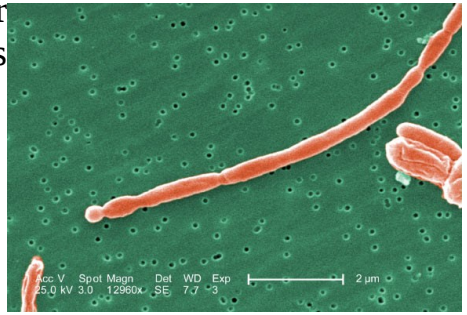
New Study Reveals Link between Gut Microbiota and Multiple Sclerosis

New study shows that gut microbiota could play a big role in the pathogenesis of multiple sclerosis

Multiple sclerosis is an immune-mediated autoimmune disease of the central nervous system that develops in genetically susceptible individuals and requires environmental triggers. A **new study**, published in the journal ***Science Translational Medicine***, shows that gut microbiota could play a big role in the pathogenesis of this disease.

In multiple sclerosis, the body's own immune system attacks and damages the protective coating around nerve cells.

This coating is made up of myelin — a biological membrane of protein and fatty substances — which is why research efforts to find the disease's target antigen have so far focused on the myelin membrane's components.



The new findings suggest that it is worth broadening the research perspective to gain a better understanding of the pathological processes.

***Under a high magnification of 12,960x, this SEM image revealed some of the morphologic details displayed by a number of joined, Gram-negative, rod-shaped* Escherichia coli *bacteria.* Janice Haney Carr, CDC.**

"T cells, i.e. the immune cells responsible for pathological processes, react to a protein called GDP-L-fucose synthase," said lead author Dr. Mireia Sospedra of the University Hospital Zurich and colleagues.

"This enzyme is formed in human cells as well as in bacteria frequently found in the gastrointestinal flora of patients suffering from multiple sclerosis."

"We believe that the immune cells are activated in the intestine and then migrate to the brain, where they cause an inflammatory cascade when they come across the human variant of their target antigen."

The researchers plan to test the immunoactive components of GDP-L-fucose synthase using an approach that they have been pursuing for several years already.

"Our clinical approach specifically targets the pathological autoreactive immune cells," Dr. Sospedra said.

"This approach differs radically from other treatments that are currently available, which throttle the whole immune system." "While these treatments often succeed in stopping the progression of the disease, they also weaken the immune system — and can thus cause severe side effects."

"Our clinical approach involves drawing blood from multiple sclerosis patients in a clinical trial and then attaching the immunoactive protein fragments onto the surface of red blood cells in a laboratory."

"When the blood is reintroduced into the bloodstream of patients, the fragments help re-educate their immune system and make it 'tolerate' its own brain tissue." "This therapeutic approach aims for effective targeted treatment without severe side effects."

Raquel Planas et al. *2018. GDP-l-fucose synthase is a CD4+ T cell–specific autoantigen in DRB3*02:02 patients with multiple sclerosis.* Science Translational Medicine *10 (462): eaat4301; doi: 10.1126/scitranslmed.aat4301*

http://bit.ly/2Ez2PFQ

NASA wants to send humans to Venus – here's why that's a brilliant idea

NASA is currently working on a conceptual manned mission to Venus

Gareth Dorrian * **Ian Whittaker** **

Popular science fiction of the early 20th century depicted Venus as some kind of wonderland of pleasantly warm temperatures, forests, swamps and even dinosaurs. In 1950, the Hayden Planetarium at the American Natural History Museum were soliciting reservations for the first space tourism mission, well before the modern era of Blue Origins, SpaceX and Virgin Galactic. All you had to do was supply your address and tick the box for your preferred destination, which included Venus.

Today, Venus is unlikely to be a dream destination for aspiring space tourists. As revealed by numerous missions in the last few decades, rather than being a paradise, the planet is a hellish world of infernal temperatures, a corrosive toxic atmosphere and crushing pressures at the surface. Despite this, NASA is currently working on a conceptual manned mission to Venus, named the High Altitude Venus Operational Concept – (HAVOC).

But how is such a mission even possible? Temperatures on the planet's surface (about 460°C) are in fact hotter than Mercury, even though Venus is roughly double the distance from the sun. This is higher than the melting point of many metals including bismuth and lead, which may even fall as "snow" onto the higher mountain peaks.

The surface is a barren rocky landscape consisting of vast plains of basaltic rock dotted with volcanic features, and several continent-scale mountainous regions.

Venus was once an Earth twin. **NASA / JPL**

It is also geologically young, having undergone catastrophic resurfacing events. Such extreme events are caused by the build up of heat below the surface, eventually causing it to melt, release heat and re-solidify. Certainly a scary prospect for any visitors.

Hovering in the atmosphere

Luckily, the idea behind NASA's new mission is not to land people on the inhospitable surface, but to use the dense atmosphere as a base for exploration. No actual date for a HAVOC type mission has been publicly announced yet. This mission is a long term plan and will rely on small test missions to be successful first. Such a mission is actually possible, right now, with current technology. The plan is to use airships which can stay aloft in the upper atmosphere for extended periods of time.

As surprising as it may seem, the upper atmosphere of Venus is the most Earth-like location in the solar system. Between altitudes of

50km and 60km, the pressure and temperature can be compared to regions of the Earth's lower atmosphere. The atmospheric pressure in the Venusian atmosphere at 55km is about half that of the pressure at sea level on Earth. In fact you would be fine without a pressure suit, as this is roughly equivalent to the air pressure you would encounter at the summit of Mount Kilimanjaro. Nor would you need to insulate yourself as the temperature here ranges between 20°C and 30°C.

The atmosphere above this altitude is also dense enough to protect astronauts from ionising radiation from space. The closer proximity of the sun provides an even greater abundance of available solar radiation than on Earth, which can be used to generate power (approximately 1.4 times greater).

The conceptual airship would float around the planet, being blown by the wind. It could, usefully, be filled with a breathable gas mixture such as oxygen and nitrogen, providing buoyancy. This is possible because breathable air is less dense than the Venusian atmosphere and, as result, would be a lifting gas.

The Venusian atmosphere is comprised of 97% carbon dioxide, about 3% nitrogen and trace amounts of other gases. It famously contains a sprinkling of sulphuric acid which forms dense clouds and is a major contributor to its visible brightness when viewed from Earth. In fact the planet reflects some 75% of the light that falls onto it from the sun. This highly reflective cloud layer exists between 45km and 65km, with a haze of sulphuric acid droplets underneath down to about 30km. As such, an airship design would need to be resistant to the corrosive effect of this acid.

Luckily we already have the technology required to overcome the problem of acidity. Several commercially available materials, including teflon and a number of plastics, have a high acidic resistance and could be used for the outer envelope of the airship. Considering all these factors, conceivably you could go for a walk on a platform outside the airship, carrying only your air supply and wearing a chemical hazard suit.

Life on Venus?

The surface of Venus has been mapped from orbit by radar on the US Magellan mission. However, only a few locations on the surface have ever been visited, by the series of Venera missions of Soviet probes in the late 1970s. These probes returned the first – and so far only – images of the Venusian surface. Certainly surface conditions seem utterly inhospitable to any kind of life.

The upper atmosphere is a different story however. Certain kinds of extremophile organisms already exist on Earth which could withstand the conditions in the atmosphere at the altitude at which HAVOC would fly. Species such as Acidianus infernus can be found in highly acidic volcanic lakes in Iceland and Italy. Airborne microbes have also been found to exist in Earth's clouds. None of this proves that life exists in the Venusian atmosphere, but it is a possibility that could be investigated by a mission like HAVOC.

The current climatic conditions and composition of the atmosphere are the result of a runaway greenhouse effect (an extreme greenhouse effect that cannot be reversed), which transformed the planet from a hospitable Earth-like "twin" world in its early history. While we do not currently expect Earth to undergo a similarly extreme scenario, it does demonstrate that dramatic changes to a planetary climate can happen when certain physical conditions arise.

By testing our current climate models using the extremes seen on Venus we can more accurately determine how various climate forcing effects can lead to dramatic changes. Venus therefore provides us with a means to test the extremes of our current climate modelling, with all the inherent implications for the ecological health of our own planet.

We still know relatively little about Venus, despite it being our nearest planetary neighbour. Ultimately, learning how two very

similar planets can have such different pasts will help us understand the evolution of the solar system and perhaps even that of other star systems.

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Disclosure statement *The authors do not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and have disclosed no relevant affiliations beyond their academic appointment.*

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Neanderthals Suffered a Lot of Traumatic Injuries. So How Did They Live So Long?

Our ancient-hominid relatives seem to have had surprisingly sophisticated health care.

David Robson

Neanderthals suffered many gruesome injuries in their day. The precious remains of our ancient-human relatives reveal crushed limbs, fractured skulls, and broken ribs—relics from hunting accidents and warfare. That's not to mention severe tooth abscesses and broken teeth that would have contributed to severe chronic pain. Behind these gory details, however, lies the fact that many of these individuals appear to have survived for months or even years after their injuries. They lived to fight another day. This is at odds with some common assumptions about Neanderthals: Compared to modern humans, they are often thought to have lacked the necessary compassion or cognitive abilities to look after the sick. "We can infer from the fact that they survived that they must have been helped by others—and in some cases that help must have been knowledgeable and quite well planned," says Penny Spikins, an archaeologist at the University of York in the United Kingdom. Their survival would have only been possible, in other words, if they had sophisticated health care.

In a recent paper in *Quaternary Science Reviews*, Spikins concludes that Neanderthals' medical skills were remarkably similar to our own ancestors' methods, and included wound dressing, fever management, midwifery, and a budding pharmacopeia of herbal remedies. Developing these abilities, she hypothesizes, might have even changed the course of their evolution.

Spikins has previously researched the *motives* of Neanderthal health care. In an attempt to debunk the myth that Neanderthals lacked the compassion of modern *Homo sapiens*, for instance, she describes one individual found in Shanidar Cave in Iraq who survived for a decade or more despite a withered arm and head injuries that would have probably resulted in sight and hearing loss. His survival would almost certainly have been impossible unless other group members had provided him with food, water, and shelter—a level of altruism not typically associated with the Neanderthal mind, Spikins says. She has now charted many other examples of individuals who could not have lived through their illnesses without the help of others.

Her latest paper builds on this analysis by examining some of the specific medical skills involved in such a level of care. In the vast array of bones that archaeologists have uncovered, the fractures had often healed without significant deformities, suggesting that they had been set with a primitive splint. Many of these wounds, such as the severe head traumas and broken ribs, probably would have resulted in significant blood loss and increased risk of infection, yet the injured individuals survived long enough for the bones to heal, and their remains lack signs of severe infection—which, Spikins says, would be apparent in lumps and bumps on the bone edges.

All of this suggests that Neanderthals had some means of dressing wounds. Spikins doesn't know exactly what those methods were, but she points out that bandages can be made from animal parts. Some Inuit groups today, for instance, use lemming skin to dress wounds and boils, since it is said to be particularly good at adhering to human

flesh. It's feasible that Neanderthals would have also come across similar methods to stem the blood flow and to keep the wound (relatively) hygienic, Spikins says.

Neanderthals may have even been in command of some natural drugs to speed their recovery. One of the other individuals in the Shanidar Cave was found to be buried with numerous plants that are believed to have medicinal properties, including yarrow, a natural antibacterial and anti-inflammatory agent that appears to accelerate wound healing. As a common folk cure, it is also said to reduce fevers and alleviate the symptoms of viral infections such as influenza, and to reduce flatulence and stomach cramps. Perhaps this was a sign of the health care he had received during his lifetime.

Supporting this hypothesis, Karen Hardy, of the Catalan Institution for Research and Advanced Studies and the Autonomous University of Barcelona, has spent the past six years analyzing the calcified plaque left on Neanderthal teeth, which can carry tiny traces of the foods they ate. In the first of these experiments, Hardy found the chemical signatures of yarrow and chamomile, which is also thought to be an anti-inflammatory agent. Since these plants taste extremely bitter, and have little nutritional value by themselves, she hypothesizes that they were instead used for self-medication.

One of Hardy's later plaque analyses of another Neanderthal individual revealed traces of poplar, which contains the natural painkiller salicylic acid, and the mold penicillium, the source of one of our most successful antibiotics. While we can't be sure that Neanderthals *deliberately* ingested these substances for medicinal purposes, it's telling that this individual suffered from a severe tooth abscess. Within the plaque, Hardy also found traces of microsporidia parasites, which cause acute diarrhea in humans. "The best guess is that it had to do with one or both of these infections," she told me.

At least one form of Neanderthal health care seems more certain: midwifery. Skeletal remains demonstrate that, like anatomically modern humans, the size and shape of a Neanderthal baby's head and the mother's pelvis would have made unassisted childbirth dangerous. "The only way those heads could have got out of the birth canal is with that characteristic 'twist' which happens with modern humans at birth," says Spikins—a maneuver that presents a high risk without assistance. From this, we can be fairly certain that they had developed some kind of midwifery to reduce the mortality rates, she says.

These findings don't just sketch out a new branch to the history of medicine, showing that Neanderthal health care was remarkably similar to our own ancestors' strategies; the research might also help us to better understand Neanderthals' long-term adaptations to their environment. Many Neanderthals lived in colder and more arid regions across Western and Central Europe and some parts of Asia, where they ventured as far north as the Altai Mountains in Siberia. In the more northern areas, the main food source would have been hulking great creatures such as mammoths and woolly rhinos, the hides of which were so thick that they could only be hunted with spears at a dangerously close range. In southern regions such as modern-day Spain, meanwhile, Neanderthals appear to have chased ibex over mountainous terrains, which came with a serious risk of falls. That's not to mention the many predators—including hyenas and saber-toothed cats—in these regions that posed their own dangers.

As a result of these challenges, injury rates were extraordinarily high, with one estimate suggesting that between 79 and 94 percent of Neanderthals sustained at least one traumatic injury in their lifetime. Spikins believes it simply would not have been possible for them to have adapted and spread so widely in these areas if they had not found the means to treat serious injuries. "As primates, we're not naturally adapted to hunting large animals," she explains of Neanderthals and *Homo sapiens* alike. "But health care allowed

groups to sustain much higher rates of injury than they would otherwise be able to sustain, so they move into an ecological niche that they weren't really well-suited for."

Spikins hypothesizes that—as with modern humans—Neanderthal health care could have also allowed greater cultural complexity to flourish, by enabling the older generation to share their knowledge with younger members of the group. "The whole population structure changes with health care, so you have more members who are older," she says; that cumulative knowledge might have allowed them to develop more sophisticated ways of hunting, for instance. She would also be interested to investigate whether midwifery allowed for the continued evolution of the brain. "We'd really hope that this study could prompt further thoughts about the ways these cultural practices can impact on our biological evolution," she says.

Other archaeologists I spoke with were intrigued by Spikins's paper, although they caution that we shouldn't yet draw firm conclusions from the available evidence, which is still somewhat circumstantial. We can only infer so much from the way their bones healed, rather than material artifacts demonstrating the specific practices involved, and it is impossible to know for certain why those Neanderthals were ingesting those bitter-tasting plants.

"There is little *hard* evidence—most of it is presumed," says April Nowell of the University of Victoria in Canada. She points out that many other animals have been known to self-medicate to a limited degree—and so it makes perfect sense that Neanderthals would be "equally if not more knowledgeable" of the medicinal benefits of plants. But she would have preferred more direct comparisons with anatomically modern humans and other primates to see whether the health-care adaptations differed between groups. It would have also been interesting to see whether the specific injuries, and the potential treatments, depended on the location and the particular challenges that it presented, and whether they changed over time. Did the Neanderthals in the north suffer from different maladies compared to those in Southern Europe?

In principle, however, the existence of more sophisticated health care chimes with the burgeoning recognition of Neanderthal intelligence. "It is totally in line with Neanderthal cognitive abilities, which there is no reason to suspect were very different from our own, and which would have allowed them to survive in their challenging environment," says Francis Wenban-Smith of the University of Southampton. It is one more reason, he says, to recognize our cousins' "capabilities as members of the human family, rather than presuming them to be the simple-minded brutes of popular folklore."

http://bit.ly/2R113P0

Age-related increase in estrogen may cause common men's hernia

Men could be treated with hormone inhibitor to strengthen muscle

CHICAGO --- An age-related increase in estrogen may be the culprit behind inguinal hernias, a condition common among elderly men that often requires corrective surgery, according to a Northwestern Medicine study was published Oct. 15 in Proceedings of the National Academy of Sciences.

The study, led by Dr. Serdar Bulun, chair and the John J. Sciarra Professor of Obstetrics and Gynecology at Northwestern University Feinberg School of Medicine, found the lower abdominal muscles of mouse models are particularly sensitive to estrogen, developing scar tissue in response to increases in estrogen levels that weakens the abdominal wall and eventually causes a hernia.

When the investigators reduced estrogen with a drug compound, it prevented the hernias, suggesting a therapy with preventive potential in humans.

"It may make sense to treat at-risk men with an aromatase inhibitor that could decrease estrogen and strengthen the muscle," said Bulun,

also a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Inguinal hernias occur when tissue, such as the intestines, protrudes through the inguinal canal, a weak spot near the groin in the human abdominal wall. These hernias are the most common reason men undergo surgery. There are more than 700,000 inguinal hernia repair surgeries performed each year in the United States, according to the Food and Drug Administration. While the chances of an inguinal hernia increase as men age, the root cause remains unknown.

One other consequence of aging in men is that a larger share of testosterone is converted to estrogen by a hormone called aromatase. Bulun, whose chief scientific interests include breast cancer and gynecology, was investigating the effects of high estrogen in female mice. One experiment involved boosting estrogen levels by incorporating the human aromatase gene into the mouse genome, creating mice who would convert testosterone into estrogen throughout the body. Originally, he wasn't even interested in the male mice -- until an animal keeper at Northwestern spotted large hernias developing in only the males.

Bulun investigated these mice, finding large swaths of fibroblasts -- scar tissue -- developing in a small muscular sphincter, a structure analogous to the inguinal canal in humans.

"We realized the lower abdominal muscle is extraordinarily sensitive to estrogen," Bulun said. "Estrogen causes these fibroblasts to divide rapidly, at a much higher pace than the muscle cells."

The proliferation of the fibroblasts weakens the integrity of the sphincter and it eventually gives way, causing a hernia. When the investigators gave the mice a drug that blocked aromatase, and therefore the conversion of testosterone to estrogen, the hernias stopped, pointing toward estrogen as the cause and indicating potential for an aromatase inhibitor therapy that may be able to prevent surgery in at-risk patients, Bulun said.

Those patients with greater risk of hernia often have common factors like age or genetics, but overall, Bulun said the best predictor of a future inguinal hernia is a previous one.

"If you have to repair a hernia for the second time, the chances of success go down," Bulun said. "If there is a recurrent case, you might be able to supplement the surgical treatment of that patient with medication."

Bulun is currently working with Dr. Jonah Stulberg, assistant professor of surgery at Feinberg and co-author of the current study, to design clinical trials that would test an aromatase inhibitor's effectiveness in human subjects.

The first author of the paper was Dr. Hong Zhao, research associate professor of obstetrics and gynecology. Other Northwestern authors include Robert Chatterton, professor emeritus of obstetrics and gynecology, and Dr. Warren Tourtellotte, adjunct professor of pathology, all at Feinberg.

This study was supported by grant R37-HD36891 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health.

http://bit.ly/2P8BSwW

New blood test could spare cancer patients from needless chemotherapy after surgery

Many cancer patients have chemotherapy after surgery, but not all of them actually need it

Jeanne Tie

Many cancer patients could soon be spared the unnecessary side effects of chemotherapy after having surgery to remove their tumour.

A blood test being trialled at more than 40 hospitals across Australia and New Zealand aims to detect whether there are any cancer cells remaining in the body after surgery, which could lead to the cancer returning.

There is currently no reliable way of knowing which patients will have their cancer return after surgery. So, early stage cancer patients

often receive chemotherapy after surgical treatment as a precaution – to mop up any cancer cells that could remain.

But chemotherapy comes with a host of serious side effects. Short-term, these include pain, fatigue, nausea and other digestive issues, bleeding problems and an increased susceptibility to infection. Long term side-effects may include heart, lung, nerve and memory problems, and fertility issues.

When cancer cells rupture and die – which they are always doing – they release their contents, including cancer-specific DNA, that float freely in the bloodstream. This is called "circulating tumour DNA" or ctDNA. If ctDNA is detected after surgery, this indicates there are remaining microscopic cancer cells in the patient that weren't picked up by standard tests.

Research shows patients positive for circulating tumour DNA after surgery have an extremely high risk of cancer relapse (close to 100%) while those with a negative test have a very low risk of relapse (less than 10%).

Current trials in early-stage bowel cancer patients started in 2015. These have shown the ctDNA test can determine whether patients can be divided into "high risk" and "low risk" groups. The trials were later extended to women with ovarian cancer in 2017 and will soon extend to pancreatic cancer.

Results from the same test could also help scale the dose for the patients who do need chemotherapy, depending on their risk of cancer returning.

Why do we need the test?

When a patient with a cancer, such as early stage bowel cancer, is diagnosed, their tumours seem to be limited to the bowel with no evidence of spread to elsewhere in the body. But after a successful surgery to remove the bowel cancer, around one-third of these patients will experience cancer recurrence elsewhere in the body in the following years.

This shows that cancer cells have already spread at the time of diagnosis, but could not be detected using our current standard blood tests and scans. If these patients had been treated with chemotherapy after surgery, these relapses would have been prevented by eradicating the microscopic residual cancer cells responsible for the cancer's return.

In the case of bowel cancer, the decision on whether to use chemotherapy is based on an assessment of the cancer removed at the time of surgery in the lab. For example, if there are cancer cells in the lymph glands next to the bowel (a stage 3 cancer), there is an increased probability the cancer has already spread elsewhere.

For other cancers, such as ovarian and pancreatic, other methods are used to determine whether chemotherapy is necessary. But they all lack precision. Ultimately, some high-risk patients will not have cancer recurrence because their cancer has been cured by surgery alone, while other apparently low-risk patients will suffer from recurrence.

So, many bowel cancer patients are currently treated with six months of chemotherapy and its associated side effects, even though they do not need to be treated. While others that would potentially benefit from treatment do not receive the necessary chemotherapy because they appear to be at low risk.

More than 400 patients have already joined in the trials but there is hope this will grow to more than 2,000. The trials are expected to run until 2021 for bowel cancer and 2019 for ovarian cancer.

The ctDNA test was developed through a collaboration between the Walter and Eliza Hall Institute and Johns Hopkins Kimmel Cancer Centre, US.

The ability to find and measure cancer DNA in patient's blood could revolutionise cancer care. The next step is to determine how it can be used in the clinic.

Associate Professor, Walter and Eliza Hall Institute

Disclosure statement Jeanne Tie receives funding from Victorian Cancer Agency and NHMRC.

https://go.nature.com/2CuyAx8

Dandelion seeds fly using 'impossible' method never before seen in nature

The seeds contain a lot of open space, which seems to be the key to sustaining flight.

Jeremy Rehm

Dandelion seeds fly using a method that researchers thought couldn't work in the real world, according to a study[1] published on 17 October in *Nature*.

When some animals, aeroplanes or seeds fly, rings of circulating air called vortices form in contact with their wings or wing-like surfaces. These vortices can help to maintain the forces that lift the animal, machine or seed into the air.

Researchers thought that an unattached vortex would be too unstable to persist in nature. Yet the light, puffy seeds of dandelions use vortices that materialize just above their surfaces and lift the seed into the air.

Up in the air

Dandelion seeds bear filaments that radiate out from a central stalk like the spokes on a bicycle wheel, a feature that seems to be the key to their flight. Many insects harbour such filter-like structures on their wings or legs, suggesting that the use of detached vortices for flight or swimming might be relatively common, says study co-author Naomi Nakayama, a plant scientist at the University of Edinburgh, UK.

Researchers were curious about how these bristly seeds stayed in the air because they looked so different from the wing-like seeds of other plants, such as maples. Those structures act like the wings of a bird or aeroplane, generating pressure differences above and below the wing to fly. To find the answer, Nakayama and her colleagues put dandelion seeds in a vertical wind tunnel and used a laser to illuminate particles that helped to visualize the airflow around the seed.

That's when they saw the vortex floating above the seeds. The amount of open space between the seed's spokes seems to be the key to the stability of these detached vortices, says study co-author Cathal Cummins, an applied mathematician at the University of Edinburgh. Pressure differences between the air moving through the spokes and the air moving around the seed creates the vortex ring.

Previous studies have found that dandelion seeds always have between 90 and 110 bristles, says Nakayama. It's "scary consistent", and that consistency turns out to be very important.

Just right

When the team designed small silicon discs to imitate these spokes, they produced models with a range of openings: from solid discs to ones that were 92% air, like the structures on the dandelion seeds. When the researchers tested these model seeds in their wind tunnel, they found that only the discs that best approximated dandelion seeds could maintain the detached vortex.

If the number of openings in the discs was even 10% off of those in dandelion seeds, the vortex destabilized. The seed looks inefficient for flight because it has so much open space, says Nakayama, but these openings are what allow the unattached vortex ring to remain stable.

It's great to see an analysis of something we see every day but didn't fully understand, says Richard Bomphrey, a comparative biomechanist at the Royal Veterinary College in Hatfield, UK. "To discover that there were aerodynamic mechanisms that we didn't already know — despite the fact that we can fly things at Mach 9 — is always exciting."

doi: 10.1038/d41586-018-07084-8

Read the related editorial, Revealed: the extraordinary flight of the dandelion.

http://bit.ly/2S2rKUO

The Lancet HIV: PrEP implementation is associated with a rapid decline in new HIV infections

Study from Australia first to evaluate a population-level roll-out of pre-exposure prophylaxis in men who have sex with men.

Rapid, targeted, and high-coverage roll-out of pre-exposure prophylaxis (PrEP) to men who have sex with men was associated with a reduction in HIV diagnoses by 25% in one year across New South Wales (Australia), according to a study published in *The Lancet HIV* journal.

Diagnoses in men who have sex with men across New South Wales reduced from 295 cases in the year before PrEP roll-out to 221 cases in the year after - the lowest levels recorded since the beginning of HIV surveillance in 1985.

The study, led by the Kirby Institute at UNSW Sydney, followed 3,700 men who had been dispensed PrEP as part of the roll-out and found generally high levels of adherence. In this group, the incidence of HIV infection was less than 1 in 2,000 per year, compared with an expected incidence of 2 per 100 per year or higher in the absence of PrEP.

Randomised controlled trials have previously demonstrated the efficacy of PrEP. In addition, mathematical models have predicted that PrEP can have a large and fast impact if rolled out rapidly and at high coverage for people at risk. However, empirical studies to confirm PrEP's population-level effectiveness have not tested these findings until now.

The study in New South Wales was possible due to the existing surveillance system for recent HIV infection in the area, which allowed researchers to quickly document the population-level effect of PrEP. It illustrates the successes possible with effective roll-out of PrEP.

Although a number of countries, including the USA, France, and England, have approved HIV PrEP, uptake has until recently been slow and geographically patchy.

"Our results support the population-level effectiveness of PrEP one year after rapid PrEP implementation at scale," says Professor Andrew Grulich, from the Kirby Institute at UNSW Sydney. "PrEP is a highly effective preventative approach when implemented alongside high levels of HIV testing and treatment. Roll-out should be prioritised as a crucial component of HIV prevention in epidemics predominantly affecting men who have sex with men." [1]

The study recruited 3,700 participants aged 18 years or older from 21 clinics across New South Wales. All participants in the study were at high risk of HIV infection, and were given PrEP for free. HIV testing was conducted at one and three months after enrolment into the trial, then every three months.

Among the 3,700 participants, 3,645 (99%) were dispensed PrEP or had a HIV test at least once during follow-up. During the year-long study, only two men became infected with HIV and these men were not adherent to PrEP.

The authors found that adherence to PrEP was high (median medication possession ratio of 98%). However, approximately 30% of participants had adherence below 80%, but this could also indicate on-demand PrEP use [2], or stopping using PrEP after a period of high-risk behaviour.

State-wide [3], the authors found that after PrEP roll-out there were 25% fewer HIV diagnoses, compared to the 12 months before PrEP roll-out (295 cases vs 221 cases).

The decline was greatest for recent HIV infections (32% decline, from 149 cases to 102 cases). These declines were greatest in men aged 45 years or older, Australian-born men, and those who lived in the gay neighbourhoods of Sydney.

In comparison with other international settings, PrEP roll-out in New South Wales was more rapid and at higher coverage - meeting the initial target of 3,700 participants on PrEP within eight months. 12 months after, 7,621 participants were taking part. By the end of the study, 9,714 people were taking part.

In the USA, PrEP was approved in 2012 and it was estimated that 492,000 men would benefit from the drug. However, uptake was sluggish before accelerating more recently, and by late 2016 it was estimated that 83,672 men in the US had commenced PrEP.

In England, the NHS announced it would provide PrEP to 10,000 patients through an implementation study in selected clinics from September 2017. Reductions in HIV diagnoses in 2017 in London have been attributed to a combination of increased testing and treatment, as well as PrEP sourced through trials or privately.

In France, 2,805 people (97% MSM) were prescribed PrEP in the first 12 months of roll-out in 2016 with only four new HIV infections in this cohort, but population-based trends in HIV have not yet been reported.

Professor Grulich adds: "This study involved a large-scale and state-wide response to ensure that PrEP was made available to men at high risk of HIV infection. This involved leadership from the NSW Government, advocacy groups working to help improve health literacy, and a network of free, publicly funded and private sexual health services serving men who have sex with men." [1]

The authors note some limitations, including that they cannot rule out that some other factors may be involved in the reduced levels of infection at a state level, and some infections may have been missed if people did not attend the last HIV test at 12 months. They also note that some men may have obtained PrEP privately and the level of coverage may have been higher than described in the study.

Writing in a linked Comment, Professor Sheena McCormack, MRC Clinical Trials Unit, UK, notes that New South Wales was an ideal location to help identify the added benefit of PrEP as it has met the 90-90-90 targets [4] for the proportion of individuals with HIV diagnosed, treated, and virally suppressed, which were surpassed in 2016, but adds that most countries are unlikely to reach these targets by 2020.

She notes: "Now, the EPIC-NSW study has provided robust evidence for the added value of PrEP at the population level, as well as endorsing the biological efficacy in individuals who use PrEP consistently during periods of possible exposure to HIV."

Peer-reviewed / Observational study / People

NOTES TO EDITORS

This study was funded by the New South Wales Ministry of Health with some study drug provided by Gilead Sciences. It was conducted by researchers from the Kirby Institute at the University of New South Wales, Macquarie University, New South Wales Ministry of Health, University of Sydney, ACON, Positive Life NSW, Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine, Sydney Sexual Health Centre, North Coast HIV/Sexual Health Services, Holden Street Clinic, Holdsworth House Medical Practice, The Albion Centre, Illawarra Sexual Health Service, St Vincent's Hospital, Liverpool Sexual Health Clinic, Albury Sexual Health Service, Brookong Sexual Health Centre, Taylor Square Private Clinic, Northern Sydney Sexual Health, Nepean Blue Mountains Local Health District Department of Sexual Health, Short Street Clinic, RPA Sexual Health, Hunter-New England Sexual Health, University of Newcastle, Coffs Harbour Sexual Health, Kirketon Road Centre.

The labels have been added to this press release as part of a project run by the Academy of Medical Sciences seeking to improve the communication of evidence. For more information, please see: http://www.sciencemediacentre.org/wp-content/uploads/2018/01/AMS-press-release-labelling-system-GUIDANCE.pdf if you have any questions or feedback, please contact The Lancet *press office pressoffice@lancet.com*

[1] Quote direct from author and cannot be found in the text of the Article.

[2] On-demand use of PrEP involves taking two tablets 2-24 hours before sex, one tablet 24 hours after sex and a further tablet 48 hours after sex. Daily use involves taking one tablet a day.

[3] The population of the state of NSW is approximately 7 million people. The first year of the roll-out of PrEP reached 7,621 people.

[4] The UNAIDS 90-90-90 target aims for 90% of all people living with HIV to know their HIV status, 90% of all people with diagnosed HIV infection to receive sustained antiretroviral therapy, and for 90% of all people receiving antiretroviral therapy to have viral suppression by 2020. .

http://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(18)30215-7/fulltext

http://bit.ly/2PL2Pnh

Case Western Reserve researchers cure drug-resistant infections without antibiotics

Results in mouse sepsis model lay foundation for clinical trials

Biochemists, microbiologists, drug discovery experts and infectious disease doctors have teamed up in a new study that shows antibiotics are not always necessary to cure sepsis in mice. Instead of killing causative bacteria with antibiotics, researchers treated infected mice with molecules that block toxin formation in bacteria. Every treated mouse survived. The breakthrough study, published in *Scientific Reports*, suggests infections in humans might be cured the same way. The molecules cling to a toxin-making protein found across Gram-positive bacterial species, called AgrA, rendering it ineffective. Treating mice with the therapeutic molecules effectively cured infections caused by *methicillin-resistant Staphylococcus aureus* (*MRSA*). *S. aureus* is notorious for its ability to overcome even the most potent antibiotics. Its resistance arsenal is broad, limiting therapeutic options to treat infections.

In a mouse model of *S. aureus* sepsis, treatment with small molecules alone resulted in 100 percent survival, while 70 percent of untreated animals died. The small molecules were as effective in promoting survival as antibiotics currently used to treat *S. aureus* infections. The molecules also appear to give antibiotics a boost. Septic mice treated with a combination of the small molecules and antibiotics had 10x fewer bacteria in their bloodstream than mice treated with antibiotic alone.

"For relatively healthy patients, such as athletes suffering from a MRSA infection, these molecules may be enough to clear an infection," said Menachem Shoham, PhD, associate professor of biochemistry at Case Western Reserve University School of Medicine, and senior author on the study. "For immunocompromised patients, combination therapy with the molecules and a low-dose antibiotic may be in order. The antibiotic in the combination could be one to which the bacteria are resistant in monotherapy, because our small molecules enhance the activity of conventional antibiotics, such as penicillin." With support from the small molecules, previously obsolete antibiotics could reenter the clinic. Said Shoham, "This could provide a partial solution to the looming, global threat of antibiotic resistance."

If available, antibiotics kill most bacteria, but a small number of bacteria with natural resistance survive. Over time, antibiotic-resistant bacteria multiply and spread. By Centers for Disease Control and Prevention estimates, at least two million Americans get an antibiotic-resistant infection annually. For some infections, effective antibiotics are no longer available. Disarming bacteria of disease-causing toxins represents a promising alternative to dwindling antibiotics.

Eliminating toxins frees up the immune system to eliminate bacterial pathogens instead of antibiotics, said Shoham. "Without the toxins the bacteria become harmless. And since they don't need the toxins to survive, there is less pressure to develop resistance."

The small molecules work against multiple bacterial species. The new study included preliminary experiments showing the molecules prevent three other bacterial species from killing immune cells. "These results indicate broad-spectrum efficacy against Gram-positive pathogens," wrote the authors. Added Shoham, "We have proven efficacy not only against MRSA but also against *Staphylococcus epidermidis* which is notorious for clogging catheters, *Streptococcus pyogenes* that causes strep throat, *Streptococcus pneumoniae*, and other pathogens."

Shoham led the study in collaboration with colleagues from the departments of biochemistry and dermatology and the Center for RNA and Therapeutics at Case Western Reserve University. The researchers developed two small molecules, F12 and F19, both of

which potentiate antibiotic efficacy in the mouse models. The researchers are now working to commercialize both potential drugs. Case Western Reserve University has issued a license to Q2Pharma, Ltd., a biopharmaceutical startup company in Israel, to perform additional preclinical studies and develop F12 and F19 for clinical trials. Their initial trials will focus on patients suffering from systemic multi-drug resistant infections.

This research was supported by a Transformational Award to Menachem Shoham by the Dr. Ralph and Marian Falk Medical Research Trust Bank of America, N.A., Trustee. Some in vitro studies were supported by NIH/NIAID Preclinical Services under contract numbers HHSN272201100012I and HHSN27200007.

Greenberg, M, et al. "Small-molecule AgrA inhibitors F12 and F19 act as antivirulence agents against Gram-positive pathogens." Scientific Reports*. 2018 Oct 1;8(1):14578. doi: 10.1038/s41598-018-32829-w. PMID: 30275455.*

http://bit.ly/2yq0Qhw

We're doing drug trials wrong – here's how to fix it

Problem in developing all new medicines lies in the tendency to research, diagnose and treat diseases as a single entity

Tracy Hussell Professor of Inflammatory Disease, University of Manchester

By the age of 65, at least half of us will suffer from two or more long-term diseases. And the chance of having multi-morbidity, as it is known, increases with age.

Only 9% of people with coronary heart disease have no other condition. The other 91% have various combinations of hypertension (high blood pressure), heart failure, stroke, diabetes, chronic obstructive pulmonary disease, depression, dementia, chronic kidney disease and so on.

And it's not just the elderly who suffer from several long-term conditions – young people do too. In poor areas, the occurrence of two or more diseases in the young can occur ten to 15 years earlier compared with those in wealthier regions.

People with multi-morbidities have to take a range of drugs: one or more for each disease. But whether drugs developed to treat single diseases are effective in patients with multi-morbidity is a matter of debate. In some patients, their body attacks the drug as though it were a pathogen. In other patients, the treatment causes [side effects] that are worse than the disease being treated, including an increased risk of infection.

A new class of drugs, so-called disease-modifying anti-rheumatic drugs, are being used to treat rheumatoid arthritis. These drugs treat the underlying disease rather than just ease the symptoms. This is a major advance, but at least 40% of the people taking them won't see an improvement in their symptoms. This is probably because most patients have another disease, which may stop the drug working properly.

The root of the problem in developing all new medicines lies in the tendency to research, diagnose and treat diseases as a single entity. The single disease approach goes right back to the way biology is taught at school and university.

Multi-morbidity is the norm

A growing number of medical researchers think we should learn from disease combinations. This may seem like an impossible task, given the number of possible combinations, but some combinations are very common, such as heart disease and high blood pressure. And not taking multi-morbidities into account affects every stage of introducing a new drug, from its discovery to testing it in patients.

The decision to develop a new drug is based on the careful analysis of thousands of patient groups. But these groups are not divided based on the presence of other existing diseases. By not grouping patients based on pre-existing conditions, many relevant new drugs specific for particular disease combinations may be missed.

Once new drugs have been developed, they are first tested in animal models of a particular disease or in tissue culture, containing an individual cell type. There is no guarantee that this type of test is relevant for human disease, and there is also no guarantee that

relevant drugs won't be missed that might have worked in more complex disease combinations.

Multi-morbidities are also not taken into account when new drugs are tested in patients. Remarkably, the patients who have the most severe disease combinations, and are the most problematic to treat, are mostly excluded from clinical trials. In coronary heart disease, for example, on average, 69% of patients with multi-mobidities are excluded from clinical trials because clinicians are wary of making their disease even worse. Yet these are the patients that most need the treatment. Also, how the drug works may differ in patients with one disease compared with patients with more than one disease.

The situation is even worse for dementia patients where 95% have other diseases, yet in 86% of trials, patients with other conditions are excluded. Instead, recruitment for clinical trials picks those patients who are potentially less affected by the disease in question, as they do not have any of the commonly associated multi-morbidities, which could also mean they are in a younger age group that responds differently to the drug.

Appetite for a new approach

Is it any wonder that little progress has been made in the treatment of the most debilitating conditions affecting the human race? New targets for drugs should not be chosen irrespective of what else is wrong with the patient. Rather patients with a particular disease should be sub-categorised and studied based on the other diseases they have, and treatment specifically tested and tailored to their needs. Also, science funding bodies and the pharmaceutical industry should drive the development of new animal and tissue culture models in which to test new drugs that encompass patient disease complexity. There is an appetite among researchers for this approach, but the momentum needs to increase.

Disclosure statement *Tracy Hussell does not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and has disclosed no relevant affiliations beyond their academic appointment.*

Partners ***University of Manchester*** *provides funding as a member of The Conversation UK.*

http://bit.ly/2OzWGOr

Distinguishing fatal prostate cancer from 'manageable' cancer now possible

Could reduce unnecessary surgeries and radiotherapy

Scientists at the University of York have found a way of distinguishing between fatal prostate cancer and manageable cancer, which could reduce unnecessary surgeries and radiotherapy.

A recent study showed that more than 25 men were being unnecessarily treated with surgery or radiotherapy, for every single life saved. It is believed that success rates could be hindered as a result of treating all prostate cancers in the same way.

A team at the University of York and the University of British Columbia, Canada, however, have designed a test that can pick out life-threatening prostate cancers, with up to 92% accuracy.

Professor Norman Maitland, from the University of York's Department of Biology, said: "Unnecessary prostate treatment has both physical consequences for patients and their families, but is also a substantial financial burden on the NHS, where each operation will cost around £10,000.

"Cancers that are contained in the prostate, however, have the potential to be 'actively monitored' which is not only cheaper, but has far fewer negative side-effects in patients with non-life threatening cancer."

It is now understood that to find the different levels of cancer, scientists have to identify genes that have been altered in different cancer types. The team analysed more than 500 cancer tissue samples and compared them with non-cancer tissue to search for patterns of

a chemical group that is added to part of the DNA molecule, altering gene expression.

A person's age, what they eat and how they sleep, for example, impacts on chemical alterations to genes and which ones are turned on and off. This is part of the normal functioning of the human body and can tell individuals apart, but the process can sometimes go wrong, resulting in various diseases.

Professor Maitland said: "In some diseases, such as cancer, genes can be switched to an opposite state, causing major health issues and threat to life.

"The challenge in prostate cancer is how to look at all of these patterns within a cell, but hone in on the gene activity that suggests cancer, and not only this, what type of cancer - dangerous or manageable?

"To put it another way: how to do we distinguish the tiger cancer cells from the pussycat cancer cells, when there are millions of patterns of chemical alterations going on, many of which will be perfectly healthy?"

The team needed to eliminate the 'noise' of the genetic patterns that make individuals unique, to leave them with the patterns that indicate cancer. They were able to do this using a computer algorithm, which left the team with 17 possible genetic markers for prostate cancer.

Dr Davide Pellacani, who began these studies in York, before moving to the University of British Columbia, said: "Using this computer analysis, not only could we see which tissue samples had cancer and which didn't, but also which cancers were dangerous and which ones less so.

"Out of almost a million markers studied, we were able to use our new tools to single out differences in cancer potency."

To take this method out of the laboratory, the team are now investigating a further trial with new cancer samples, and hope to involve a commercial partner to allow this to be used for patients being treated in the NHS.

The research, published in the *British Journal of Cancer*, was funded by The Freemasons of the Province of Yorkshire (North and East Ridings) and The Masonic Samaritan Fund. Yorkshire Cancer Research; Prostate Cancer UK; The British Columbia Cancer Agency Strategic Priorities Fund.

https://wb.md/2CudSNW

C diff Spores on Bedsheets Survive Hospital Laundering

60% of spores behind, increasing the risk of contamination

Troy Brown, RN

Conventional laundering methods for hospital bedsheets left 60% of *Clostridium difficile* spores behind, increasing the risk of contaminating other bed linens and patients, new data show.

"The findings of this study may explain some sporadic outbreaks of *C difficile* infections in hospitals from unknown sources, however, further research is required in order to establish the true burden of hospital bedsheets in such outbreaks," senior author Katie Laird, PhD, head of the Infectious Disease Research Group, School of Pharmacy, De Montfort University, Leicester, United Kingdom, said in a news release.

Joanna Tarrant, PhD, from the Infectious Disease Research Group, School of Pharmacy, De Montfort University, and colleagues report their findings in an article published online October 16 in *Infection Control and Hospital Epidemiology*.

To test the effect of laundering on *C difficile* spores, the investigators used both naturally contaminated bedsheets from patients infected with *C difficile* and experimentally inoculated sheets. The sheets were washed according to the current UK National Health Service (NHS) laundry policy, as specified in Health Technical Memorandum (HTM) 01-04.

With the experimentally inoculated sheets, the authors initially tested the effects of washing without detergent (a control cycle), exposing the spores to the heat and agitation specified in the NHS protocol, and found that the sheets remained heavily contaminated.

After washing with detergent, the experimentally inoculated sheets still contained 0 to 9 colony-forming units (cfu) per 25 cm^2 swatch. Moreover, previously sterile swatches washed in the load with the experimentally inoculated sheets held 0 to 14 cfu/25 cm^2. Thus, the washing not only did not sterilize the original bedsheets but also spread the contamination to other items in the laundry load.

When the team repeated the analysis with naturally contaminated sheets laundered at a commercial laundry in accordance with the NHS protocol, the results were similar. Prior to washing, the sheets were contaminated with an average of 51 cfu/cm^2. After laundering, the spore count was 33 cfu/cm^2.

"The thermal disinfection conditions, described in HTM 01-04, were inadequate to fully decontaminate linen that had been naturally contaminated with *C. difficile* spores," the authors write.

The residual contamination could be contributing to sporadic outbreaks, the authors note, especially if facilities rent linens from companies that distribute bedding to multiple hospitals or healthcare facilities.

The study received no financial support. The authors have disclosed no relevant financial relationships.

Infect Control Hosp Epidemiol. Published online October 16, 2018. Abstract

https://wb.md/2EyhPne

Breast Tomosynthesis Better Than Mammography?

Simplified digital breast tomosynthesis detects significantly more breast cancers

Liam Davenport

A simplified version of an advanced breast imaging technique known as digital breast tomosynthesis detects significantly more breast cancers than standard digital mammography and can potentially reduce the radiation dose and the screen-screen-reading burden of breast cancer screening, say Swedish investigators.

Breast tomosynthesis could replace mammography for breast cancer screening in the future, suggest Sophia Zackrisson, PhD, Department of Translational Medicine, Diagnostic Radiology, Lund University, Skåne University Hospital Malmö, Sweden, and colleagues.

For the Malmö Breast Tomosynthesis Screening Trial (MBTST), almost 15,000 women underwent screening with both two-view mammography and a single-view, low-compression version of digital breast tomosynthesis, which uses low-dose X-rays to capture multiple breast images.

Tomosynthesis had a higher sensitivity, although slightly lower specificity, than mammography for detecting breast cancer.

Overall, the more modern technique detected a significantly higher proportion of cancers than standard mammography, at a lower overall radiation dose than the older approach.

If these findings are "supported by cost-effectiveness studies, one-view digital breast tomosynthesis warrants consideration as the preferred breast cancer screening method in the future," the researchers comment.

The research was published online October 12 in *Lancet Oncology*.

In an accompanying comment, Martin J. Yaffe, PhD, from Sunnybrook Research Institute, Ontario Institute for Cancer Research, and the University of Toronto, Canada, said that this study "suggests that single-view tomosynthesis is more accurate for screening than digital mammography."

He adds that tomosynthesis "could potentially also be associated with reductions in radiation dose, complexity, patient discomfort, and cost as compared with two-view digital breast tomosynthesis plus two-view digital mammography, which is used in some settings".

Furthermore, "In this study, digital breast tomosynthesis detected more invasive cancers, more invasive lobular cancers, and fewer ductal carcinomas in situ than digital mammography."

Yaffe believes that the results will therefore "go a long way towards motivating a change away from the use of digital mammography in national breast cancer screening and towards adoption of digital breast tomosynthesis."

He notes, however, that technical differences as well as differences in image acquisition and processing between systems "might reduce the generalisability of the results."

Taken together, this means that the "question of whether digital breast tomosynthesis detects more of the cancers which, if undetected, would result in death or increased morbidity remains unanswered."

He suggests that some answers to these questions are likely to come from the ongoing Tomosynthesis Mammographic Imaging Screening Trial, sponsored by the Sunnybrook Health Sciences Center. This trial includes systems from all manufacturers and takes into account the nature of the cancers detected.

Improvements in Screening

Standard digital mammography is hampered by suboptimal sensitivity and specificity, particularly for women who have radiographically dense breasts.

This is not least in part due to the overlapping of breast tissue when generating the images. This can hide tumor tissue and thus lead to a false negative result, or healthy tissue can have the appearance of a tumor, creating a false positive result.

Digital breast tomosynthesis improves on standard mammography by obtaining multiple low-dose X-ray projection images at a range of angles by passing the X-ray tube over the breast in an arc.

These projection images are used to create a quasi–three dimensional set of thin image slices of the breast, reducing the overlapping effect seen in standard mammography.

"Thus, breast cancer screening with digital breast tomosynthesis might increase both sensitivity and specificity in comparison with digital mammography," Zackrisson and colleagues write.

Indeed, two previous prospective, population-based screening trials indicated that two-view tomosynthesis combined with two-view digital mammography increased cancer detection in comparison with digital mammography alone. A further study in which tomosynthesis was combined with simulated mammography had promising results.

Yaffe points out, however, that tomosynthesis is more expensive than mammography and that its interpretation is "more time consuming."

He adds that "when used in conjunction with standard digital mammography, the radiation dose to the breast can be twice that of a digital mammography examination alone."

These factors, he says, have restricted the incorporation of tomosynthesis into population-based screening programs.

Study Details

The MBTST was a prospective, population-based study. Every third woman aged 40 to 74 years who was invited to undergo regular national breast cancer screening at a single hospital was invited to take part.

During screening, the women underwent standard two-view digital mammography from the craniocaudal and mediolateral oblique views, followed by one-view digital breast tomosynthesis from the mediolateral oblique view, with a wide 50º angle.

The pressure on the breast for digital tomosynthesis was approximately half that used in the mammography examinations.

The images were read and scored by two groups of radiologists, one for each screening method; there were seven radiologists in total. A consensus meeting of at least two readers was held for any cancer for

which the malignancy probability score was ≥3. At those meetings, it was decided whether or not to recall the patient.

Of 21,691 women invited to take part in the study between 2010 and 2015, 14,851 (68%) agreed. Three women withdrew consent during follow-up and were excluded.

The mean age at baseline was 57 years, and all participants were followed up until their next screening in 1.5 to 2 years, depending on their age.

The mean glandular radiation dose was lower with tomosynthesis than mammography, at 2.3 mGy vs 2.7 mGy, as was the mean compression force, at 71 N vs 118 N, a mean reduction of 40%.

The team reports that 139 cancers were detected in 137 of 14,848 women; 131 cancers were detected in 129 women in the tomosynthesis group, and 97 cancers were detected in 96 women in the mammography group.

The sensitivity was higher for tomosynthesis than for mammography, at 81.1% vs 60.4%, whereas the specificity was slightly lower, at 97.2% vs 98.1%.

The cancer detection rate per 1000 women screened was significantly higher for digital tomosynthesis than digital mammography, at 8.7 vs 6.5, as was the recall rate, at 3.6% vs 2.5% ($P < .0001$ for both).

Overall, the positive predictive value for screen recalls was slightly lower with tomosynthesis than mammography, at 24.1% vs 25.9%. The negative predictive value was similar, at 99.8% and 99.6%.

Twenty-two cancers were detected during the follow-up screening interval, giving an interval cancer incidence of 1.48 per 1000 women screened. Of these cancers, two were high-grade octal carcinomas in situ, and two were invasive.

Discussing the study, Jaffe points out that the impact of the reduced compression force used for tomosynthesis on image quality, radiation dose, and patient comfort "was not quantified."

Although inadequate compression in digital mammography can increase the radiation dose and worsen the image quality, "in this study, these factors were clearly not a problem," Jaffe says. Nevertheless that "information regarding the effect of the reduced compression on breast thickness would have been useful."

Jaffe also says that, in the United States, screening specificity is approximately 90%, and so digital breast tomosynthesis would provide increased specificity.

In the current study, the specificity of digital mammography in the hospital "was already 98%, so there was little room for improvement in screening specificity."

Moreover, the sensitivity calculation was affected by the lack of an independent, absolute measure of the number of cancers, with the result that "the additional cancers found by use of digital breast tomosynthesis alone increased its sensitivity, but at the same time decreased the estimated sensitivity of digital mammography."

The study was funded by the Swedish Cancer Society, the Swedish Research Council, the Breast Cancer Foundation, the Swedish Medical Society, the Crafoord Foundation, the Gunnar Nilsson Cancer Foundation, the Sk å ne University Hospital Foundation, governmental funding for clinical research, the South Swedish Health Care Region, the Malmö Hospital Cancer Foundation and the Cancer Foundation at the Department of Oncology, Skåne University Hospital. Several study authors have disclosed relevant financial relationships, which are listed in the original article. Dr Yaffe's institution has a research collaboration on topics related to breast tomosynthesis with GE Healthcare.

Lancet Oncol. Published online October 12, 2018. Abstract, Comment

http://bit.ly/2PMV3cr

Cancer-associated mutations are common in normal human esophagus

Unexpectedly, a new study finds that cancer-associated genetic mutations are surprisingly common in aged, healthy esophageal epithelium tissue.

日本のニュース

Unexpectedly, a new study finds that cancer-associated genetic mutations are surprisingly common in aged, healthy esophageal epithelium tissue.

The results further our understanding of cancer and aging and underscore how little is known about the mutational evolution within normal tissues, a process likely ubiquitous in the tissues of all living things.

As people get older, they accumulate mutations in the healthy cells of normal tissues. Generally, these mutations accumulate passively and do not alter cell behavior.

However, if a genetic alteration provides a mutant cell with a competitive edge, these cells become persistent mutant clones, which are thought to be the origin of cancer.

Human skin, exposed to the powerful mutagenic power of the sun's light, is the most highly mutated normal tissue - nearly 25% of cells in the sun-exposed skin of middle-aged individuals carry cancer driver mutations.

Despite its importance, the extent to which cells accumulate somatic mutations throughout life is poorly understood, particularly in tissues not exposed to mutagens like ultraviolet light.

To explore the mutational burden of other tissues, Iñigo Martincorena and colleagues performed targeted gene sequencing of normal esophageal epithelium - a tissue-like skin, which lines the esophagus - from nine human donors ranging from 20 to 75 years of age.

While the mutation rate was lower in the esophageal tissue than in skin, Martincorena et al. revealed a strong positive selection of cellular clones carrying mutations in 14 cancer-associated genes.

According to the results, by middle age, over half of the esophageal epithelium tissue contained mutant clones.

What's more, Martincorena et al. observed a high frequency of mutations in the cancer driver gene NOTCH1 in aged normal esophageal epithelium.

These mutations were more common in normal cells than in esophageal cancer cells, suggesting that esophageal cancers are more likely to evolve from cells in epithelium without NOTCH1 mutations.

http://bit.ly/2EEtqtJ

Before nerves, there were peptides

Researchers map communication pathways in an organism that has no nervous system.

Nick Carne reports.

Animal nervous systems evolved from much more simple structures in part because of a novel form of communication, according to new research.

An international team of scientists has found that simple multicellular organisms called Placozoa can coordinate their movement and body shape in the absence of a nervous system by signalling between cells using short chains of amino acids known as peptides.

That's significant because it echoes how more complex organisms use similar structures, known as neuropeptides, for signalling within the nervous system.

"It might seem strange to use an animal with no neurons or synapses to study nervous system evolution, but although Placozoans are nerveless, you can still find within their cells the basic molecules needed for communication in complex nervous systems," says Frédérique Varoqueaux, from the University of Lausanne in Switzerland.

"So studying Placozoans can tell us more about the origins of neurons and how they became the body's control system."

The organisms are just one millimetre in size and look like tiny hairy discs. Although they have only three cell layers and no true nerve or

muscle cells, they glide across surfaces in the ocean with apparent ease.

The new study found that their cells contain a variety of small peptides, made up of between four and 20 amino acids that are secreted from one cell and detected by neighbouring ones.

Experiments revealed that the peptides changed Placozoan behaviour within seconds. Each had a unique effect, which in some cases was very dramatic. The main changes included crinkling, turning, flattening, and internal churning, a behaviour associated with feeding.

“Each peptide can be used individually as a different signal, but the peptides could also be used sequentially or together in different combinations which allows for very high numbers of unique signals between cells,” says Gáspár Jékely from the University of Exeter in the UK.

“This explains how Placozoans can coordinate sophisticated behavioural sequences such as feeding."

The paper is published in *Current Biology*.

https://wb.md/2S68q1C

More Evidence Herpes Virus Strongly Tied to Alzheimer's

Mounting research is helping to cement a proposed link between the herpes virus and Alzheimer's disease (AD).

Pauline Anderson

The researcher who got the ball rolling nearly 30 years ago by first uncovering the herpes-AD relationship believes it's time to investigate the use of antivirals in mid-life with the view of preventing AD later on.

Ruth F. Itzhaki, PhD, professor emeritus, University of Manchester, United Kingdom, reviews her own research and that of others that examines the viral concept of AD in an article published online October 19 in Frontiers in Aging Neuroscience.

Causal Link?

Over the past few decades, research has shown that individuals who are infected with herpes simplex virus type 1 (HSV1) are at increased risk for dementia and that use of antiviral drugs decreases this risk.

Results of more recent studies suggest the link is more than a mere association.

"Some very important epidemiological work is being done that suggests that it's not just an association but that it's causal," Itzhaki told *Medscape Medical News*.

Most of the population is infected with HSV1 by age 70. Researchers believe the virus travels to the brain, where it remains in a latent state. Reactivation occurs intermittently, caused by events such as immunosuppression, peripheral infection, and inflammation.

Data suggest that HSV1 may cause amyloid beta plaques, and Itzhaki and others have shown that abnormal tau protein accumulates in HSV1-infected cell cultures.

In addition, the *APOE-ε4* allele appears to boost the risk. HSV1 is present in the brain of *APOE-ε4* carriers in approximately about half of dementia cases, said Itzhaki.

She and others estimate that the risk for AD is about 12 times greater for those who have both the virus in the brain and the *APOE-ε4* allele than for those who have neither.

"Our theory is that in *APOE-ε4* carriers, reactivation is more frequent or more harmful in HSV1-infected brain cells, which, as a result, accumulate damage that culminates in development of Alzheimer's," she said.

In her article, Itzhaki reviews three recent "very significant" studies from Taiwan, a country that is unique in that records are available for more than 99% of the population through the National Health Insurance Research Database.

The database is being extensively mined for information on microbial infections and disease, said Itzhaki.

In the Taiwan articles, the word "infection" is used for people who show overt signs of the disease, such as shingles (herpes zoster [HZ]), cold sores (herpes labialis), or genital sores. The term "senile dementia" (SD) is used rather than AD because in some cases, the diagnosis was uncertain.

Two of the studies investigated varicella zoster virus (VZV) infection in relation to long-term neurocognitive changes and development of dementia. VZV causes chickenpox. After acute infection, it remains in the body in latent form, and in some individuals, it reactivates later, causing shingles.

Antivirals Preventive?

The first study included 846 patients (mean age, 62.2 years) who were diagnosed with herpes zoster ophthalmicus (HZO) in 2005 and who developed dementia in the following 5 years.

The patients who developed dementia were compared with an age-matched control group of 2538 persons during the same 5-year period.

Of the patients with HZO, 4.16% developed SD, compared to 1.65% of the control persons ($P < .001$). The crude hazard ratio (HR) of developing SD within 5 years of HZO diagnosis was 2.97 after adjustment for patient characteristics and comorbidities.

In the second study, 39,205 patients with HZ were followed for an average of 6.2 years. The incidence of dementia was compared with that among 39,205 control persons (mean age of both groups, 63.5 years).

At 1.11, the HR was small. However, for HZ patients who were treated with antivirals, including acyclovir, valacyclovir, tromantadine, and famciclovir, the incidence of dementia was about half that of untreated persons (adjusted HR, 0.55; 95% confidence interval [CI], 0.40 - 0.77; $P < .0001$).

Itzhaki noted that although antiviral treatment seemed to prevent dementia, the mechanism is unclear. She speculated that such treatment may not prevent the onset of dementia, but it may stop further deterioration, which is still a "very valuable result.

"Even if the effects were merely a delay in onset of the disease, this would still be enormously beneficial for patients, carers, and the economy," she said.

Itzhaki noted that the study did not provide data on the effect of antivirals on those already suffering from dementia.

The third study was the "most striking," said Itzhaki. That study investigated 8362 patients aged 50 years or older who were newly diagnosed with HSV infections. The control group of 25,086 age- and sex-matched persons was not infected with HSV.

The risk of developing SD in the HSV group during a 10-year period was 2.56-fold greater than in the control group (95% CI, 2.351 - 2.795; $P < .001$).

Itzhaki acknowledged that the results of the Taiwanese studies apply only to severe herpes infections, which are rare.

"Ideally, we would study dementia rates amongst people who have suffered mild HSV1 infection, including cold sores or mild genital herpes, but these are far less likely to be documented," she said.

No Cause and Effect

Commenting on the research for *Medscape Medical News*, James A. Hendrix, PhD, director of global science initiatives, Alzheimer's Association, pointed out that although the studies demonstrate an association between herpes and AD, they do not show cause and effect.

In the antiviral trial, the worse outcome for those not taking the antiviral could be due to a number of factors, including simply having poorer health overall, said Hendrix.

"We know that people who don't get state-of-the-art healthcare have higher rates of dementia," he said.

He was also concerned that the trials investigated senile dementia, which is not necessarily AD.

Itzhaki said the increasing research she outlined in her article suggests that it might be time to test whether antiviral treatment may prevent cognitive deterioration. Such treatment would be more likely to succeed if it was initiated before middleage, even if the treatment were for only a relatively short period.

In the United Kingdom, the proportion of 30- to 40-year-olds who are HSV1 seropositive is estimated to be at most about 70%, and the proportion of those who are carriers of the *APOE-ε4* allele is about 25%. So overall, only about 18% of the persons in that age group would be most at risk and would be most likely to benefit from antiviral treatment, said Itzhaki.

She emphasized that antivirals are "harmless" and are relatively inexpensive. "They are probably less expensive than taking a statin, which a lot of people are taking, at least in the UK," she said.

The types of antiviral used to treat AD should be "carefully chosen," said Itzhaki. The exact stage at which the drug would be most effective and how long it should be used should also be closely calculated, she added.

Treatments would probably be more effective if combined with an anti-inflammatory, she said. The herpes virus, she noted, causes inflammation as well as direct damage.

Itzhaki and her colleagues hope to secure funding to test a "double treatment" of an antiviral and an anti-inflammatory in patients with mild AD to see whether this prevents further deterioration.

She sugggested that clinicians keep a note in the patient record of cold sores and other signs of herpes infection. This would make it easier to track whether they were more likely to develop dementia later on, should they be treated in mid-life with an antiherpes agent.

Not Enough Direct Evidence...Yet

For Hendrix, it's still "way too early" to recommend that adults take antivirals for the primary prevention of AD. "We don't have enough direct evidence to even go there yet," he said.

Vaccination against HSV1 would be ideal to prevent the disease, but unfortunately, there's currently no such vaccine. Developing a vaccine would be expensive and would take years to complete, said Itzhaki.

Although there have now been upwards of 150 studies investigating the link between herpes and dementia, Itzhaki said the accumulating data "have been ignored or dismissed."

She said she and others have been battling for years to draw attention to research linking herpes to AD, to little avail.

This, she said, has been "very unfortunate" for patients who developed the disease. "Surely, now is the time to rectify the situation," she said.

She has two theories as to why this area of research has been all but dismissed.

One is that "people have very entrenched views," and the prevailing view and the focus of research is that beta amyloid and tau cause Alzheimer's.

"We think amyloid is involved; we just don't think it's a cause or primary cause," she said.

Hendrix acknowledged that although the Alzheimer's Association funds "a whole range" of different topics and "doesn't pick the winners and losers," past budget limitations forced it to focus more on "mainstream" areas.

But now that more federal funding has been secured, the association will be able to take a more diverse approach, he said.

And that approach should include the role of viruses. He noted that research on the immune system in AD is "exploding."

"Whether herpes or other viruses are actually having an impact on the immune system is a very important area and probably one of the hottest areas of AD research today," he said.

Compelling Evidence

Hendrix referred to a "very important" article published earlier this year, funded in part by the Alzheimer's Association, in which researchers conducted genetic studies of brain tissue from individuals with AD and found compelling evidence of the presence of herpes.

Another reason Itzhaki believes this area of research has not been taken more seriously is that "very few people in the Alzheimer's field know anything about microbes, particularly virology."

That's changing, too, said Hendrix. The increased dedicated funding that the Alzheimer's Association now has will likely "bring in experts" from this and other fields.

"The situation is changing by the week, month, and year," he said.

Dr Itzhaki and Dr Hendrix have disclosed no relevant financial relationships.

Front Aging Neurosci. Published online October 19, 2018.

http://bit.ly/2NTW68H

By Middle Age, Healthy People Have Way More Cancer-Causing Mutations Than We Thought

Changes wrought by aging could be a lot greater than we previously thought.

By Yasemin Saplakoglu, Staff Writer | October 19, 2018 09:57am ET

Aging causes changes in our bodies and our cells. But a new study finds that the extent of these changes could be a lot greater than we previously thought.

Middle-age and elderly people have more mutant cells in their esophagus than they do normal cells, a group of researchers reported yesterday (Oct. 18) in the journal Science. Further, some of these mutations are associated with esophageal cancer.

Our bodies are created from a set of instructions that we carry around in every one of our cells, an individualized manual that we call our genes. But this manual never gathers dust — throughout our lifetime, it changes (as biologists would say, it "mutates"), which creates new instructions.

For the most part, these mutations don't have any effect on healthy cells, and those cells continue chugging along, unfazed. But sometimes mutations can be detrimental— the new set of instructions can, for example, tell a healthy cell to divide and multiply rapidly and prevent other cells from stopping this uncontrolled cell growth. Healthy cells can thus turn cancerous.

In the new study, the researchers wanted to understand what mutations are present in healthy people. The team examined the tissue that lines the esophagus from nine donors between the ages of 20 and 75. They used gene sequencing — a method that reveals the genetic makeup of a tissue — to see how many known cancer-associated mutations each donor carried.

They found that, by the time people reached middle age, over half of the tissue that lines the esophagus contained mutated genes associated with esophageal cancer: 14 in total. Surprisingly, they found that one of the mutated genes, NOTCH1, was more common in healthy tissues than in cancerous ones.

Specifically, in middle-age and elderly people, NOTCH1 mutants were present in 12 to 80 percent of cells, and TP53 mutants — another mutation also associated with esophageal cancer— was found in 2 to 37 percent of cells. Their findings show that researchers may need to reconsider the role that these genes play in cancer, according to a statement.

"We have found that genetic mutations associated with cancer are widespread in normal tissues, revealing how our own cells mutate, compete and evolve to colonize our tissues as we age," co-author Iñigo Martincorena, a group leader at the Wellcome Sanger Institute in the United Kingdom, said in the statement. "Given the importance of these mutations to cancer, it is remarkable that we have been unaware of the extent of this phenomenon until now."

The esophagus is not the only body in the tissue that carries such mutations. Similarly, thanks to the sun, a quarter of a middle-age person's skin cells have mutations that can drive cancer, according to the study.

"While the work sheds light on early cancer development, it also raises many questions about how these mutations may contribute to aging and other diseases, opening interesting avenues for future research," Martincorena said.

https://bbc.in/2CzK8z0

Length of ring and index fingers 'linked to sexuality'

Women whose left index and ring fingers are different lengths are more likely to be lesbians, a study suggests.

Scientists measured the fingers of 18 pairs of female identical twins, where one was straight and the other gay.

On average, the lesbians, but not the straight twins, had different sized index and ring fingers, typically a male trait, but only on the left hand. This may be the result of exposure to more testosterone in the womb, the University of Essex researchers said.

The scientists also measured the fingers of 14 pairs of male identical twins, where one was straight and the other gay, but found no link.

Both men and women were exposed to the "male" hormone, testosterone, in the womb - but some may be exposed more than others, the scientists said.

Study author Dr Tuesday Watts, from the psychology department at Essex University, said: "Because identical twins, who share 100% of their genes, can differ in their sexual orientations, factors other than genetics must account for the differences.

"Research suggests that our sexuality is determined in the womb and is dependent on the amount of male hormone we are exposed to or the way our individual bodies react to that hormone, with those exposed to higher levels of testosterone being more likely to be bisexual or homosexual.

"Because of the link between hormone levels and difference in finger lengths, looking at someone's hands could provide a clue to their sexuality."

The findings are published in Archives of Sexual Behaviour.

http://bit.ly/2CWxNpD

How Fish and Chips Migrated to Great Britain

The fried fish was introduced by Jews fleeing religious persecution.

by Abbey Perreault

The powerful pairing of fish and chips has long been considered a British staple. Dubbed “the undisputed national dish of Great Britain” by the National Federation of Fish Friers, it’s been enjoyed on the island for over a century, with an estimated 35,000 chip shops in business by 1935. During World War II, Winston Churchill exempted the beloved dish from rationing. Today, “Fish & Chip Friday” is a weekly ritual for Brits ringing in the weekend.

Fish and chips by the sea at Hunstanton, Norfolk. **© Andrew Dunn, http://www.andrewdunnphoto.com/CC BY-SA 2.0**

Fish and chips’s origin story, however, is a bit more complex than this nationalist sentiment might imply.

As told by Simon Majumdar in his podcast, *Eat My Globe*, it all began outside of the U.K., hundreds of years ago. From the 8th to the 12th century, Jews, Muslims, and Christians lived in relative peace in Portugal, known as Al-Andalus under Moorish rule. Sephardic Jews, who likely comprised around 20 percent of the population, were relatively well-respected and held positions in the high court. For this reason, the area became somewhat of a haven for those fleeing the Spanish Inquisition. However, in 1496, after the end of

Moorish rule, King Manuel I married Isabel of Spain, who was not so aligned with the idea of religious freedom. Her ultimatum: Their betrothal would mean the expulsion of Jews from Portugal. Manuel I mandated that all Jews be baptized, or otherwise expelled.

While many fled, some Jews stayed, and either converted to Christianity or pretended to do so. *Marranos*, also referred to as "Crypto-Jews," continued to practice Judaism in secret. But when Portugal fell under Spanish rule, the Inquisition targeted individuals with Jewish lineage, threatening anyone claiming to be a *Converso*. As religious violence worsened, many fled Portugal and resettled in England, bringing with them culinary treasures founded in Sephardic cuisine—including fish.

Peshkado frito (in Andalusian dialect, *pescaíto frito*) was one of them. The dish of white fish, typically cod or haddock, fried in a thin coat of flour, was a favorite particularly among Portuguese Marranos, who fried it on Friday nights to prepare for the Sabbath, as the Mosaic laws prohibited cooking. Allegedly, the batter preserved the fish so it could be eaten cold, and without sacrificing too much flavor, the following day.

It was a hit. Fish prepared "in the Jewish manner" was sold on the streets of London on any given day. And at the end of the week, eating fish on Friday was a part of religious observance for Jews and Christians alike—as "fish fasting" to avoid consuming warm-blooded animals has been a part of the Catholic tradition for centuries. But the Friday-night tradition was likely chipless until the late-19th century. The general popularity of the potato bloomed late in Europe, and it wasn't until the late 1800s that the tuber was accepted, due especially to the promotional efforts of a French scientist. Though there are several theories of how the potato came to England—and how it became the "chip" we know and love today—one historical account credits a tripe vendor by the name of Mrs. "Granny" Duce with selling the first fried cut potatoes to the public.

There are also competing theories about who created the pairing of, as Churchill called them, "good companions." Most trace it back to the early 1860s, when Joseph Malins, a Jewish immigrant, opened up a fish and chips shop in London. Others point to John Lee, a man living outside of Manchester, who ran a "chipped potato" restaurant that sold the beloved pairing.

Whether the winning combo was first slapped together by John or Joseph or someone else entirely, it soon became everybody's dish. British natives and immigrants alike began slathering their cod in batter and frying up husky chips. Industrialization in the 19th and early 20th centuries launched the fish dish to even greater heights, as it became a favorite for factory and mill workers in London and beyond. And while its religious connotations are hidden today, many admirers remain devoted to the beloved international, national dish.