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## UA researchers discover component of cinnamon prevents colorectal cancer in mice

*University of Arizona College of Pharmacy study shows compound that gives cinnamon its distinctive flavor and smell is a potent inhibitor*

Research conducted at the University of Arizona College of Pharmacy and the UA Cancer Center indicates that a compound derived from cinnamon is a potent inhibitor of colorectal cancer.

Georg Wondrak, Ph.D., associate professor, and Donna Zhang, Ph.D., professor, both of the UA College of Pharmacy Department of Pharmacology and Toxicology, recently completed a study in which they proved that adding cinnamaldehyde, the compound that gives cinnamon its distinctive flavor and smell, to the diet of mice protected the mice against colorectal cancer. In response to cinnamaldehyde, the animals' cells had acquired the ability to protect themselves against exposure to a carcinogen through detoxification and repair.

'This is a significant finding,' says Zhang, who, along with Wondrak, is a member of the UA Cancer Center. 'Because colorectal cancer is aggressive and associated with poor prognoses, there is an urgent need to develop more effective strategies against this disease.'

'Given cinnamon's important status as the third-most-consumed spice in the world,' Wondrak adds, 'there's relatively little research on its potential health benefits. If we can ascertain the positive effects of cinnamon, we would like to leverage this opportunity to potentially improve the health of people around the globe.'

Drs. Wondrak and Zhang's study, 'Nrf2-dependent suppression of azoxymethane/dextrane sulfate sodium-induced colon carcinogenesis by the cinnamon-derived dietary factor cinnamaldehyde,' has been published online and will appear in a print issue of Cancer Prevention Research later this spring. A story about the cinnamaldehyde study appears on the UA College of Pharmacy's website.

The next step in the research is to test whether cinnamon, as opposed to cinnamaldehyde, prevents cancer using this same cancer model. Because cinnamon is a common food additive already considered safe -- it's not a synthetic, novel drug -- a study in humans may not be too far off.

Wondrak outlines questions to investigate going forward: 'Can cinnamon do it, now that we know pure cinnamaldehyde can? And can we use cinnamaldehyde or cinnamon as a weapon to go after other major diseases, such as inflammatory

dysregulation and diabetes? These are big questions to which we might be able to provide encouraging answers using a very common spice.'

Research reported in this release was supported by the National Cancer Institute of the National Institutes of Health under grant number 5R21CA166926-02.

<http://nyti.ms/1fhcdfE>

## To Lose Weight, Eating Less Is Far More Important Than Exercising More

*When it comes to reaching a healthy weight, what you don't eat is much, much more important*

One of my family's favorite shows is "The Biggest Loser." Although some viewers don't appreciate how it [pushes people so hard to lose weight](#), the show probably inspires some overweight people to regain control of their lives.

But one of the most frustrating parts of the show, at least for me, is its overwhelming emphasis on [exercise](#). Because when it comes to reaching a healthy weight, what you don't eat is much, much more important.

Think about it this way: If an overweight man is consuming 1,000 more calories than he is burning and wants to be in energy balance, he can do it by exercising. But exercise consumes far fewer calories than many people think. Thirty minutes of [jogging or swimming laps](#) might burn off 350 calories. Many people, fat or fit, can't keep up a strenuous 30-minute exercise regimen, day in and day out. They might exercise a few times a week, if that. Or they could achieve the same calorie reduction by eliminating two [16-ounce sodas](#) each day.

Proclamations that people need to be more active are ubiquitous in the media. The importance of exercise for proper [weight management](#) is reinforced when people [bemoan the loss of gym class in schools as a cause of the obesity epidemic](#). Michelle Obama's [Let's Move](#) program places the focus on exercise as a critical component in combating excess weight and [obesity](#).

Exercise has many benefits, but there are problems with relying on it to control weight. First, it's just not true that Americans, in general, aren't listening to calls for more activity. From 2001 to 2009, the percentage of people who were sufficiently physically active [increased](#). But so did the percentage of Americans who were obese. The former did not prevent the latter.

Studies confirm this finding. A [2011 meta-analysis](#), a study of studies, looked at the relationship between physical activity and fat mass in children, and found that being active is probably not the key determinant in whether a child is at an unhealthy weight. In the adult population, interventional studies [have difficulty showing](#) that a physically active person is less likely to gain excess weight than a sedentary person. Further, studies of energy balance, and there are [many of them](#), show that total energy expenditure and physical activity levels in developing and

industrialized countries are similar, making activity and exercise unlikely to be the cause of differing obesity rates.

Moreover, exercise increases one's appetite. After all, when you burn off calories being active, your body will often signal you to replace them. Research confirms this. A [2012 systematic review](#) of studies that looked at how people complied with exercise programs showed that over time, people wound up burning less energy with exercise than predicted and also increasing their caloric intake.

Other metabolic changes can negate the expected weight loss benefits of exercise over the long term. When you lose weight, metabolism often slows. Many people believe that [exercise can counter or even reverse](#) that trend. Research, however, shows that the resting metabolic rate in all dieters slows significantly, regardless of whether they exercise. This is why weight loss, which might seem easy when you start, becomes harder over time.

This isn't to say that exercise plays no role. There are many studies that show that adding exercise to diets can be beneficial. A [1999 review](#) identified three key meta-analyses and other randomized controlled trials that found statistically significant, but overall small, increases in weight loss with exercise.

A [meta-analysis](#) published last year found that, in the long term, behavioral weight management programs that combine exercise with diet can lead to more sustained weight loss (three to four pounds) over a year than diet alone. Over a six-month period, though, adding exercise made no difference. Another [systematic review from last fall](#) found similar results, with diet plus exercise performing better than diet alone, but without much of an absolute difference.

All of these interventions included dietary changes, and the added weight-loss benefit from activity was small. Far too many people, though, can manage to find an hour or more in their day to drive to the gym, exercise and then clean up afterward — but complain that there's just no time to cook or prepare a healthful, home-cooked meal. If they would spend just half the time they do exercising trying to make a difference in the kitchen, they'd most likely see much better results.

Many people think of dieting as a drastic and rigid change, with a high risk of putting the pounds back on. What is more likely to succeed is gradual change, made in a [much more sustainable way](#). I also don't mean to make it seem that weight loss with diet is easy and exercise is hard. They're both hard. The challenge of a slowing metabolism, and the desire to eat more, occurs in both cases, although dietary change still works better than exercise.

But I can't say this enough: Exercise has a big upside for health beyond potential weight loss. Many studies and reviews detail how physical activity can improve outcomes in [musculoskeletal disorders, cardiovascular disease, diabetes,](#)

[pulmonary diseases, neurological diseases](#) and [depression](#). The Academy of Medical Royal Colleges declared it a "[miracle cure](#)" recently, and while I'm usually loath to use that term for anything in medicine, a fairly large evidence base corroborates that exercise improves outcomes in many domains.

But that huge upside doesn't seem to necessarily apply to weight loss. The data just don't support it. Unfortunately, exercise seems to excite us much more than eating less does. After all, as a friend said to me recently, "[The Biggest Loser](#)" would be really boring if it were shot after shot of contestants just not overeating.

[http://www.eurekalert.org/pub\\_releases/2015-06/ru-bch061515.php](http://www.eurekalert.org/pub_releases/2015-06/ru-bch061515.php)

### **Bacteria could help clean groundwater contaminated by uranium ore processing**

*A strain of bacteria that "breathes" uranium may hold the key to cleaning up polluted groundwater at sites where uranium ore was processed to make nuclear weapons.*

A team of Rutgers University scientists and collaborators discovered the bacteria in soil at an old uranium ore mill in Rifle, Colorado, almost 200 miles west of Denver. The site is one of nine such mills in Colorado used during the heyday of nuclear weapons production.

The research is part of a U.S. Department of Energy program to see if microorganisms can lock up uranium that leached into the soil years ago and now makes well water in the area unsafe to drink.

The team's discovery, published in the April 13, 2015 issue of PLOS ONE, is the first known instance where scientists have found a bacterium from a common class known as betaproteobacteria that breathes uranium. This bacterium can breathe either oxygen or uranium to drive the chemical reactions that provide life-giving energy.

"After the newly discovered bacteria interact with uranium compounds in water, the uranium becomes immobile," said Lee Kerkhof, a professor of marine and coastal sciences in the School of Environmental and Biological Sciences. "It is no longer dissolved in the groundwater and therefore can't contaminate drinking water brought to the surface."

Kerkhof leads the Rutgers team that works with U.S. Department of Energy researchers.

Breathing uranium is rather rare in the microbial world. Most examples of bacteria which can respire uranium cannot breathe oxygen but often breathe compounds based on metals - typically forms of solid iron. Scientists had previously witnessed decreasing concentrations of uranium in groundwater when

iron-breathing bacteria were active, but they have yet to show that those iron-breathing bacteria were directly respiring the uranium.

While the chemical reaction that the bacteria perform on uranium is a common process known as "reduction," or the act of accepting electrons, Kerkhof said it's still a mystery how the reduced uranium produced by this microorganism ultimately behaves in the subsurface environment.

"It appears that they form uranium nanoparticles," he said, but the mineralogy is still not well known and will be the subject of ongoing research.

The Rutgers team was able to isolate the uranium-breathing bacterium in the lab by recognizing that uranium in samples from the Rifle site could be toxic to microorganisms as well as humans. The researchers looked for signs of bacterial activity when they gradually added small amounts of dissolved uranium at the right concentration back to the samples where uranium had become immobilized. Once they found the optimal uranium concentrations, they were able to isolate the novel strain.

Exactly how the strain evolved, Kerkhof said, "we are not sure." But, he explained, bacteria have the ability to pass genes to each other. So just like bacteria pick up resistance to things like antibiotics and heavy metal toxicity, this bacterium "picked up a genetic element that's now allowing it to detoxify uranium, to actually grow on uranium." His research team has completed sequencing its genome to support future research into the genetic elements that allow the bacterium to grow on uranium.

What Kerkhof is optimistic about is the potential for these bacteria to mitigate the specific groundwater pollution problem in Rifle. Scientists at first expected the groundwater to flush into the Colorado River and carry the dissolved uranium with it, where it would get diluted to safer levels. But that hasn't happened. Other potential methods of remediation, such as digging up the contaminated soil or treating it with harsh chemicals, are thought to be too expensive or hazardous.

"Biology is a way to solve this contamination problem, especially in situations like this where the radionuclides are highly diluted but still present at levels deemed hazardous," said Kerkhof. If the approach is successful, it could be considered for other sites where uranium was processed for nuclear arsenals or power plant fuel. While the problem isn't widespread, he said there's potentially a lot of water to be concerned about. And the problem could spread beyond traditional places such as ore processing sites.

"There is depleted uranium in a lot of armor-piercing munitions," he said, "so places like the Middle East that are experiencing war could be exposed to high levels of uranium in the groundwater."

[http://www.eurekalert.org/pub\\_releases/2015-06/b-eut061215.php](http://www.eurekalert.org/pub_releases/2015-06/b-eut061215.php)

## **Eating up to 100 g of chocolate daily linked to lowered heart disease and stroke risk**

***There may be no need to cut out chocolate to protect cardiovascular health, say researchers***

Eating up to 100 g of chocolate every day is linked to lowered heart disease and stroke risk, finds research published online in the journal Heart.

There doesn't seem to be any evidence for cutting out chocolate to lower the risk of cardiovascular disease, conclude the researchers.

They base their findings on almost 21,000 adults taking part in the EPIC-Norfolk study, which is tracking the impact of diet on the long term health of 25,000 men and women in Norfolk, England, using food frequency and lifestyle questionnaires.

The researchers also carried out a systematic review of the available international published evidence on the links between chocolate and cardiovascular disease, involving almost 158,000 people--including the EPIC study participants.

The EPIC-Norfolk participants (9214 men and 11 737 women) were monitored for an average of almost 12 years, during which time 3013 (14%) people experienced either an episode of fatal or non-fatal coronary heart disease or stroke. Around one in five (20%) participants said they did not eat any chocolate, but among the others, daily consumption averaged 7 g, with some eating up to 100 g. Higher levels of consumption were associated with younger age and lower weight (BMI), waist: hip ratio, systolic blood pressure, inflammatory proteins, diabetes and more regular physical activity - all of which add up to a favourable cardiovascular disease risk profile.

Eating more chocolate was also associated with higher energy intake and a diet containing more fat and carbs and less protein and alcohol. The calculations showed that compared with those who ate no chocolate higher intake was linked to an 11% lower risk of cardiovascular disease and a 25% lower risk of associated death.

It was also associated with a 9% lower risk of hospital admission or death as a result of coronary heart disease, after taking account of dietary factors.

And among the 16,000 people whose inflammatory protein (CRP) level had been measured, those eating the most chocolate seemed to have an 18% lower risk than those who ate the least. The highest chocolate intake was similarly associated with a 23% lower risk of stroke, even after taking account of other potential risk factors. Of nine relevant studies included in the systematic review, five studies each assessed coronary heart disease and stroke outcome, and they found a

significantly lower risk of both conditions associated with regular chocolate consumption. And it was linked to a 25% lower risk of any episode of cardiovascular disease and a 45% lower risk of associated death.

This is an observational study so no definitive conclusions about cause and effect can be drawn. And the researchers point out that food frequency questionnaires do involve a certain amount of recall bias and underestimation of items eaten.

Reverse causation--whereby those with a higher cardiovascular disease risk profile eat less chocolate and foods containing it than those who are healthier--may also help to explain the results, they say.

Nevertheless, they add: "Cumulative evidence suggests that higher chocolate intake is associated with a lower risk of future cardiovascular events."

And they point out that as milk chocolate, which is considered to be less 'healthy' than dark chocolate, was more frequently eaten by the EPIC-Norfolk participants, the beneficial health effects may extend to this type of chocolate too.

"This may indicate that not only flavonoids, but also other compounds, possibly related to milk constituents, such as calcium and fatty acids, may provide an explanation for the observed association," they suggest. And they conclude: "There does not appear to be any evidence to say that chocolate should be avoided in those who are concerned about cardiovascular risk."

[http://www.eurekalert.org/pub\\_releases/2015-06/aqu-nsf061515.php](http://www.eurekalert.org/pub_releases/2015-06/aqu-nsf061515.php)

### **New study favors cold, icy early Mars**

#### ***A cold and icy planet billions of years ago better explains water drainage and erosion features seen on Mars today***

WASHINGTON, D.C. - The high seas of Mars may never have existed, according to a new study that looks at two opposite climate scenarios of early Mars and suggests that a cold and icy planet billions of years ago better explains water drainage and erosion features seen on the planet today.

For decades, researchers have debated the climate history of Mars and how the planet's early climate led to the many water-carved channels seen today. The idea that 3 to 4 billion years ago Mars was once warm, wet and Earth-like with a northern sea -- conditions that could have led to life -- is generally more popular than that of a frigid, icy planet where water is locked in ice most of the time and life would be hard put to evolve.

To see which early Mars better explains the modern features of the planet, researcher Robin Wordsworth of the Harvard Paulson School of Engineering and Applied Sciences and his colleagues used a 3-dimensional atmospheric circulation model to compare a water cycle on Mars under different scenarios 3 to 4 billion years ago, during what's called the late Noachian and early Hesperian periods. One scenario looked at Mars as a warm and wet planet with an average global

temperature of 10 degrees Celsius (50 degrees Fahrenheit) and the other as a cold and icy world with an average global temperature of minus 48 degrees Celsius (minus 54 degrees Fahrenheit).

The study's authors found that the cold scenario was more likely to have occurred than the warm scenario, based on what is known about the history of the Sun and

the tilt of Mars's axis 3 to 4 billion years ago. The cold

model also did a better job

explaining the water erosion

features that have been left

behind on the Martian surface,

and which have puzzled and

intrigued scientists since they

were first discovered by the

Viking orbiters in the 1970s. A

paper presenting the results has

been accepted for publication in

AGU's Journal of Geophysical

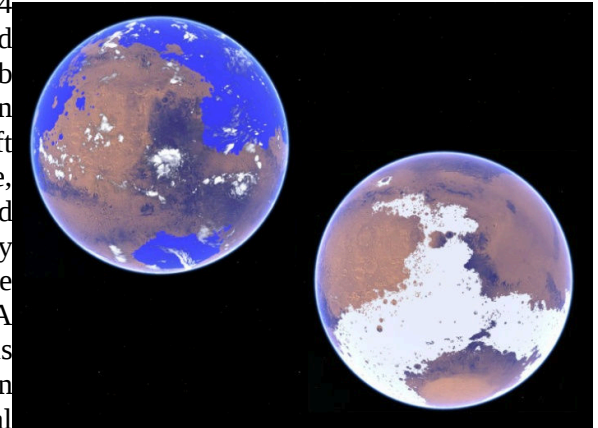
Research - Planets.

*This is a conceptual rendition of the competing warm and cold scenarios for early Mars. Robin D. Wordsworth*

The colder scenario was more straightforward to model, Wordsworth explained, because Mars only gets 43 percent of the solar energy of Earth, and early Mars was lit by a younger Sun believed to have been 25 percent dimmer than it is today. That makes it very likely early Mars was cold and icy, he said.

An extreme tilt of the Martian axis would have pointed the planet's poles at the Sun and driven polar ice to the equator, where water drainage and erosion features are seen today. More importantly, under a thicker atmosphere that likely existed under the colder scenario, highland regions at the equator get colder and northern low-lying regions get warmer - the so-called 'icy highlands effect' that is responsible for making the peaks of mountains snow-covered on Earth today. Despite a number of warming factors - including a thicker atmosphere filled with climate-warming carbon dioxide -- Mars still would have been quite cold, Wordsworth added.

Creating a warm/wet Mars took more work, Wordsworth said. Previous studies have shown that even when the effects of climate-warming clouds, dust and carbon dioxide are taken into account, climate models still don't show early Mars developing any warm and wet periods, he said.



But the conditions on early Mars may have been different than scientists' thought, Wordsworth said. The study's authors added to their model different climate effects to force Mars into a warmer, wet state.

Even then, however, the warm/wet early Mars does not explain the patchwork of Martian water erosion features and valley networks observed on the planet today, and why these features tend to be concentrated near the planet's equator, Wordsworth said.

Under the warm/wet model, rainfall rates varied a lot with longitude and latitude. The warm/wet model predicts that on early Mars rain was greatest in an area called Arabia and around the Hellas basin, including in the west and southeast areas of the basin, where few water drainage features are found today. At the same time, several regions with many water-carved valleys, such as Margaritifer Sinus, received one-tenth to one-twentieth as much rain as Arabia and the Hellas basin under the warm/wet scenario.

In the warm/wet scenario, mountains also created rain shadows, like those that wring water from clouds to create deserts on Earth. On Mars, the bulge of Tharsis would have caused more rain to fall on the windward western side of the volcanic plateau, where few water features are seen today. To the east, downwind of the bulge, drier air would flow over Margaritifer Sinus, causing less rain to fall there - a situation that doesn't match the drainage features observed there.

The cold/icy scenario isn't perfect but it's a better fit to the observations in general, Wordsworth said. While this scenario accumulates frozen water closer to the drainage features observed today on Mars, something had to have melted the ice which carved the valleys, he said. In this scenario, the climate is cool most of the time, and short-lived events like meteor impacts and volcanic eruptions likely caused the necessary melting, he said.

"I'm still trying to keep an open mind about this," said Wordsworth. "There is lots of work to be done. But our results show that the cold/icy scenario matches the surface distribution of erosion features more closely. This strongly suggests that early Mars was generally cold, and water was supplied to the highland regions as snow, not as rain."

Proving that a cold climate on early Mars led to the features seen on the planet today is a "big question", said Bethany Ehlmann, a planetary scientist at California Institute of Technology and NASA's Jet Propulsion Laboratory in Pasadena, California, who was not involved in the new study.

The new paper answers part of that question by showing that locations with snow accumulation in the cold and icy scenario roughly correspond to valley network locations seen today, she said. Further, the model of the cold and icy early Mars shows that some melting of ice would occur, she said.

"We know from rover- and orbiter-based data that there were lakes on ancient Mars," she said. "Key questions are: how long did they persist? Were they episodic or persistent? And does the feeder valley network demand rain or is snow and ice melt sufficient?"

The 3-D climate modeling used in the new study begins to address these questions with a new level of sophistication by investigating how specific locations might have accumulated rain or snow, she said.

<http://www.bbc.com/news/health-33135100>

### **Half 'have natural flu protection'**

*Nearly half of people already have some defences that can prevent flu taking hold, research suggests.*

Tests on 1,414 people showed that part of the immune system - called T-cells - was able to attack regions of the virus that were common to many different strains of flu. The team at University College London says it may be possible to develop a "universal flu vaccine". However, virologists warned flu was an expert at mutating.

The body produces antibodies in response to an infection or flu vaccine that bind to the surface of a virus. But flu is skilled at changing its appearance and rendering antibodies useless, which is why a new flu vaccine is needed each year. T-cells are a different weapon in the immune system. They are able to target the hidden parts of flu, which change less frequently. This means that after being exposed to one strain of flu, people may have resistance to other strains too.

Tests on nearly 1,500 unvaccinated people over the course of four years indicated 43% had "cross-protection" to seasonal and pandemic flus. The data was published in the American Journal of Respiratory and Critical Care Medicine.

However, the flu vaccines given to adults do not generate a T-cells response, meaning a new type of vaccine is needed.

Prof Andrew Hayward, from University College London, told the BBC News website that developing a T-cell vaccine for flu could protect against a wide range of strains - a "universal flu vaccine". He said: "It may increase the level of protection we can give to elderly people, who currently often have an immune response to the current vaccine which is not as good as in young people.

"From time-to-time we predict the antibodies that go into the seasonal flu vaccine wrong, so we get a mismatch between the vaccine and the circulating flu."

He said this cross-protection could minimise the impact of such a mismatch and play a role in pandemics when new flu viruses emerged. "Having a cross-protective vaccine could allow it to be used much earlier in the pandemic and could make a difference to the spread and ultimate size of the pandemic," he added.

Prof Jonathan Ball, from the University of Nottingham, said: "Our immune system deploys two types of weapon to combat viral infections - antibodies and T-cells, and both are important. "The current study shows that the other arm of our adaptive immune response - the T-cells - might offer some protection against genetically different strains of the virus.

"We know that influenza's response to host immunity is mutation - so, whether or not these findings can be translated into a vaccine that can yield a level of cross-protection that the virus can't escape from is still a big unknown. "

[http://www.eurekalert.org/pub\\_releases/2015-06/kift-srf061615.php](http://www.eurekalert.org/pub_releases/2015-06/kift-srf061615.php)

### **Speech recognition from brain activity**

***Spoken sentences can be reconstructed from activity patterns of human brain surface; 'Brain-to-Text' combines knowledge from neuroscience, medicine, and informatics***

Speech is produced in the human cerebral cortex. Brain waves associated with speech processes can be directly recorded with electrodes located on the surface of the cortex. It has now been shown for the first time that is possible to reconstruct basic units, words, and complete sentences of continuous speech from these brain waves and to generate the corresponding text. Researchers at KIT and Wadsworth Center, USA present their "Brain-to-Text" system in the scientific journal *Frontiers in Neuroscience* (doi: 10.3389/fnins.2015.00217).

"It has long been speculated whether humans may communicate with machines via brain activity alone," says Tanja Schultz, who conducted the present study with her team at the Cognitive Systems Lab of KIT. "As a major step in this direction, our recent results indicate that both single units in terms of speech sounds as well as continuously spoken sentences can be recognized from brain activity."

These results were obtained by an interdisciplinary collaboration of researchers of informatics, neuroscience, and medicine. In Karlsruhe, the methods for signal processing and automatic speech recognition have been developed and applied. "In addition to the decoding of speech from brain activity, our models allow for a detailed analysis of the brain areas involved in speech processes and their interaction," outline Christian Herff und Dominic Heger, who developed the Brain-to-Text system within their doctoral studies.

The present work is the first that decodes continuously spoken speech and transforms it into a textual representation. For this purpose, cortical information is combined with linguistic knowledge and machine learning algorithms to extract the most likely word sequence. Currently, Brain-to-Text is based on audible speech. However, the results are an important first step for recognizing speech from thought alone.

The brain activity was recorded in the USA from 7 epileptic patients, who participated voluntarily in the study during their clinical treatments. An electrode array was placed on the surface of the cerebral cortex (electrocorticography (ECoG)) for their neurological treatment. While patients read aloud sample texts, the ECoG signals were recorded with high resolution in time and space. Later on, the researchers in Karlsruhe analyzed the data to develop Brain-to-Text. In addition to basic science and a better understanding of the highly complex speech processes in the brain, Brain-to-Text might be a building block to develop a means of speech communication for locked-in patients in the future.

*A video on the functioning of Brain-to-Text:*

[http://csl.anthropomatik.kit.edu/publikationen\\_2934.php](http://csl.anthropomatik.kit.edu/publikationen_2934.php)

The study online: <http://journal.frontiersin.org/article/10.3389/fnins.2015.00217>

[http://www.eurekalert.org/pub\\_releases/2015-06/jhub-ero061515.php](http://www.eurekalert.org/pub_releases/2015-06/jhub-ero061515.php)

### **Experts: Risk of hepatitis E outbreak 'very high' in earthquake-ravaged Nepal**

***Statement calls for nation to use unapproved vaccine to protect pregnant women, others at highest risk***

During the coming monsoon season, survivors of the recent earthquake that destroyed parts of Nepal face a "very high" risk of a hepatitis E outbreak that could be especially deadly to pregnant women, according to a consensus statement from a group of infectious disease experts from around the world.

The document, published in the *Lancet* June 16 and signed by the Johns Hopkins Bloomberg School of Public Health's Alain Labrique and six others, states that the conditions in the April tremor that killed 8,800 people and injured more than 23,000 have left conditions ripe for hepatitis E virus (HEV), which is primarily spread from feces to mouth via contaminated water. The researchers say that 500 pregnant women could die from the virus in the coming months and many more could be sickened.

"Earthquake-affected areas are faced with a 'perfect storm' of risk factors: large displaced populations with limited access to clean drinking water, lack of sanitary facilities, the approaching monsoon, overburdened healthcare infrastructure, large amounts of circulating HEV, and an at-risk population that mostly lacks protective antibodies," the researchers write.

There are an estimated 20 million hepatitis E infections in the world annually. While the virus can lead to liver disease, it mostly runs its course with few long-term complications. Yet pregnant women have a mortality rate of 25 percent when infected by the virus.

There is a safe and effective vaccine available, the researchers say, but it is currently only licensed for use in China. The World Health Organization has not

recommended its routine use because there is a need for additional safety and efficacy data, particularly in pregnant women. They have also said, however, that its use should be "considered" in outbreaks such as this. The researchers estimate more than 400 pregnant women could be saved if the vaccine were used in Nepal during monsoon season, which runs from July to September.

The group recommends that Nepalese health authorities actively work to identify cases of the disease where pregnant women are being treated; that the Nepalese Ministry of Health should initiate a request for the vaccine and build a stockpile; and develop targeted deployment strategies for the use of the vaccine, based on identification of high-risk populations and the available organizational capacity for safe implementation and monitoring of outcomes.

"Hepatitis E is a neglected virus that isn't well understood but we are now seeing that it is likely a major cause of maternal deaths in countries where it is common," says Labrique, PhD, an associate professor in the Bloomberg School's departments of international health and epidemiology. "We are compelled to advocate for measures that reduce the risk of preventable mortality."

*"Nepali Earthquakes and the risk of an epidemic of Hepatitis E" was written by Buddha Basnyat, Harry R. Dalton, Nassim Kamar, David Rein, Alain Labrique, Jeremy Farrar and Peter Piot. Collaborating institutions include Oxford University Clinical Research Unit-Patan Academy of Health Sciences, Kathmandu, Nepal; University of Exeter; Université Paul Sabatier; University of Chicago; Wellcome Trust; and the London School of Hygiene & Tropical Medicine.*

*Other Johns Hopkins Bloomberg School of Public Health researchers who signed the consensus statement include Lisa J. Krain, Brittany L. Kmush, Christopher D. Heaney and Kenrad E. Nelson.*

[http://www.eurekalert.org/pub\\_releases/2015-06/tes-pde061015.php](http://www.eurekalert.org/pub_releases/2015-06/tes-pde061015.php)

## **Prenatal DDT exposure tied to nearly 4-fold increase in breast cancer risk**

### ***Fifty year-long study first to directly connect breast cancer risk to in utero chemical exposure***

Washington -- Women who were exposed to higher levels of the pesticide DDT in utero were nearly four times more likely to be diagnosed with breast cancer as adults than women who were exposed to lower levels before birth, according to a new study published in the Endocrine Society's Journal of Clinical Endocrinology and Metabolism (JCEM). A more estrogenic form of DDT that is found in commercial DDT, o,p'-DDT, was largely responsible for this finding.

Despite being banned by many countries in the 1970s, DDT remains widespread in the environment and continues to be used in Africa and Asia. Many women who were exposed in utero in the 1960s, when the pesticide was used widely in the United States, are now reaching the age of heightened breast cancer risk.

DDT was among the first recognized endocrine disruptors, according to the introductory guide to endocrine-disrupting chemicals published by the Endocrine Society and IPEN. DDT and related pesticides can mimic and interfere with the function of the hormone estrogen. Past studies have found DDT exposure is linked to birth defects, reduced fertility and increased risk of Type 2 diabetes.

'This 54-year study is the first to provide direct evidence that chemical exposures for pregnant women may have lifelong consequences for their daughters' breast cancer risk,' said one of the study's authors, Barbara A. Cohn, PhD, of the Public Health Institute in Berkeley, Calif. 'Environmental chemicals have long been suspected causes of breast cancer, but until now, there have been few human studies to support this idea.'

The case-control study is prospective, having tracked the daughters of women who participated in the Child Health and Development Studies (CHDS) for 54 years beginning in utero. CHDS studied 20,754 pregnancies among women who were members of the Kaiser Foundation Health Plan from 1959 through 1967. CHDS participants gave birth to 9,300 daughters during that period.

For the analysis published in JCEM, researchers used state records and a survey of CHDS participants' grown daughters to determine how many were diagnosed with breast cancer by age 52. To determine levels of DDT exposure in utero, the researchers analyzed stored blood samples from CHDS to measure DDT levels in the mothers' blood during pregnancy or in the days immediately after delivery. The researchers measured DDT levels in mothers of 118 women who were diagnosed with breast cancer. The scientists identified 354 daughters who did not develop cancer to use as controls and tested their mothers' blood for comparison.

The researchers found that independent of the mother's history of breast cancer, elevated levels of o,p'-DDT in the mother's blood were associated with a nearly four-fold increase in the daughter's risk of breast cancer. Among the women who were diagnosed with breast cancer, 83 percent had estrogen-receptor positive breast cancer, a form of cancer that may receive signals from the hormone estrogen to promote tumor growth.

Researchers also determined that exposure to higher levels of o,p'-DDT was associated with women being diagnosed with a more advanced stage of cancer. In addition, the scientists found women with greater exposure to o,p'-DDT were more likely to develop HER2-positive breast cancer, where the cancer cells have a gene mutation that produces an excess of a specific protein. Basic research studies where breast cancer cells were exposed to DDT have found the pesticide activated the HER2 protein.

'This study calls for a new emphasis on finding and controlling environmental causes of breast cancer that operate in the womb,' Cohn said. 'Our findings should

prompt additional clinical and laboratory studies that can lead to prevention, early detection and treatment of DDT-associated breast cancer in the many generations of women who were exposed in the womb. We also are continuing to research other chemicals to see which may impact breast cancer risk among our study participants.'

*Other authors of the study include: Michele La Merrill of the University of California, Davis, in Davis, CA; Nickilou Y. Krigbaum, Lauren Zimmermann and Piera M. Cirillo of the Public Health Institute in Berkeley, CA; and Gregory Yeh and June-Soo Park of the California Department of Toxic Substances Control in Berkeley, CA.*

*The research was supported with funding from the California Breast Cancer Research Program, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, the California Public Health Department, the National Cancer Institute's Surveillance, Epidemiology and End Results Program, and the U.S. Centers for Disease Control and Prevention's National Program of Cancer Registries.*

*The study, 'DDT exposure in utero and breast cancer,' will be published online at <http://press.endocrine.org/doi/10.1210/jc.2015-1841>, ahead of print.*

[http://www.eurekalert.org/pub\\_releases/2015-06/cu-wyd061715.php](http://www.eurekalert.org/pub_releases/2015-06/cu-wyd061715.php)

### **Weighing yourself daily can tip the scale in your favor**

***For those wishing to lose weight and keep it off, here's a simple strategy that works: step on a scale each day and track the results.***

ITHACA, N.Y. - A two-year Cornell study, recently published in the Journal of Obesity, found that frequent self-weighing and tracking results on a chart were effective for both losing weight and keeping it off, especially for men.

Subjects who lost weight the first year in the program were able to maintain that lost weight throughout the second year. This is important because studies show that about 40 percent of weight lost with any dietary treatment is regained in one year, and almost 100 percent of weight loss is regained at the end of five years.

"You just need a bathroom scale and an excel spreadsheet or even a piece of graph paper," said David Levitsky, professor of nutrition and psychology at Cornell and the paper's senior author.

The method "forces you to be aware of the connection between your eating and your weight," said Levitsky. "It used to be taught that you shouldn't weigh yourself daily, and this is just the reverse."

In the study, 162 subjects were randomly separated into an intervention group and a control group. Individuals in the intervention group were first given a target of 1 percent weight loss, which they could lose in any manner they chose.

"Because we didn't prescribe, everyone found their own way of losing the weight," whether they reduced portion size, stopped snacking or skipped a meal, Levitsky said. Losing 1 percent of body weight requires most people to cut only

about 150 calories a day for two weeks. Once they maintained that weight loss for 10 days, the program then gave them a new target to lose another 1 percent, and so on. The goal was to lose a total of 10 percent of their starting body weight.

Still, there was a significant difference between men and women, with women losing weight on the program, but far less than the men. "It seems to work better for men than women, for reasons we cannot figure out yet," Levitsky said.

Overall, the researchers believe that stepping on a scale and tracking one's weight acts as a reinforcement for some behaviors, such as eating less, and it strengthens others such as going for a walk in order to maintain body weight.

"We think the scale also acts as a priming mechanism, making you conscious of food and enabling you to make choices that are consistent with your weight," Levitsky said.

[http://www.eurekalert.org/pub\\_releases/2015-06/loa-dy061715.php](http://www.eurekalert.org/pub_releases/2015-06/loa-dy061715.php)

### **'What don't you understand about 'yes' and 'no'?'**

***New issue of Language features 8 linguistic studies***

The words 'yes' and 'no' may seem like two of the easiest expressions to understand in any language, but their actual behavior and interpretation are surprisingly difficult to pin down. In a paper published earlier today in the scholarly journal *Language*, two linguists examine the workings of 'yes' and 'no' and show that understanding them leads to new insights concerning the understanding of questions and statements more generally.

Floris Roelofsen (University of Amsterdam) and Donka F. Farkas (UC - Santa Cruz) provide a comprehensive account of 'polarity particles', as these words are called, across languages, and explain the intricate pattern of their distribution. For example, "Yes, it is" and "No, it isn't" are acceptable answers to the question "Is the door open or is it not open?", but not to "Is the door open or is it closed?". Furthermore, the intonation used when pronouncing a sentence can affect whether 'yes' or 'no' are appropriate responses to it.

The distribution of these particles, it turns out, is also affected by the polarity of the sentence they respond to. For example, both "No, he hasn't" and "Yes, he hasn't" are acceptable as agreeing responses to "Ben has not called today", but in an agreeing response to "Ben has called today", "Yes, he has" is acceptable but "No, he has" is not.

Roelofsen and Farkas build on previous insights from semantics and discourse models, as well as on quantitative surveys of how speakers judge various responses. The framework they create not only explains the distribution and interpretation of these particles in English, but also predicts what patterns one expects to find across languages. These predictions are then checked and verified against data from French, German, Romanian, and Hungarian.



An open-access version of this article is now available from the Linguistic Society of America, the publishers of *Language*:

<http://www.linguisticsociety.org/files/news/LanguageFarkasRoelofsen.pdf>

[http://www.eurekalert.org/pub\\_releases/2015-06/ip-rni061715.php](http://www.eurekalert.org/pub_releases/2015-06/ip-rni061715.php)

## Restoring natural immunity against cancers

### *Infiltrating immune cells into tumors to induce the immune system to block tumor growth*

Scientists at the Institut Pasteur and Inserm have successfully increased the infiltration of immune cells into tumors, thus inducing the immune system to block tumor growth. In an article published in *Nature Immunology*, the scientists show that, in combination with existing immunotherapies, this process efficiently destroys cancer cells.

Chemokines are small molecules that can attract immune cells towards inflammatory tissues, acting for example during tumor development or upon infection, in order to support migration of lymphocytes into diseased tissues. However, these molecules may be degraded by enzymes, a process that limits the influx of immune cells. For example, the chemokine CXCL10, which induces the recruitment of T lymphocytes into pathological tissues, is rapidly degraded by the enzyme dipeptidylpeptidase 4 (DPP4).

The Dendritic Cell Immunobiology Unit, led by Matthew Albert (Institut Pasteur and Inserm), had previously shown that increased levels of DPP4 and the degraded form of CXCL10 in hepatitis C patients correlate with patients' inability to respond to interferon treatment. Following these results, the scientists predicted and have now confirmed that inhibiting this enzyme could improve the efficacy of immune responses, in particular antitumor responses.

In a recently published study, Rosa Barreira da Silva, Matthew Albert and their colleagues showed that oral administration of a specific DPP4 inhibitor (sitagliptin) slows the development of several types of cancer in mice. In addition, the authors demonstrated that DPP4 inhibition increased the infiltration of T lymphocytes into tumors, and that the combination of this innovative treatment with existing immunotherapies eradicated the tumor.

Since health authorities have already approved DPP4 inhibitors for the treatment of type 2 diabetes, the conclusions drawn from these studies may quickly translate into clinical studies in humans. In fact, Matthew Albert's team, in collaboration with clinical colleagues, has already submitted a proposal for a phase I clinical trial, to evaluate the impact of sitagliptin treatment in patients with hepatocellular carcinoma.

The cross-disciplinary nature of the projects undertaken by the teams at the Institut Pasteur and Inserm, along with collaboration between scientists and

clinicians, allows clinical observations and scientific discoveries to be rapidly applied for the management of human disease.

*This project has received funding from the Pasteur-Roux grant, the French Cancer League (Ligue Contre le Cancer), the Fondation ARC cancer research organization and the French National Research Agency (ANR) as part of the "Immuno-Onco" LabEx (Laboratories of Excellence) program.*

[http://www.eurekalert.org/pub\\_releases/2015-06/tl-tlp061615.php](http://www.eurekalert.org/pub_releases/2015-06/tl-tlp061615.php)

## Patients with complications after major surgery more likely to survive if readmitted to the same hospital

### *26% more likely to survive if they return to the hospital where they had their operation*

Patients rehospitalized with complications after major surgery are 26% more likely to survive if they return to the hospital where they had their operation compared to those readmitted to a different hospital, according to a national study involving over 9 million Medicare patients in the USA, published in *The Lancet*. The findings stand in contrast to current health policies that aim to regionalise major surgical procedures into high volume centres of excellence.

"With up to one in four patients rehospitalized following complex surgery, our results could potentially translate into thousands of lives saved every year in the USA alone if patients returned to the hospital where they had the procedure and received care from their original surgical team" [1], explains lead author Dr Benjamin Brooke from the University of Utah School of Medicine in Salt Lake City, USA.

Brooke and colleagues examined data from more than 9 million (9440503) Medicare beneficiaries in the USA between January, 2001 and November, 2011, who underwent 12 common high-risk operations [2]. They used different statistical models to investigate the association between readmission destination (ie, the index hospital where the procedure took place vs a different hospital) and risk of death within 90 days of the procedure. This included instrumental variable analyses to account for potential unmeasured bias. This approach effectively allows researchers to simulate randomisation of patients who were readmitted following surgery and to generate unbiased estimates.

The number of patients rehospitalised with complications within 30 days of their operation ranged from 5.6% (154203 patients) of knee replacement patients, to 22% (3665) of oesophagectomy (surgical removal of all or part of the oesophagus) patients. Of patients rehospitalized, those readmitted to the same hospital ranged from two-thirds (186336) after coronary artery bypass grafting, to 83% (142142) following colectomy (surgical removal of all or part of the colon).

The researchers found that patients readmitted to the same hospital were 26% less likely to die within 90 days than those readmitted to a different hospital, even after taking into account measures of surgical quality that can affect mortality such as hospital size, teaching status, and volume of procedures. When confounding was controlled with instrumental variable analysis, patients returning to the index hospital were 8% less likely to die than those returning to a different hospital.

According to Dr Brooke, "Patients increasingly travel long distances to have their operations done at hospitals that are recognised as providing high-quality care or because of lower costs for health insurers. The assumption has been that if patients need readmission for complications they can seek care at local hospitals without compromising outcomes. However, our findings suggest that maintaining continuity of care when readmissions occur is a more important predictor of survival than other established surgical quality measures such as hospital procedure volume and needs to be considered in the trade-offs when choosing a hospital for surgery."<sup>[1]</sup>

Dr Justin Dimick and Dr David Miller from the University of Michigan, Ann Arbor, Michigan, USA, authors of a linked Comment, say, "After many years of evidence supporting the advantages of regionalizing complex surgery, Brooke and colleagues provide the first definitive empirical evidence that travelling to a remote hospital for surgery may be potentially life threatening. These findings have important implications for existing selective referral and centre of excellence programmes. If patients need to travel long distances to receive care, every effort should be made to ensure that the post-surgical patient is readmitted to the hospital where they had surgery."<sup>[1]</sup>

<sup>[1]</sup> Quotes direct from authors and cannot be found in text of Article / Comment.

<sup>[2]</sup> Open abdominal aortic aneurysm repair, infrainguinal arterial bypass, aortobifemoral bypass, coronary artery bypass surgery, oesophagectomy (surgical removal of all or part of the oesophagus), colectomy (surgical removal of all or part of the colon), pancreatectomy (surgery to remove all or part of the pancreas), cholecystectomy (surgical removal of the gallbladder), ventral hernia repair, craniotomy, hip replacement, or knee replacement.

[http://www.eurekalert.org/pub\\_releases/2015-06/uoc--hbq061715.php](http://www.eurekalert.org/pub_releases/2015-06/uoc--hbq061715.php)

### Humans' built-in GPS is our 3-D sense of smell

***Like homing pigeons, humans have a nose for navigation because our brains are wired to convert smells into spatial information, according to new research***

Like homing pigeons, humans have a nose for navigation because our brains are wired to convert smells into spatial information, new research from the University of California, Berkeley, shows.

While humans may lack the scent-tracking sophistication of, say, a search-and-rescue dog, we can sniff our way, blindfolded, toward a location whose scent we've smelled only once before, according to the UC Berkeley study published today (June 17) in the journal PLOS ONE.

Similar investigations have been conducted on birds and rodents, but this is the first time smell-based navigation has been field-tested on humans. The results evoke a GPS-like superpower one could call an "olfactory positioning system."

"What we've found is that we humans have the capability to orient ourselves along highways of odors and crisscross landscapes using only our sense of smell," said study lead author Lucia Jacobs, a UC Berkeley psychology professor who studies evolution and cognition in animals and humans.

Smell is a primitive sense that our early ancestors used for foraging, hunting and mating, among other skills necessary for survival. Early sailors and aviators gave anecdotal reports of using odors to navigate, but there have been no experiential scientific studies on this until now.

The process of smelling, or olfaction, is triggered by odor molecules traveling up the nasal passage, where they are identified by receptors that send signals to the olfactory bulb - which sits between the nasal cavity and the brain's frontal lobe - and processes the information. A key to the connection between smell, memory and navigation is that olfactory bulbs have a strong neural link to the brain's hippocampus, which creates spatial maps of our environment.

"Olfaction is like this background fabric to our world that we might not be conscious of, but we are using it to stay oriented," Jacobs said. "We may not see a eucalyptus grove as we pass it at night, but our brain is encoding the smells and creating a map."

Pigeons and rats, for example, are known to orient themselves using odor maps, or "smellscapes," but sighted humans rely more heavily on visual landmarks, and so the study turned up some surprising results.

Two dozen young adults were tested on orientation and navigation tasks under various scenarios in which their hearing, sight or smell was blocked. The test location was a 25-by-20-foot room where 32 containers with sponges were placed at points around the edge of the room. Two of the sponges were infused with essential oils such as sweet birch, anise or clove.

In the smell-only experiment, study participants were led, one at a time, into the room wearing blindfolds, earplugs and headphones and walked in circles for disorientation purposes. They spent a minute at a specific point on the grid, where they inhaled a combination of two fragrances. After being walked in circles again for disorientation purposes, they were tasked with sniffing their way back to the starting point where they had smelled the two fragrances.

Overall, study participants navigated relatively closely to the targeted location when using only their sense of smell, compared to when other sensory inputs were blocked. Moreover, they were not just following one scent, but using information from both scents to orient themselves toward a point on an odor grid.

"We never thought humans could have a good enough sense of smell for this," said Jacobs. But in retrospect, she noted, the results are "as obvious as the nose on my face." Jacobs will be exploring this mechanism further as a scientist selected to be on the team of the National Science Foundation's "Cracking the Olfactory Code" Ideas Lab, which takes place this summer.

*In addition to Jacobs, co-authors on the study are UC Berkeley researchers Jennifer Arter, Amy Cook and Frank Sulloway.*

[http://www.eurekalert.org/pub\\_releases/2015-06/uu-iws061615.php](http://www.eurekalert.org/pub_releases/2015-06/uu-iws061615.php)

### **Individuals with social phobia have too much serotonin -- not too little**

*It was believed that individuals with social anxiety disorder have too little serotonin, a new study shows the situation is exactly the opposite*

Previous studies have led researchers to believe that individuals with social anxiety disorder/ social phobia have too low levels of the neurotransmitter serotonin. A new study carried out at Uppsala University, however, shows that the situation is exactly the opposite. Individuals with social phobia make too much serotonin. The more serotonin they produce, the more anxious they are in social situations.

Many people feel anxious if they have to speak in front of an audience or socialise with others. If the anxiety becomes a disability, it may mean that the person suffers from social phobia which is a psychiatric disorder.

Social phobia is commonly medicated using SSRI compounds. These change the amount of the neurotransmitter serotonin in the brain. Based on previous studies, it was believed that individuals with social phobia had too little serotonin and that SSRIs increased the amount of available serotonin. In a new study published in the scientific journal JAMA Psychiatry, researchers from the Department of Psychology at Uppsala University show that individuals with social phobia make too much serotonin.

The research team, led by professors Mats Fredrikson and Tomas Furmark, used a so-called PET camera and a special tracer to measure chemical signal transmission by serotonin in the brain. They found that patients with social phobia produced too much serotonin in a part of the brain's fear centre, the amygdala. The more serotonin produced, the more anxious the patients were in social situations.

A nerve cell, which sends signals using serotonin, first releases serotonin into the space between the nerve cells. The nerve signal arises when serotonin attaches itself to the receptor cell. The serotonin is then released from the receptor and pumped back to the original cell.

'Not only did individuals with social phobia make more serotonin than people without such a disorder, they also pump back more serotonin. We were able to show this in another group of patients using a different tracer which itself measures the pump mechanism. We believe that this is an attempt to compensate for the excess serotonin active in transmitting signals', says Andreas Frick, a doctoral student at Uppsala University Department of Psychology.

This discovery is a major leap forward when it comes to identifying changes in the brain's chemical messengers in people who suffer from anxiety. Earlier research has shown that nerve activity in the amygdala is higher in people with social phobia and thus that the brain's fear centre is over-sensitive. The new findings indicate that a surplus of serotonin is part of the underlying reason.

'Serotonin can increase anxiety and not decrease it as was previously often assumed', says Andreas Frick.

*Frick et al. (2015) Serotonin Synthesis and Reuptake in Social Anxiety Disorder: A Positron Emission Tomography Study, JAMA Psychiatry*

[http://www.eurekalert.org/pub\\_releases/2015-06/oifn-jvm061615.php](http://www.eurekalert.org/pub_releases/2015-06/oifn-jvm061615.php)

### **JAMA Viewpoint: Middle East respiratory syndrome: A global health challenge**

***Middle East respiratory virus requires constant vigilance and could spread to other countries***

WASHINGTON - The ongoing outbreak in the Republic of Korea (South Korea) is an important reminder that the Middle East respiratory virus (MERS-CoV) requires constant vigilance and could spread to other countries including the United States. However, MERS can be brought under control with effective public health strategies, say two Georgetown University public health experts.

In a JAMA Viewpoint published online June 17, Georgetown public health law professor Lawrence O. Gostin and infectious disease physician Daniel Lucey outline strategies for managing the outbreak, focusing on transparency, trust and infection control in health care settings. The duo also outline weaknesses in a World Health Organization's (WHO) framework designed to govern patents on certain viruses, which is likely to impact critical future research.

MERS-CoV, which affects the respiratory system and is sometimes fatal, was first diagnosed in 2012 in Saudi Arabia. The first outbreak occurred that year in Jordan with nine laboratory-confirmed cases. In May 2015, South Korea reported what has been described as a "super-spreading" event with dozens diagnosed MERS-

CoV cases after exposure to a single patient. While more difficult to spread person-to-person than its cousin, SARS, MERS-CoV is most likely to spread in health care environments.

"South Korea repeated many of the fundamental mistakes evident during the SARS and Ebola epidemics: lack of transparency, poor infection control, and social disruption, including unnecessary school closures," says Gostin.

"Public health measures--infection prevention and control, isolation, contact tracing, and quarantine--historically have controlled MERS-CoV and were also widely employed during SARS and Ebola outbreaks," Gostin and Lucey write.

However, they point out that public fear and government mistrust can hinder effective epidemic response.

"In the case of MERS-CoV, health authorities initially withheld the names of hospitals handling cases. Transparency builds public trust; given the scientific uncertainty, health authorities should fully disclose what is and is not known about the MERS-CoV outbreak."

Key points Gostin and Lucey make about MERS-CoV infection control include:

***Training health workers and conducting diagnostic testing of certain travelers;***

***Limiting quarantine quarantines use to well-documented exposures using the least restrictive means possible;***

***Restricting travel should be avoided as it would be ineffective as evidence is lacking of MERS-CoV community transmission; and***

***Closing schools also should be avoided given the lack of community transmission of MERS-CoV.***

In addition, Gostin and Lucey point out that deficiencies in a WHO framework for virus sharing have led to challenges of intellectual property ownership of MERS-CoV that could hinder research.

After Saudi Arabia sent blood samples to Erasmus Medical Center in the Netherlands and MERS-CoV was identified, Erasmus filed for a patent. Saudi Arabia says that action violates national rules and that Erasmus acted unethically. Gostin and Lucey say the WHO's Pandemic Influenza Preparedness Framework fails to cover non-influenza pathogens like MERS-CoV noting, "...there remain substantial holes in international rules needed to facilitate critical research."

In conclusion, the two public health experts say that by fully funding and implementing requirements put forth in WHO's International Health Regulations, such as building core capacities (diagnosis, treatment, laboratories contact tracing and human forms of quarantine) offers "the best assurance of global health security."

*Gostin is professor of global health law and faculty director of the O'Neill Institute for National and Global Health Law. Lucey is adjunct professor of microbiology and*

*immunology at Georgetown University School of Medicine and is a Senior Scholar at the O'Neill Institute.*

<http://www.bbc.com/news/science-environment-33054762>

### **Building the face of a criminal from DNA**

***The face of a killer constructed from DNA left at the scene of a crime: it sounds like science fiction. But revealing the face of a criminal based on their genes may be closer than we think.***

Today scientists are using genetic markers from DNA to build up a picture of an offender's face, a process known as molecular photo fitting. A DNA profile is only useful to detectives if a match can be found on a database.

As surgeon Gabriel Weston explains in the BBC series [Catching History's Criminals: The Forensics Story](#), this technology offers the tantalising prospect of generating a face from nothing more than a few cells.



***The face was based solely on the genetic make-up of presenter Gabriel Weston***

To find out just how effective this process can be, DNA was extracted from Gabriel's saliva and the results sent anonymously to a group of scientists in Belgium. From that data they set about building a picture of Gabriel's face - as predicted by her genes. The question was: Would it look anything like her?

The job of turning the cells in her saliva into a picture of her face was carried out by Dr Peter Claes, a medical imaging specialist at the University of Leuven. Along with colleagues in the US, he's built up a database of faces and DNA. And armed with this information, he's able to model how a face is constructed based on just 20 genes.



***Gabriel's DNA results were sent anonymously to a team of scientists in Belgium***

It is possible to judge just how much the picture of Gabriel's face - based on her genetic makeup - looks like her by comparing it to her actual image.

Dr Claes believes it contains a lot of information that would be useful to detectives: "I can tell you that your eyebrows are sticking forward more, and your chin as well," he explains.

"You have a very prominent specific chin compared to an average European, which in my eyes is not a bad result. You do tend to have flat cheeks, but of course that's a tricky area to actually predict accurately because it's heavily based on diet, which is an environmental factor."

If this predicted face is superimposed over a photo of Gabriel, the accuracy of the technique is revealed.

The eyes, nose, mouth and chin are all in roughly the right place. But the features are more rounded than in reality.



**Scientists were able to compare the faces when they were superimposed**

At the moment, police couldn't publish a molecular photo-fit like this and hope to catch a killer. But that's not how Dr Claes sees the technique being used in a criminal investigation.

"If I were to bring this result to an investigator, I wouldn't necessarily give him the image to broadcast. I would talk to him and say okay, you're looking for a woman, with a very specific chin and eyebrow structure. "So if you're having suspects or candidates that you're looking for, just focus on those."

This may be new science, but Dr Claes and his colleagues are rapidly developing the technology. The number of genes used is being expanded from 20 to 200, and it seems clear that molecular photo-fitting is only going to become more accurate in the coming years.

<http://www.bbc.com/news/health-33183330>

### **Record 'fake drugs' haul worth £16m by UK agency**

***Dangerous counterfeit and unlicensed medicines worth nearly £16m have been seized in a record haul by the UK's Medicines and Healthcare products Regulatory Agency (MHRA).***

By James Gallagher Health editor, BBC News website

Slimming pills, drugs for erectile dysfunction and cancer medicines were taken in a series of raids. The MHRA said criminals were making money at the expense of people's health and it was a growing problem. Nearly 1,400 websites were closed as part of the operation. Seven suspects are now under investigation.

The seizures were part of Operation Pangea - an international clampdown on the illegal trade in fake medicines by 115 countries. In the UK, 6.2 million doses or medical devices were seized, worth £15.8m. Internationally, £51.6m of goods were taken. Items seized in the UK included:

***two million doses of erectile dysfunction drugs***

***slimming drugs - some of which can increase the risk of heart attacks and strokes***

***narcolepsy pills***

***abortion pills***

***diabetes medication***

***hair-loss drugs***

***cancer medicines, particularly for breast and prostate***

***medical devices, including fake condoms and dental laboratories***

"It's amazing to me that people will buy those types of medicines over the internet," said the MHRA's head of enforcement, Alastair Jeffrey.

The drugs are not always used for their medical purposes. Breast cancer drugs are used by some body builders to reduce their breast tissue, for example.

Many packs of narcolepsy pills were seized en route to universities, where students take them for "cognitive enhancement" - to stay awake around exam time.

Mr Jeffrey added: "Criminals involved in the illegal supply of medical products through the internet aren't interested in your health, they are interested in your money and are able to get this by selling you a potentially dangerous product or by stealing your bank details.

"To protect your health, visit your GP, get a correct diagnosis and buy medicines from a legitimate High Street or registered pharmacy which can trade online."

It is thought that people buying the drugs are made up of those who think they are buying genuine drugs and those who are getting hold of drugs a doctor would never prescribe. The "vast majority" of the drugs came from India and China - neither country was involved in Operation Pangea. It is unclear what the total size of the illegal drugs market in the UK is.

The MHRA said counterfeit medicines were the greatest source of profit "across the whole criminal spectrum" but insisted the UK was "way ahead of the game".

Mr Jeffrey said criminal gangs were moving into the field because, compared with illegal narcotics, sentencing was low. "It's two years, it's not a police priority, you can use the internet as a facilitator, the risk is low and the profits are very high," he said. He added there were "some indications" that terrorist groups were involved in "pharmaceutical crime" in the Middle East.

[http://www.eurekalert.org/pub\\_releases/2015-06/vumc-vs061715.php](http://www.eurekalert.org/pub_releases/2015-06/vumc-vs061715.php)

### **Vanderbilt-led study finds significant drop in new prostate cancer diagnoses**

***Decline follows USPSTF recommendation against PSA testing***

A new study led by Vanderbilt University Medical Center investigators found new diagnoses of prostate cancer in the U.S. declined 28 percent in the year following the draft recommendation from the United States Preventive Services Task Force (USPSTF) against routine PSA screening for men. The new research, led by first author Daniel Barocas, M.D., MPH, assistant professor of urological

surgery and medicine, was posted online in the June 15 issue of The Journal of Urology in advance of publication.

In October 2011, the USPSTF issued a draft guideline discouraging the use of prostate-specific antigen (PSA)-based screenings for prostate cancer after concluding the harms outweigh potential benefits. Harmful side effects of treatment may include incontinence, erectile dysfunction and radiation cystitis.

However, the 'grade D' recommendation was considered controversial because of uncertainty about the risk-benefit ratio of screening since prostate cancer is the second leading cause of cancer death among men in the U.S., with nearly 30,000 deaths annually, and some studies show that screening saves lives.

To assess the effects of this recommendation, the investigators identified new cancers diagnosed between January 2010 and December 2012 in the National Cancer Database. They studied the trend of prostate cancers diagnosed each month before and after the draft guideline, compared with new colon cancer cases. The research revealed that 12 months after the draft USPSTF guidelines were published diagnoses of new low-risk cancers had fallen by 37.9 percent while colon cancer cases remained stable.

New prostate cancer diagnoses also declined by 23 to 29.3 percent among men over age 70 and 26 percent among men considered infirm. The authors note these are populations who are unlikely to live long enough to benefit from early detection and are at risk of harms of treatment.

However, the investigators suggest that withholding screening may also result in failure to detect higher-risk cancers during the window of curability. Timely treatment of intermediate and high-risk localized disease is associated with superior overall survival, disease-specific survival and decreased spread of the disease to other locations in the body.

The study identified a drop of 28.1 percent in diagnoses of intermediate-risk disease and 23.1 percent in high-risk prostate cancer one year after the draft guideline. The decline did not vary across age or comorbidity features.

'These findings suggest that reduced screening may result in missed opportunities to spare these men from progressive disease and cancer death,' said Barocas.

While the observation period was too limited to determine the impact on the diagnosis of metastatic prostate cancer, which is associated with a high treatment burden, decrease in quality of life and increased mortality, the authors did observe a small upward trend in diagnoses of non-localized disease.

'The results raise concern that if this trend continues more men may be diagnosed at a point when their disease is advanced. Younger, healthier men with intermediate or high-risk disease would normally be candidates for aggressive local therapy and they may not be receiving a timely diagnosis under this policy,'

said Barocas. The authors suggest that future research should focus on screening regimens that minimize harms and maximize potential benefits of screening, while also considering patient preferences.

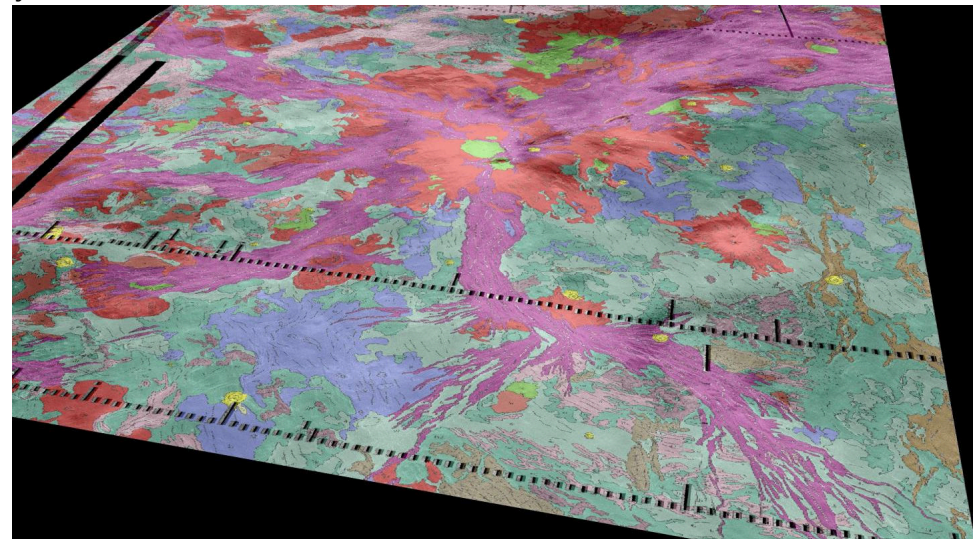
*Other investigators participating in the study include Amy Graves, S.M., MPH, David Penson, M.D., MPH, Sam Chang, M.D., Vanderbilt; Katherine Mallin, Ph.D., Bryan Palis, and David Winchester, M.D., National Cancer Database, American College of Surgeons, Chicago.*

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### Study suggests active volcanism on Venus

***An international team of scientists has found some of the best evidence yet that Venus, Earth's nearest neighbor, is volcanically active.***

PROVIDENCE, R.I. [Brown University] - In combing through data from the European Space Agency's Venus Express mission, the scientists found transient spikes in temperature at several spots on the planet's surface. The hotspots, which were found to flash and fade over the course of just a few days, appear to be generated by active flows of lava on the surface.



***This perspective view of the geology of Venus superposed on topography shows a broad topographic rise (Atla Regio) in the center (red, with radiating purple spokes) and surrounding volcanic plains (green and blue).***

***The large Venus volcano Oza Mons (red, center) is several hundreds of miles across. Radiating from this rise are numerous tectonic rift zones (mapped in purple), regions of stretched and faulted crust of Venus. Although geologically relatively recent in the 4.5 billion year history of Venus, these terrains could be many hundreds of million years old and no longer active. Ivanov/Head/Dickson/Brown University***

"We were able to show strong evidence that Venus is volcanically, and thus internally, active today," said James W. Head, a geologist at Brown University and co-author of a paper describing the new research. "This is a major finding that helps us understand the evolution of planets like our own."

The research is published online in *Geophysical Research Letters*.

The hotspots turned up in thermal imaging taken by the Venus Express spacecraft's Venus Monitoring Camera. The data showed spikes in temperature of several hundred degrees Fahrenheit in spots ranging in size from 1 square kilometer to over 200 kilometers.

The spots were clustered in a large rift zone called Ganiki Chasma. Rift zones are formed by stretching of the crust by internal forces and hot magma that rises toward the surface. Head and Russian colleague Mikhail Ivanov had previously mapped the region as part of a global geologic map of Venus generated from the Soviet Venera missions in the 1980s and U.S. Magellan mission in the 1990s. The mapping work had shown that Ganiki Chasma was quite young, geologically speaking, but just how young wasn't clear until now.

"We knew that Ganiki Chasma was the result of volcanism that had occurred fairly recently in geological terms, but we didn't know if it formed yesterday or was a billion years old," Head said. "The active anomalies detected by Venus Express fall exactly where we had mapped these relatively young deposits and suggest ongoing activity."

The latest finding is consistent with other data from Venus Express that have hinted at very recent volcanic activity. In 2010, infrared imaging from several volcanoes seemed to indicate lava flows from thousands to a few million years old. A few years later, scientists reported transient spikes in sulfur dioxide in Venus' upper atmosphere, another potential signal of active volcanism.

The observation of hotspots by Venus Express, combined with the geologic mapping from Venera and Magellan, make a strong case for a volcanically active Venus, Head says.

"This discovery fits nicely with the emerging picture of very recent activity in Venus' geologic history," he said. "These remarkable findings were the result of collaborations spanning many years and many political borders. They underscore the importance of international collaboration in exploring our solar system and understanding how it evolves."

*The work was led by Eugene Shalygin and Wojciech Markiewicz of the Max Planck Institute. Additional co-authors were Alexander Basilevski (Russia's Vernadsky Institute and Brown University), Dima Titov (European Space Agency) and N.I. Ignatiev (Russia's Space Research Institute).*

[http://www.eurekalert.org/pub\\_releases/2015-06/uotm-gdo061115.php](http://www.eurekalert.org/pub_releases/2015-06/uotm-gdo061115.php)  
**Genomic discovery of skin cancer subtypes provides potential 'signpost' for drug targets**

***MD Anderson researchers lead The Cancer Genome Atlas analysis of cutaneous melanoma identifying four subtypes***

Cutaneous melanoma, the most deadly form of skin cancer, is now believed to be divided into four distinct genomic subtypes, say researchers at The University of Texas MD Anderson Cancer Center, a finding that could prove valuable in the ever-increasing pursuit of personalized medicine.

As part of The Cancer Genome Atlas, researchers identified four melanoma subtypes: BRAF, RAS, NF1 and Triple-WT, which were defined by presence or absence of mutations from analysis of samples obtained from 331 patients. The five-year study resulted from an international collaboration of over 300 researchers from more than five countries, including Australia, Germany and Canada.

'A major achievement in the clinical management of patients with advanced melanoma has been the development of effective targeted therapies,' said Jeffrey E. Gershenwald, M.D., professor of surgery, Surgical Oncology. 'This comprehensive classification of melanomas allows us to create a framework that could be used to further personalize therapeutic decision-making in both the targeted and immunotherapy arena, as well as to develop more impactful prognostic and predictive models to inform patient care.'

Results from the study are published in the June 18 issue of *Cell*. Analysis of the TCGA effort was chaired by Gershenwald, Ian Watson, Ph.D., instructor of Genomic Medicine and Lynda Chin, M.D., former chair of Genomic Medicine and now associate vice chancellor for health transformation and chief innovation officer for health affairs at The UT System. Gershenwald is also co-leader of MD Anderson's Melanoma Moon Shot Program, which aims to accelerate the conversion of scientific discoveries into clinical advances and significantly reduce cancer deaths.

The scientists found all four genomic subtypes share common 'downstream' signaling pathways, but differ in how they activate these pathways. Understanding the genomic underpinnings of melanoma may provide additional information on other existing therapies.

'For example, BRAF and MEK inhibitor combinations are now used to treat patients with BRAF mutant melanomas, and MEK inhibitor combinations are being explored for RAS mutant melanomas,' said Watson. 'Pre-clinical studies have already demonstrated that some NF1 melanoma cell lines respond to MEK

inhibitors, but more work is needed to identify responders and non-responders within this new melanoma subtype, as well as to determine strategies to treat Triple Wild-type melanoma patients.'

Interestingly, no significant correlation was found between the genomic subtypes and patient outcome. However, within each genomic subtype, they found a subset with evidence of immune infiltration that did correlate with improved survival.

'Detailed analyses showed that these lymphocytic elements were not merely 'bystanders,' said Chin. 'They had infiltrated the tumor and were likely associated with melanoma biology.' The study also revealed the importance of a T cell biomarker called LCK, a protein found in lymphocytes or white blood cells. The biomarker was shown to be associated with improved patient survival.

The team hypothesizes that this information could prove useful in the emerging field of immunotherapy, which has shown success in treating late-stage melanoma patients. In particular, recently approved checkpoint blockade drugs have shown incredible potential in treatment for melanomas. Yet, it is not entirely clear which patients respond to the therapy.

'We believe this international collaboration from more than 20 tissue source sites and 50 institutions around the globe, which included pathologists who analyzed samples for immune infiltration, computational biologists who identified significant driving genetic alterations, and clinician scientists who aided in acquiring samples and interpreting data, have generated a dataset that is a treasure trove, and that will seed studies for many years to come,' said Chin. 'We could not have carried out this study without the families and patients who donated samples by participating in research protocols.'

*The study was funded by the National Institutes of Health (U54HG003273, U54HG003067, U54HG003079, U24CA143799, U24CA143835, U24CA143840, U24CA143843, U24CA143845, U24CA143848, U24CA143858, U24CA143866, U24CA143867, U24CA143882, U24CA143883, U24CA144025, and P30CA016672.*

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## **Diet that mimics fasting appears to slow aging**

### ***Benefits demonstrated in mice and yeast; piloted in humans***

Want to lose abdominal fat, get smarter and live longer? New research led by USC's Valter Longo shows that periodically adopting a diet that mimics the effects of fasting may yield a wide range of health benefits.

In a new study, Longo and his colleagues show that cycles of a four-day low-calorie diet that mimics fasting (FMD) cut visceral belly fat and elevated the number of progenitor and stem cells in several organs of old mice -- including the brain, where it boosted neural regeneration and improved learning and memory. The mouse tests were part of a three-tiered study on periodic fasting's effects --

testing yeast, mice and humans - set to be published by Cell Metabolism on June 18.

Mice, which have relatively short life spans, provided details about fasting's lifelong effects. Yeast, which are simpler organisms, allowed Longo to uncover the biological mechanisms that fasting triggers at a cellular level. And a pilot study in humans found evidence that the mouse and yeast studies were applicable to humans.

Bimonthly cycles that lasted four days of an FMD which started at middle age extended life span, reduced the incidence of cancer, boosted the immune system, reduced inflammatory diseases, slowed bone mineral density loss and improved the cognitive abilities of older mice tracked in the study. The total monthly calorie intake was the same for the FMD and control diet groups, indicating that the effects were not the result of an overall dietary restriction.

In a pilot human trial, three cycles of a similar diet given to 19 subjects once a month for five days decreased risk factors and biomarkers for aging, diabetes, cardiovascular disease and cancer with no major adverse side effects, according to Longo.

'Strict fasting is hard for people to stick to, and it can also be dangerous, so we developed a complex diet that triggers the same effects in the body,' said Longo, Edna M. Jones professor of biogerontology at the USC Davis School of Gerontology and director of the USC Longevity Institute. Longo has a joint appointment at the USC Dornsife College of Letters, Arts and Sciences. 'I've personally tried both, and the fasting mimicking diet is a lot easier and also a lot safer.'

The diet slashed the individual's caloric intake down to 34 to 54 percent of normal, with a specific composition of proteins, carbohydrates, fats and micronutrients. It decreased amounts of the hormone IGF-I, which is required during development to grow, but it is a promoter of aging and has been linked to cancer susceptibility. It also increased the amount of the hormone IGFBP-, and reduced biomarkers/risk factors linked to diabetes and cardiovascular disease, including glucose, trunk fat and C-reactive protein without negatively affecting muscle and bone mass.

Longo has previously shown how fasting can help starve out cancer cells while protecting immune and other cells from chemotherapy toxicity.

'It's about reprogramming the body so it enters a slower aging mode, but also rejuvenating it through stem cell-based regeneration,' Longo said. 'It's not a typical diet because it isn't something you need to stay on.'

For 25 days a month, study participants went back to their regular eating habits -- good or bad -- once they finished the treatment. They were not asked to change their diet and still saw positive changes.



Longo believes that for most normal people, the FMD can be done every three to six months, depending on the abdominal circumference and health status. For obese subjects or those with elevated disease risk factors, the FMD could be recommended by the physician as often as once every two weeks. His group is testing its effect in a randomized clinical trial, which will be completed soon, with more than 70 subjects.

'If the results remain as positive as the current ones, I believe this FMD will represent the first safe and effective intervention to promote positive changes associated with longevity and health span, which can be recommended by a physician,' Longo said. 'We will soon meet with FDA officers to pursue several FDA claims for disease prevention and treatment.'

Despite its positive effects, Longo cautioned against water-only fasting and warned even about attempting the fasting mimicking diet without first consulting a doctor and seeking their supervision throughout the process.

'Not everyone is healthy enough to fast for five days, and the health consequences can be severe for a few who do it improperly,' he said. 'Water-only fasting should only be done in a specialized clinic. Also, certain types of very low calorie diets, and particularly those with high protein content, can increase the incidence of gallstones in women at risk'.

'In contrast,' he added, 'the fasting mimicking diet tested in the trial can be done anywhere under the supervision of a physician and carefully following the guidelines established in the clinical trials.'

Longo also cautioned that diabetic subjects should not undergo either fasting or fasting mimicking diets while receiving insulin, metformin or similar drugs. He also said that subjects with body mass index less than 18 should not undergo the FMD diet.

For the study, Longo collaborated with researchers and clinicians from USC as well as from Texas, Italy and England. The study was funded by the National Institute on Aging.

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### **Scientists find evidence of key ingredient during dawn of life**

***UNC School of Medicine researchers provide first direct experimental evidence for the rapid synthesis of two classes of proteins necessary to create the first life on Earth***

CHAPEL HILL, NC - Before there were cells on Earth, simple, tiny catalysts most likely evolved the ability to speed up and synchronize the chemical reactions necessary for life to rise from the primordial soup. But what those catalysts were, how they appeared at the same time, and how they evolved into the two modern superfamilies of enzymes that translate our genetic code have not been understood.

In the Journal of Biological Chemistry, scientists from the UNC School of Medicine provide the first direct experimental evidence for how primordial proteins developed the ability to accelerate the central chemical reaction necessary to synthesize proteins and thus allow life to arise not long after Earth was created. This finding provides another insight into the dramatic inventions nature made as prebiotic chemistry evolved into life billions of years ago. Earlier this month, Carter and his UNC colleague Richard Wolfenden, PhD, reported in the Proceedings of the National Academy of Sciences more evidence for how amino acids were selected to match with a genetic blueprint to form proteins, the machines of living cells.

This latest paper provides evidence that the two major superfamilies of enzymes that translate the genetic code in modern biology evolved from opposite strands of the same remarkable ancestral gene.

"We found, quite surprisingly, that a single ancient gene probably used its two opposite strands of DNA to code for different catalysts that both activated amino acids," said Charles Carter, PhD, professor of biochemistry and biophysics, and senior author of the JBC paper. "The peptide made from one strand activated those amino acids needed for the insides of proteins, and the peptide made from the other strand activated those amino acids needed for the outsides of proteins."

### **Comprehending catalysis**

A key obstacle in creating living things is speeding up chemical reactions that normally proceed at very slow and different speeds so that all reactions proceed at about the same rate inside cells. From this standpoint, one reaction in modern biochemistry towers above the others as an obstacle to the formation of life: the reaction that combines amino acids with adenosine triphosphate, or ATP, a molecule that transfers chemical energy within cells. This combination allows proteins to assemble spontaneously. Without a catalyst, this reaction would be slower than any of the other steps in protein synthesis by about a thousand-fold.

Scientists know that inside modern living cells there are enzymes called aminoacyl-tRNA synthetases that dramatically speed up this reaction. Like all enzymes, synthetases are remarkably sophisticated machines. They belong to two different families: Class I synthetases activate half of the twenty amino acids that link together to form proteins, and Class II synthetases activate the other half.

Carter's team devised experiments to physically take apart the synthetases to show that the necessary catalytic activity comes from parts of the enzymes that all members of each synthetase family share: the parts that bind to ATP. These parts - chains of 46 amino acids - compose about 5 to 10 percent of the total size of modern enzymes but exhibit more than 40 percent of their total activity.

Carter calls these enzyme fragments protozymes - from the Greek root "protos" meaning first. His team found that the enzymatic activity of these protozymes focuses on the activation reaction with ATP.

This catalytic activity means that the protozymes were able to form very tight complexes with the least stable, slowest-to-form structures during the transitions that occur during the chemical reactions that form proteins. These tight complexes of enzymes within these "transition states", Carter said, would be very necessary during catalysis and thus for the creation of the first life on Earth.

### Designer evidence

Carter then got help from colleague Brian Kuhlman, PhD, professor of biochemistry and biophysics, to create "designer" protozymes from a single gene in which one strand codes for a protozymic ancestor of class I synthetases and the other strand codes for a protozymic ancestor of class II synthetases.

Surprisingly, their experiments revealed that both designer protozymes exhibited the same catalytic activity as did the protozymes Carter's team had isolated from the modern synthetases.

"We discovered that nature solved the problem of activating amino acids destined to be inside (class I) folded proteins and outside (class II) folded proteins by evolving a single gene to do both jobs," Carter said. "Moreover, the protozymes managed to do this in a most unusual way: by relying on two entirely different interpretations of the same genetic information."

Carter's previous work on Earth's earliest enzymes had pointed strongly in this direction. But his team's current research marks the first direct, experimental "proof of principle" of a hypothesis originally proposed in 1994 by two theoretical evolutionary biologists - Sergei Rodin, PhD, DSc, and Susumu Ohno, PhD, DVM - who said that one gene could encode different proteins from each of its two strands.

"We now have more information about how amino acids eventually evolved into complex molecules necessary to create life as we know it," Carter said. "But perhaps more importantly, we've been able to provide a new set of tools that will enable others to approach questions about the origin of life in ways that are scientifically sound and productive."

And there are still questions about how all this happened.

"This doesn't yet solve the central chicken and the egg problem," Carter said. "Even the designed protozyme requires a ribosome to synthesize it and lead to protein creation. But what we've shown is that blueprints for life actually contained more information than anyone had realized because both strands of the ancestral gene were responsible for encoding the two classes of synthetases needed for the creation of proteins."

This result unifies what scientists previously considered to be two distinct superfamilies of modern enzymes and greatly simplifies the complex process of forming the diversity of catalysts necessary for life: both catalysts were available at the same times and places before there were cells to package life's machinery.

*This research was sponsored by the National Institutes of Health. JBC paper first author, Luis Martinez, an undergraduate, conducted many experiments as part of the UNC Summer Undergraduate Research Experience (SURE). Other undergraduates contributed to this work thanks to the American Biophysical Society summer course in biophysics at UNC and the UNC Post-baccalaureate Research Experience Program (PREP). Each program is offered by the UNC School of Medicine Office of Graduate Education.*

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## MRSA contamination found in supermarket sausages and minced pork

### Survey has found first evidence of MRSA in sausages and minced pork from supermarkets in the UK

A survey carried out earlier this year has found the first evidence of the 'superbug' bacteria Methicillin-Resistant Staphylococcus aureus (MRSA) in sausages and minced pork obtained from supermarkets in the UK. However, researchers stress that this does not pose a significant immediate risk to the public.

In February, a team of researchers funded primarily by the Medical Research Council (MRC) bought and analysed a total of 103 (52 pork and 51 chicken) pre-packaged fresh meat products, labelled as being of UK farm origin, from supermarkets in five different locations across in England.

All of the meat products were frozen at -20°C and sent to the Department of Veterinary Medicine at the University of Cambridge for testing. After thawing, researchers disinfected the exterior packaging before removing the meat. They then tested a 10g sample of meat from each packet and screened for MRSA. Two of the pork samples - one from sausages, one from minced pork - tested positive for MRSA; the sausage sample contained two strains of the bacteria.

In collaboration with the Wellcome Trust Sanger Institute an analysis of the genetic make-up of the bacteria and confirmed the presence of antibiotic resistant genes. The analysis showed that the bacteria belonged to a type of MRSA known as LA-MRSA CC398, which has emerged over the last few years in continental Europe, particularly in pigs and poultry, but was not previously believed to be widely distributed in the UK.

In many countries, LA-MRSA CC398 represents an occupational risk for those in close contact with livestock, particularly pigs and veal calves. Humans in contact with pigs (farm workers, abattoir workers and veterinarians, etc.) have significantly higher rates of the bacteria in their nasal carriage, according to

epidemiological studies, for example. Other studies have revealed an association between clinical disease resulting from LA-MRSA CC398 infection and recent contact with pigs or pig farms. As with other MRSA, this type may be responsible for serious illness following wound or surgery site infections, although many people will carry MRSA on their skin or in their noses without showing signs of disease.

The researchers stress that adequate cooking (heating above 71°C) and hygienic precautions during food preparation should minimise the likelihood of transmission to humans via contaminated pork. However, they argue that the discovery of MRSA in pork identifies a potential way that the bacteria can spread from farms to the wider population.

While human contamination of carcasses or meat products in the abattoir or at the meat packing plant may occur, there is good evidence that these isolates are of animal origin - possibly through the use of antibiotics to treat or control infection in livestock.

As the tests use a highly sensitive method of detection of bacterial contamination, the numbers of MRSA bacteria present may be low. The researchers say that as the two infected samples contained processed pork (sausages and minced pork), they cannot rule out that the meat packing plants from which the MRSA from this study originated also handle imported meat. If this were the case, it is conceivable that cross-contamination might have occurred between non-UK to UK sourced meat.

Dr Mark Holmes from the Department of Veterinary Medicine at the University of Cambridge says: "This is the first time that MRSA has been detected in retail meat products in the UK. The public should not be overly worried by this as sensible food precautions and good hygiene should prevent its spread. It's also usually pretty harmless and only causes health problems if it infects someone in poor health or gets into a wound.

"However, this does suggest that MRSA is established in our pig farms and provides a possible route of transmission from livestock, through those in direct contact with pigs, into the wider population."

Dr Des Walsh, Head of Infections and Immunity at the MRC, added: "Studies like this are crucial not just to reveal concerns to human health through contaminated livestock, but to show resistance to antibiotics is a problem growing far beyond just humans. To win the fight against antimicrobial resistance, we need an all hands on deck approach, and that's why we've teamed up with leading experts in biological, social and others sciences in a joint initiative designed to find new solutions, fast."

The research was funded by the Medical Research Council, with additional support from the Alliance to Save our Antibiotics. The results of the study are published in the online journal Eurosurveillance.

Dr Holmes was recently awarded a further £1.58 million from the MRC to look into the effects of antibiotic use on the entire population of animal gut flora, not just the disease causing bacteria. His work, using research in pigs, will help scientists understand the evolution of antibiotic resistance and help to make better choices about how to reduce the spread of antimicrobial resistance on farms.

<http://nyti.ms/1d9qzwR>

## **Meningitis Vaccine Mandate for Seventh Graders in New York Passes**

***Seventh graders in New York State would be required to be vaccinated for meningitis, a deadly disease spread by saliva droplets, and could be excluded from school if they were not, under a bill passed this week by the State Legislature.***

By [ANEMONA HARTOCOLLIS](#) JUNE 18, 2015

Beginning in September 2016, the bill would require students entering seventh grade to have received the [meningitis vaccine](#), with a booster shot to be given in the 12th grade. The United States Centers for Disease Control and Prevention recommends meningitis vaccination around that time, so many doctors have provided it.

Assemblywoman Aileen M. Gunther, a Democrat from Sullivan County who was the bill's prime sponsor, said it had been passed after testimony from medical experts as well as from several people who had lost children to meningitis, or who had been afflicted with meningitis and suffered amputations as a result.

"It's a disaster," Ms. Gunther said of the disease. "The science tells us that we can do something."

The bill was opposed by some people who believe that vaccination can cause [autism](#) - a belief [discredited by scientific studies](#). But Ms. Gunther, who is a [registered nurse](#), said that in any case, this particular vaccine would be administered long after the period when autism typically develops and is diagnosed. As with other mandated vaccines, parents can apply to their child's school for a [religious exemption](#) from the requirement.

A spokeswoman for Gov. Andrew M. Cuomo, who can sign the bill into law, said that it was under review.

Among supporters of the bill was Patti Wukovits, whose daughter, [Kimberly Coffey](#), died of meningitis in 2012 when she was 17, just before she was to go to her senior prom for East Islip High School on Long Island.

Ms. Wukovits described how easy it was to confuse meningitis with [the flu](#) and how quickly the disease progressed. She said her daughter was feeling achy and had a [fever](#) of 101. But overnight, she developed purple spots on one of her ankles, which then progressed to a rash all over her body. Ms. Wukovits took her to the emergency room. She died after being in the hospital for nine days and being declared brain-dead.

"If she had survived, she would have been a quadruple amputee," Ms. Wukovits said. "She would have had a tough life."

Ms. Coffey was buried in her prom dress, and her mother began a foundation, the Kimberly Coffey Foundation, to spread awareness of the disease.

Meningitis is an infection of the covering of the brain and the spinal cord, which can also cause blood infections. It can be spread through kissing, or drinking from the same cup. It can lead to death within a few hours, is fatal in one out of 10 cases and leaves one in seven survivors with a severe disability like amputation, [paralysis](#) or [seizures](#).

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### **Thick cortex could be key in Down syndrome**

*The thickness of the brain's cerebral cortex could be a key to unlocking answers about intellectual development in youth with Down Syndrome.*

It could also provide new insights to why individuals with this genetic neurodevelopmental disorder are highly susceptible to early onset Alzheimer's Disease later in life.

New brain-imaging research published in the journal Cerebral Cortex and led by Nancy Raitano Lee, PhD, an assistant professor at Drexel University, has found that the cortex is thicker on average in youth with Down Syndrome than in typically developing youth, even though the overall volume of the cortex is lower in those with Down Syndrome.

The cerebral cortex is the outer layer of brain tissue, a folded region about 2-4 millimeters thick, that is involved in many important aspects of brain function including sensory and cognitive processes.

Lee, a psychologist in Drexel's College of Arts and Sciences, conducted the research with colleagues at the National Institute of Mental Health who perform structural magnetic resonance imaging (MRI) of the brains of children and youth to better understand aspects of brain development. They compared MRI measurements from 31 youth with Down Syndrome and 45 typically developing peers.

Lee is particularly interested in brain development in youth with Down Syndrome, the most common genetic cause of intellectual disability (occurring in 1 in 700 live births), because there is surprisingly little known about childhood brain

development in this condition. What has been established is that the brain volume of the cortex is lower on average in people with Down Syndrome than in people who are typically developing.

"Volume is a gross measure that can mask differences between thickness and surface area in the cortex," said Lee. "We wanted to learn more about how the brain is different in Down Syndrome compared to typical development, so we measured surface area and thickness, which both contribute to cortical volume but are determined by different genetic factors."

She wasn't surprised to find that the cortex's surface area was lower in the youth with Down Syndrome because surface area is a component of the total volume, which was lower.

"The part that was surprising was our finding that the thickness of the cortex was greater in many regions in the group with Down Syndrome," she said.

The cause of the increased cortical thickness in Down Syndrome is still uncertain, but one possibility is that the brain in Down Syndrome doesn't prune excess neural connections as effectively as in typical development, a process believed to occur during childhood and young adulthood as part of reaching cognitive maturity.

Some of the brain regions with increased cortical thickness were nodes in the Default Mode Network (DMN), the part of the brain that is active when a person is at rest. Because deterioration in the DMN has been associated with Alzheimer's Disease, Lee said the difference found between Down Syndrome and typical development in youth could turn out to be an early indicator of susceptibility to Alzheimer's later in life. Individuals with Down Syndrome are more likely to develop early-onset Alzheimer's disease than the general population.

Lee hopes that her finding will highlight the importance of the cortex for understanding developmental processes in Down Syndrome and spur further research on animal models. Such studies could more clearly draw the connection of how genetic abnormalities cause brain abnormalities--knowledge that could inform potential biomedical treatment approaches for intellectual disability.

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### **How to wipe out polio and prevent its re-emergence**

*Public health officials stand poised to eliminate polio from the planet.*

ANN ARBOR- But a new study shows that the job won't be over when the last case of the horrible paralytic disease is recorded.

Using disease-transmission models, University of Michigan graduate research fellow Micaela Martinez-Bakker and two colleagues demonstrate that silent transmission of poliovirus could continue for more than three years with no reported cases.

To ensure that the disease is truly eradicated, aggressive surveillance programs and vaccination campaigns must continue in endemic countries for years after the last reported case, they conclude.

"Using transmission models, we show that you can have sustained chains of silent transmission in populations for more than three years, without a single person ever showing up as a reported polio case," said Martinez-Bakker, who completed the six-year polio study as part of her doctoral dissertation in the U-M Department of Ecology and Evolutionary Biology.

"Once we've eradicated polio--or think we've eradicated polio--we probably should intensify the environmental surveillance to make sure the virus is not just lurking under the hood at very low levels," she said. "Polio eradication is about eradicating the virus. It's not about eradicating the disease paralytic polio."

The new findings are scheduled for publication June 19 in the open access journal PLOS Biology in a study titled "Unraveling the transmission ecology of polio." The co-authors are Martinez-Bakker's dissertation advisers, Aaron King and Pejman Rohani of the U-M Department of Ecology and Evolutionary Biology.

Pakistan, Afghanistan and Nigeria are the only countries where polio remains endemic, down from more than 125 countries in 1988. The disease mainly affects children under 5, and one in 200 infections leads to irreversible paralysis, according to the World Health Organization, which reported 416 cases of polio worldwide in 2013.

Martinez-Bakker analyzed polio case reports from large-scale U.S. epidemics in the pre-vaccine era, along with birth statistics and census numbers from every state. This enormous data set provided a unique glimpse into the ecology of polio infection in the relative absence of human intervention.

And it led her to conclude that the leading explanation for the marked increase in U.S. polio incidence from the 1930s to the 1950s--an idea known as the hygiene hypothesis or the disease of development hypothesis--is likely wrong.

In particular, the sharp increase in cases that occurred after the mid-1940s appears to be a straightforward consequence of a surging birth rate during the post-war baby boom, not the result of improvements in sanitation and hygiene, as textbooks suggest.

"If you have more kindling, you can have a much larger forest fire," Martinez-Bakker said. "The baby boom provided more kindling for polio epidemics--young children and infants over 6 months of age--so much more explosive outbreaks were now possible."

Disease transmission models allowed her to track the movement of poliovirus and reconstruct the millions of unobserved, symptomless infections that spread the disease in the first half of the 20th century.

The number of U.S. polio cases peaked in 1952 at 57,000. Three years later, mass inoculations with Jonas Salk's vaccine began after it was declared "safe, effective and potent" during an April 1955 scientific meeting at U-M.

The new U-M research shows for the first time that more than 3 million Americans were likely infected with poliovirus during that peak year of 1952. The study also explains why U.S. polio epidemics in the pre-vaccine era were explosive, seasonal and varied geographically.

"Reaching eradication and preventing re-emergence of polio requires intimate knowledge of how the virus persists," Martinez-Bakker said. "Historical epidemics that predate the use of vaccines can be used to disentangle the epidemiology of disease from vaccine effects. They allow us to establish a baseline by studying the system in the absence of intervention."

*Martinez-Bakker is supported by the National Science Foundation's Graduate Research Fellowship Program and U-M's Rackham Merit Fellowship. Rohani and King are supported by the Department of Homeland Security and the National Institutes of Health. This research was supported in part through computational resources and services provided by Advanced Research Computing at U-M and by UAF Life Science Informatics.*

[http://www.eurekalert.org/pub\\_releases/2015-06/uoc--nbi061915.php](http://www.eurekalert.org/pub_releases/2015-06/uoc--nbi061915.php)

### **New biomarker identified in women with mental illness**

#### ***Findings could lead to easier diagnoses and new treatment options***

Psychiatric disorders can be difficult to diagnose because clinicians must rely upon interpreted clues, such as a patient's behaviors and feelings. For the first time, researchers at University of California, San Diego School of Medicine report identifying a biological marker: the over-production of specific genes that could be a diagnostic indicator of mental illness in female psychiatric patients.

The study was published this week in the journal EBioMedicine.

Researchers found that the gene XIST, which is responsible for inactivating one of the two copies of the X chromosome in cells that store genetic material, works overtime in female patients with mental illnesses, such as bipolar disorder, major depression and schizophrenia.

The study suggests that over-production of XIST and genes from the inactive X chromosome are common denominators in the development of psychiatric disorders in patients with rare chromosome disorders, such as Klinefelter syndrome and Triple X syndrome, and in the general population of female psychiatric patients.

"There has been an utmost urgency to identify biomarkers for mental illness that could significantly impact research and drug development," said Xianjin Zhou, PhD, assistant professor in the Department of Psychiatry at UC San Diego School of Medicine and lead author.

The study was conducted on 60 lymphoblastoid cell lines from female patients, most of whom had a family history of mental illness. Approximately 50 percent of the female patients exhibited abnormally higher levels of XIST and other genes related to the X chromosome.

Zhou and his team said reversing the abnormal activity of the inactive X chromosome in patients suffering from mental illness may offer a potential new strategy for treating psychiatric disorders.

"Our results indicate that a large subpopulation of female psychiatric patients from the general population may have abnormal function of the inactive X chromosome," said Zhou. "These results are powerful in that early diagnosis of mental illness could possibly happen with a simple blood test, leading to better interventions, therapy and treatment options."

Co-authors include Baohu Ji, Kerin K. Higa and John R. Kelsoe, all of UC San Diego.

<http://bit.ly/1Fw2dUN>

**Cradle of creation: Evolution shapes up new ecosystem in the lab**  
*The longest running evolutionary lab experiment has reproduced yet another aspect of the natural world, showing how a major change in one creature can transform its environment, and alter the evolutionary trajectory of all the creatures inhabiting that space.*

- 18:55 19 June 2015 by [Michael Le Page](#)

The [Long-term Experimental Evolution Project](#) began in 1988. [Richard Lenski](#) at Michigan State University took a single strain of the *E. coli* bacterium and set up 12 cultures.

Every day since then, a sample of each culture has been transferred to fresh growth medium, containing glucose as the main nutrient. The bacteria have now undergone more than 60,000 generations since the experiment began.

Evolutionary experiments [in the lab are now routine](#). Many biologists are also studying [evolution in the wild](#) and some think that [rapid evolution](#) may be the norm rather than the exception.

But Lenski's experiment has allowed us to witness evolution in unprecedented detail. Because samples are frozen every 75 days, the team can go back and identify the precise genetic mutations underlying the changes they see.

The experiment has become a poster child for evolution, causing consternation among [creationists trying to explain away](#) its compelling evidence.

The biggest [evolutionary shift occurred](#) after about the 31,500 generation, when one line in one of the 12 populations evolved the ability to feed on citrate, another chemical in the growth medium. Now, [Caroline Turner](#) and other members of Lenski's team [have described](#) some of the consequences of this change in a paper posted on a preprint server.

**Revolving door solution**

*E. coli* don't normally feed on citrate because they can't carry it into their cells. But a mutation in the citrate-eaters allowed them to make an "antiporter" protein, CitT, that allows citrate to cross the membrane and enter the cell. The gene for this protein already existed, but it's usually switched off when oxygen is present. The antiporter is a kind of revolving door. It allows one molecule to be swapped for another. In this case, the citrate is imported into the cell in exchange for one of three smaller, less-valuable molecules: succinate, fumarate or malate. Once this ability to feed on citrate evolved the population boomed because the same growth medium could now sustain more cells.

Those citrate feeders soon became dominant, outcompeting all but one other strain of *E. coli*, which in turn evolved to exploit the changed environment – which now contained the three exported molecules.

It did this by making more of a transporter protein called DctA, which imports - at a small energy cost - succinate and other molecules exported by the citrate-eating strain.

But things did not stop there. The citrate-eaters then also started making more DctA to try to claw back some of the succinate and other molecules they were losing in the process of acquiring citrate.

Lenski did not want to discuss the findings prior to full publication in a peer-reviewed journal, but the work is a neat example of how evolution and ecosystems are inextricably linked.

"Our findings show how evolutionary novelties can change environmental conditions, thereby facilitating diversity and altering both the structure of an ecosystem and the evolutionary trajectories of coexisting organisms," the paper says.

The researchers compare this to [the evolution](#) of photosynthetic bacteria [some 2.4 billion years ago](#): just as [oxygen excreted by the first photosynthesisers](#) transformed Earth and changed the course of evolution, so the appearance of citrate eaters altered the growth medium and changed the evolutionary path of all the bacteria living in it.

It's just what biologists expect to happen, but thanks to this experiment [and others like it](#) we can now watch evolution in action.

Turner's findings are also yet another example of the [mindlessness of evolution](#). The best solution would be to use a little energy to import citrate directly, the paper says, rather than swapping it for succinate and then spending energy to try to get that succinate back before other bacteria can feed on it.

Journal reference: *bioRxiv*, DOI: [10.1101/020958](https://doi.org/10.1101/020958)

<http://nyti.ms/1GBPljX>

## Genome Studies Show How Ebola Spread Initially

*After tracking tiny mutations in the genome of [Ebola](#), scientists from around the world are developing a fuller picture of how the virus spread and evolved genetically during the world's worst outbreak of the disease.*

By [SHERI FINK](#) JUNE 19, 2015

The latest studies, which reported the genetic sequences of viruses from more than 400 patients in [Sierra Leone](#), [Guinea](#) and [Liberia](#), suggested that early efforts to combat the epidemic in the spring of 2014 nearly stamped it out in the forested border region of Guinea where the outbreak started.

But before those efforts even began, sick people from the area had already [crossed the border into Sierra Leone](#). And at least one of them infected other people, who then crossed back into Guinea and into Liberia, reigniting the epidemic.

“That second wave was a much bigger wave than the first one,” said Miles W. Carroll of [Public Health England](#), the lead author of a paper published Wednesday in the journal *Nature*, which analyzed 179 [Ebola](#) virus sequences from Guinea.

Although officials in Guinea and with the [World Health Organization](#) knew that sick people had crossed into Sierra Leone by March 2014, the illness continued to spread silently in Sierra Leone for two more months before the outbreak was detected there.

“It does seem to be what has seeded the rest of the outbreak,” said Pardis Sabeti, a Harvard professor and computational biologist at the [Broad Institute](#) who helped write a [study published](#) Thursday in the journal *Cell*.

The study analyzed Ebola virus genomes from 232 blood samples taken over seven months in Sierra Leone.

It found that once the virus entered the country, it continued spreading, with few new introductions from outside after the borders between neighboring countries were closed.

“Most of the movement seems to be within country, not between, once the outbreak got going,” said Daniel J. Park, the study’s lead author, also with the Broad Institute.

Scientists have wondered whether the variant of the virus that spread to Sierra Leone from Guinea mutated in a way that made it more capable of propagating in humans.

But other researchers have found evidence that the earlier version of the virus in Guinea did not completely go away.

Instead, it spread to the capital, Conakry. It has continued to be among the versions of the virus propagating in Guinea and later in Sierra Leone.

Two dozen new cases were reported in both countries in the week ending June 14.

“That lineage, ‘A,’ does persist and is still persisting as far as we know in Conakry and that area,” said Andrew Rambaut of the University of Edinburgh, who helped analyze the genetic relationships between viruses.

The new studies have also calmed fears that Ebola in West Africa was mutating at a higher rate than scientists had anticipated based on past outbreaks.

“It’s evolving at the speed we’d expect of a virus of this type, which is pretty high, but not as high as [flu](#),” Dr. Rambaut said.

An early flurry of genetic changes appeared to have been winnowed by natural selection, as viruses that were presumably less capable of causing infection died out.

Also reassuring, the scientists said, was that all of the viruses sampled so far appeared to have descended from one another, suggesting that the entire outbreak in West Africa was caused by a single introduction of the virus from nature.

For the first time, scientists have found evidence of a few instances where Ebola genome might have been “edited” by human enzymes during its prolonged rampage through the human population.

“That hasn’t really happened with Ebola before, because it’s never really persisted in a human context for so long,” Dr. Park said.

His group and one from China, which released [a paper](#) in May in *Nature* based on 175 sequences in Sierra Leone, detected the evidence of those mutations.

As more researchers release their sequencing results, with more to come soon from Guinea and Liberia, some scientists are attempting to put a whole picture of the epidemic together.

Trevor Bedford, a computational biologist at the [Fred Hutchinson Cancer Research Center](#) in Seattle, and Richard Neher, a physicist at the [Max Planck Institute for Developmental Biology](#) in Germany, prepared [a graphic](#) that is something of a genetic family tree of the outbreak.

“We’re trying to connect things,” Dr. Bedford said. “We basically had no idea what was going on for a long time.”

That was because for many months, samples were not easily transported across borders; the affected countries did not have the technology to sequence samples; and some scientists were reluctant to share data before publishing their results.

“It would have been great if these papers came out six months ago,” Dr. Bedford said.

“You could imagine a situation where you don’t really have to publish your *Nature* paper; instead, you make a blog post. It could have been a bit more timely.”

<http://www.bbc.com/news/health-33190297>

## The 'ugly truth' about Body Dysmorphic Disorder

*It is often dismissed as a "first world" problem and a "bad case of vanity" caused by today's obsession with appearance and celebrity.*

But, writes Susanna Jolly, Body Dysmorphic Disorder (BDD) affects up to one in 50 people and many with the condition "self-medicate" by undergoing frequent and repeated plastic surgery procedures. Former glamour model Alicia Douvall famously spent over £1m on over 300 procedures - [but two years ago she spoke about her addiction to surgery was driven by her undiagnosed battle with BDD.](#)

The condition is a disabling preoccupation with an imagined, or slight, flaw in appearance. Symptoms often start in adolescence. Minnie Wright, 47, has suffered from BDD for most of her life. "The symptoms started when I was 11 after being bullied at school. "A lot focused on the size of my nose."Minnie says she would apply "shading" make-up and hold her head in a particular way to avoid showing her nose in profile.

### Vanity? Not fair

People with BDD delay seeking help for fear of being dismissed as vain.

Dr David Veale, one of the foremost BDD experts, specialised in this area 20 years ago following the suicide of a BDD patient under his care.

He says: "Ideally, we want to try and diagnose people with BDD early, as treating them is easier than once the thoughts and anxieties have really become entrenched. "The most important message is that BDD is a treatable illness."

### BDD - POTENTIAL SIGNS

- *Spend hours in front of a mirror, sometimes picking at skin to make it smooth*
- *Make extensive attempts to camouflage perceived defects*
- *Feel anxious around others and avoid social situations*
- *Obsessively cut or comb hair to make it 'just so'*

BDD treatment is typically a combination of an anti-depressant medication and cognitive behavioural therapy - but the wait for diagnosis and treatment can be lengthy.

### Plastic not 'fantastic'

During these delays, BDD sufferers may try to "cure" their perceived imperfections with plastic surgery.

Minnie explains, "I wanted something done, but was still a child. I had a nose job done privately on my 18th birthday. "Initially, I did feel better, but ultimately I was unhappy. "It was a bit like moving the furniture around - the underlying problem was still there, it just all looked a bit different".

Later in life Minnie's focus shifted to unhappiness with her hair and the symptoms were so "immobilising" she contemplated suicide.

Studies have suggested people with the condition have a much higher suicide rate than the general population. Minnie herself has known four people who have committed suicide while they had BDD.

Dr Veale, who also works with the [Body Dysmorphic Disorder Foundation](#), acknowledges this higher risk: and reports that a third of his patients have had at least one cosmetic procedure. Crucially, less than 10% of BDD patients will be satisfied with the results. Their anxieties are often transferred to another aspect of their appearance, sometimes leading to multiple procedures.

Around 15% of people seeking plastic surgery are thought to have BDD. Mr Simon Withey, a consultant plastic surgeon, said: "BDD is extremely complicated and surgeons will never be experts. "However, you get a sixth sense that something is not right if you ask the right questions. For me, one of the signs is if the patient is 'over-prepared'. "If I sense something is not right, I won't operate".

### 'Gold standard'

Psychiatrists have a number of assessment tools they use to identify BDD, but these are too long to be useful in a surgeon's clinic.

Dr Alex Clarke studies the psychological aspects of plastic surgery. Her team has been developing a more accessible BDD screening questionnaire. She said: "Primarily surgeons want to operate. Their concern is that if they say no, the patient will walk out the door and go and see someone else a few doors down".

The questionnaire identifies the presence of classic BDD symptoms and explores the patient's expectations. Both surgeons and patients have been accepting of this new tool in current trials. "Over the past 15 years we've seen surgeons go from being quite resistant to recognising that these are part of delivering a gold standard service," says Dr Clarke.

But the question is how to reach those unscrupulous individuals who will do anything for the right price?

Mr Marc Pacifico, a consultant plastic surgeon and spokesman for the British Association of Aesthetic and Plastic Surgeons (BAAPS) said: "It's a wild west out there. "It is a sad fact that if you look hard enough, you will find someone who will do whatever surgery you want. Anyone can call themselves a "cosmetic surgeon" and set up a practice. "People can easily be fooled by a flashy website or renowned address."

BAAPS recommend for looking for "badges" of credibility such as Fellowship of the Royal College of Surgeons (FRCSPlast) and the surgeon being a BAAPS member. Poor practice includes being seen initially by a salesperson, rather than a surgeon, and surgery offered at a low price, or part of a time-limited deal.

The comments that follow any online article about BDD often dismiss it as a "first-world problem".



But there is evidence that is not the case. Prof Leo Fontanelle is a BDD specialist from Rio de Janeiro. Brazil has the second highest rate of plastic surgical procedures performed in the world. He says: "We have seen patients from across the socio-economic classes. We don't yet have the data to tell us how many of our patients have surgery prior to being diagnosed and treated. "However, it remains important for our plastic surgeons to be aware and refer patients to the appropriate services".

### Is the selfie to blame?

Media images have long been cited as one potential factor in leading people to develop poor body image, and recent years have also seen the rise of the selfie. A recent survey showed that 16-25 year olds spend on average 16 minutes and seven attempts to take the perfect selfie.

Research showed young adults average seven attempts to take the perfect selfie So is this pressure to look perfect affecting people's mental state?

Dr Veale says not. "It is difficult to draw the line where body dissatisfaction stops and BDD starts. But he says it is actually earlier life events such as poor child-mother attachment and bullying that are more significant. "The media pressures are out there, but they are only a small part of the story". Dr Clarke wants education and awareness in schools needs to improve. "Children need to be taught some 'media literacy' to understand that all the airbrushed images they see aren't real. "It is too easy to become a victim of this pressure if you are not socially robust enough."

<http://bit.ly/1GhmX4m>

### **Left in the Brain: Potentially Toxic Residue from MRI Drugs** *Researchers raise alarms about unknown health risks of GE's Omniscan and Bayer's Magnevist, drugs injected to get better MRI pictures that contain the heavy metal gadolinium.*

by Jeff Gerth ProPublica, June 11, 2015, 11:22 a.m.

With a family history of breast cancer, Marcie Jacobs decided in June 2001 that an MRI screening was her best preventive option.

As is common with MRIs, Jacobs was injected beforehand with a contrast agent, a drug that helps sharpen the resulting images. But after a few of these treatments, she began noticing some strange cognitive effects. Jacobs began missing meetings. Over the next several years she had additional MRIs. The math skills that were crucial to her job as finance manager started deteriorating, she said.

Jacobs eventually wound up on disability. She stopped worrying about cancer – and started worrying about imaging drugs.

This month, two prominent experts in the radiology community joined in the concern, calling for more research into the possible health risks after three recent

studies found that gadolinium, a potentially toxic metal, wound up in the brain tissue of MRI patients who used two different contrast agents.

Editorializing in the journal "Radiology," Dr. Emanuel Kanal at the University of Pittsburgh Medical Center, and Michael Tweedle at Ohio State University, said the studies "called into question" the "safety of at least some" of these agents. The two urged radiologists to change their prescribing habits, although not to stop using the drugs because of their proven benefits to patients. (Related video.)

Nine gadolinium-based contrast agents are sold in the United States. The two in question, Omniscan, made by GE Healthcare, and Magnevist, manufactured by Bayer HealthCare, once dominated the contrast agent market. Both GE and Bayer, in statements, said they were monitoring the issue and noted the new studies had not found any clinical impact, such as brain injury.

As ProPublica has reported, contrast agents like Omniscan had been on the market for years when, in 2006, they were linked to a crippling, sometimes fatal condition called nephrogenic systemic fibrosis, or NSF. The Food and Drug Administration put a "black box" warning on the drugs the following year, saying patients with kidney impairment may be at risk of NSF because they were unable to excrete the gadolinium.

ProPublica first disclosed in 2009 that the agency ignored two of its own medical reviewers who wanted to ban Omniscan for patients with severe kidney disease. In 2010, the FDA did act, recommending that GE's drug and two other agents shouldn't be used in patients with impaired kidneys. The other drugs were Magnevist and Optimark, sold by Mallinckrodt Pharmaceuticals.

The new studies cited by Kanal and Tweedle have set off alarms because they show that even patients with healthy kidneys are retaining gadolinium from Omniscan and Magnevist. Estimates are that about one-third of the 20 million MRIs in the United States each year use one of the nine contrast agents.

Doctors now routinely screen MRI patients for kidney problems before injecting them with contrast agents, and scientists believe that NSF has essentially disappeared. The new studies don't speak to the clinical effects, if any, of gadolinium in the brain. But in an interview, Kanal said the findings ought to make radiologists think twice about which agents to prescribe.

"We can use an agent today that does not retain gadolinium in the brain to the degree that those other agents do," he said, referring to Omniscan and Magnevist. Given that the alternatives are "at least as efficacious" as the other two, he asked, "Why are some still prescribing the agents that do accumulate in the brain over the other options?"

Jacobs has no medical proof, but she's convinced the two drugs are behind her problems.

As her symptoms worsened, Jacobs said she underwent a series of tests that found accumulated traces of gadolinium in her breast, thigh, liver and brain. Doctors were puzzled because she had no history of kidney disease and did not fit into the identified at-risk group.

She recovered old records and determined that she received Omniscan for her first 11 imagings and Magnevist before the last, in 2007. Jacobs said she eventually began a difficult, extended program to remove gadolinium from her body.

Researching on the Internet, Jacobs found a support group around the issue. Then in March, a radiology journal, Health Imaging, featured the group in an article on the new gadolinium research. That same month Jacobs started a Facebook group that is now composed of researchers as well as dozens of patients with similar gadolinium experiences and no evidence of kidney disease.

Jacobs said the new studies “confirm that the linear gadolinium-based contrasting agents such as GE’s product Omniscan and Bayer’s product Magnevist are being retained at much higher levels than radiologists and the FDA have acknowledged.” She hopes the FDA might pull the two agents from the market.

In a statement, an FDA spokesperson said the agency is “carefully reviewing” the new studies to “better understand the potential consequences to determine what further action is needed, which may include taking steps to ensure the public is aware of these preliminary findings.”

Kanal, who has been advising the FDA and also chairs the American Board of MR Safety, said the new studies have “the entire international radiological community – and the FDA – on edge, as this is an entirely unanticipated finding.” GE Healthcare told ProPublica that as part of its commitment to safety a new company internal task force reviewed the studies and other data and continues its work.

After finding “no signs or symptoms of potential injury to the brain” associated with Omniscan and “no evidence of cytotoxicity (cell toxicity) in published autopsy studies” the task force concluded that “continued use of Omniscan according to approved product labeling” is appropriate, GE said.

Bayer told ProPublica patient safety is its “primary concern” and said it had reached out to the authors of the original research studies “to clarify their findings,” even though “none of these studies indicate any clinical implications.” The company said it was continuing to monitor the situation.

GE and Bayer have confidentially settled hundreds of lawsuits – many involving deaths – while denying liability for their contrast agents.

In 2013, one case went to trial in Cleveland and resulted in a \$5 million verdict against GE. A federal appeals court upheld the verdict last year. By then the plaintiff, who had NSF, had died.

The contours of the contrast agent market have changed in recent years. Both Magnevist, once the leading agent, and Omniscan, also a top seller, have lost market share since the FDA restrictions in 2010. GE said its market share was about 10 percent last year; Bayer declined to cite a figure.