https://go.nature.com/2JJs0rL

Roadworks ahead: Pompeiians patched potholes with iron

Ancient city's streets are paved with volcanic rock, studded with hundreds of repairs.

A carriage ride in ancient Pompeii would have been a bone-shaking ordeal, thanks to the sad state of many of the city's streets. But observations from a survey of these highways indicate that Pompeiians tried to restore their roads — by pouring molten iron into ruts and potholes.

More than a century before the city's destruction in ad 79, Pompeiian workers began paving some of the roads with stone, which was soon ravaged by traffic. Eric Poehler at the University of Massachusetts at Amherst and his colleagues surveyed some 5.5 kilometres of Pompeii's stone streets and found more than 400 iron features, including patches, drips and splatters. The team calculates that on one particularly dilapidated thoroughfare, a road crew may have poured more than 70 litres of iron or iron-rich slurry onto a section of road carved by ruts 10–20 centimetres deep.

The authors say that the repairs show the Romans could melt iron, contrary to past thinking that Roman technology could not achieve sufficiently high temperatures to do so.

Am. J. Archaeol. (2019)

http://bit.ly/2HTbdju

Bacteria may travel thousands of miles through the air globally

Study could shed light on harmful bacteria that share antibiotic resistance genes

Bacteria may travel thousands of miles through the air worldwide instead of hitching rides with people and animals, according to Rutgers and other scientists. Their "air bridge" hypothesis could shed light on how harmful bacteria share antibiotic resistance genes.

"Our research suggests that there must be a planet-wide mechanism that ensures the exchange of bacteria between faraway places," said senior author Konstantin Severinov, a principal investigator at the Waksman Institute of Microbiology and professor of molecular biology and biochemistry in the School of Arts and Sciences at Rutgers University-New Brunswick.

"Because the bacteria we study live in very hot water - about 160 degrees Fahrenheit - in remote places, it is not feasible to imagine that animals, birds or humans transport them," Severinov said. "They must be transported by air and this movement must be very extensive so bacteria in isolated places share common characteristics."

Severinov and other researchers studied the "molecular memories" of bacteria from their encounters with viruses, with the memories stored in bacterial DNA, according to a study in the journal *Philosophical Transactions of the Royal Society B*.

Bacteriophages - viruses of bacteria - are the most abundant and ubiquitous forms of life on the planet, the study notes. The viruses have a profound influence on microbial populations, community structure and evolution.

The scientists collected heat-loving Thermus thermophilus bacteria in hot gravel on Mount Vesuvius and hot springs on Mount Etna in Italy; hot springs in the El Tatio region in northern Chile and southern Chile's Termas del Flaco region; and hot springs in the Uzon caldera in Kamchatka, Russia.

In bacterial cells infected by viruses, molecular memories are stored in special regions of bacterial DNA called CRISPR arrays. Cells that survive infections pass the memories - small pieces of viral DNA - to their offspring. The order of these memories allows scientists to follow the history of bacterial interaction with viruses over time.

Initially, the scientists thought that bacteria of the same species living in hot springs thousands of miles apart - and therefore isolated from each other - would have very different memories of their encounters with viruses. That's because the bacteria all should have independent histories of viral infections. The scientists also thought that bacteria should be evolving very rapidly and become different, much like the famous finches Charles Darwin observed on the Galapagos Islands.

"What we found, however, is that there were plenty of shared memories - identical pieces of viral DNA stored in the same order in the DNA of bacteria from distant hot springs," Severinov said. "Our analysis may inform ecological and epidemiological studies of harmful bacteria that globally share antibiotic resistance genes and may also get dispersed by air instead of human travelers."

The scientists want to test their air bridge hypothesis by sampling air at different altitudes and locations around the world and by identifying the bacteria there, he said. They would need access to planes, drones or research balloons.

The study included scientists at the Russian Academy of Sciences; Skolkovo Institute of Science and Technology in Russia; Pasteur Institute in France; University of Santiago de Chile; and Weizmann Institute of Science in Israel.

http://bit.ly/2OrY3v0

New angle of attack drives cellular HIV-reservoirs to self-destruction

Novel angle of attack could selectively eradicate viral reservoir cells, yet leave healthy cells unscathed

While current therapies for HIV can successfully manage active infection, the virus can survive in tissue reservoirs, including macrophage cells, and remain a persistent problem. Now, Dr. David Russell, William Kaplan Professor of Infection Biology at Cornell University College of Veterinary Medicine, and his research team have pinpointed a novel angle of attack that could selectively eradicate these viral reservoir cells while leaving healthy cells untouched.

In their study published on March 25th in the journal *PNAS*, Russell's team, lead by first author and postdoctoral fellow Dr. Saikat Boliar, describe how a genetic regulator called SAF helps HIV-infected macrophages avoid cell death. After blocking SAF in HIV-infected cells, the researchers found that these reservoir cells then self-destructed. "We were all surprised by the specificity of the cell death," says Russell. "Only infected cells die while bystander cells, exposed to the same treatment at the same dose, showed no death at all."

While macrophages, immune cells that consume foreign entities in the body, are helpful in fighting off certain microbes, they provide the perfect foxhole for HIV. Some researchers believe these infected macrophages are the reservoirs for persistent HIV infection. "Current HIV drugs work really well on active infection, but it is the tissue reservoirs that are the problem," Russell explains. "These sites of persistent virus are resistant to all current therapies."

Russell, Boliar, and their colleagues wanted to investigate what cellular mechanisms were at play that helped keep infected macrophages alive, and turned their attention to long non-coding RNAs (lncRNAs) -- genetic coding elements that turn genes up or down, but do not translate directly into proteins themselves. "We were interested in long-noncoding RNAs because they are known 'master regulators' of cell pathways, and had not really been looked at systematically in HIV infection," Russell explains.

The team screened a panel of 90 well-characterized lncRNAs in three distinct populations of human macrophages: healthy cells, HIV-infected cells, and 'bystander' cells -- those that had been exposed to HIV, but not infected.

The investigators found that one lncRNA, called SAF, was significantly up-regulated in the HIV-infected macrophages.

Previous studies had found that SAF prevented apoptosis, or self-destruction, in cells. Russell and his team suspected SAF was protecting HIV-infected macrophages from dying.

To prove this theory, the team blocked SAF's action using another non-coding RNA called small interfering RNA (siRNA), which effectively degrade targeted RNAs such as SAF. The researchers silenced SAF in the healthy, infected, and bystander macrophage populations; the HIV-infected cells suddenly self-destructed, while the healthy and bystander cells remained unscathed.

"This showed us that when cells are infected with HIV, the virus alters the long non-coding RNAs' expression in that cell," says Russell. This would explain why bystander cells that are exposed to the HIV virions, but not actually infected by them, do not have the same response.

This discovery taps into a novel angle in curing HIV: selectively destroying persistently infected cells--and the Russell team is eager to exploit it for potential therapies.

"We plan to do a drug screen for compounds that drive HIV-infected cells into programmed cell death," says Russell. The team will start by looking for SAF inhibitors, but also will look for other molecules that effectively eradicate reservoir cells through other mechanisms.

http://bit.ly/2FxDkC0

Sex-based bias: Women in Japan are less likely to receive cardiopulmonary resuscitation in public places from bystanders

Large Japanese study of sex-based disparities in treating out-of-hospital cardiac arrest found that women under 65 were less likely to receive bystander CPR in public locations than men, report scientists in Mayo Clinic Proceedings

Rochester, MN - Japanese women under 65 are less likely to receive cardiopulmonary resuscitation (CPR) by bystanders when they suffer a sudden cardiac arrest in a public location compared to in a residential location, report investigators in *Mayo Clinic Proceedings*, published by Elsevier. They speculate that cultural attitudes may influence bystanders and propose that correct knowledge of CPR and better understanding of sex-based disparities are needed to facilitate public health intervention.

Out-of-hospital cardiac arrest (OHCA) is a major public health problem in industrialized countries, affecting more than 350,000 individuals in the United States and 123,000 individuals in Japan each year. Around 1,000 adults suffer from sudden cardiac arrest in prehospital settings each day in the US alone, and only one in nine OHCA victims survives to hospital discharge. Bystander CPR is associated with improved outcomes in prehospital settings, and international guidelines on resuscitation emphasize its importance as one of the essential components of the "chain of survival." However, recent studies have highlighted sex-based disparities, pointing out that women suffering cardiac arrest in a public location were less likely to receive bystander CPR.

"The reasons for this sex-based disparity should be better understood to facilitate public health intervention," explained Tasuku Matsuyama, MD, PhD, Department of Emergency Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan who led the investigation.

Dr. Matsuyama and colleagues report on a large nationally-representative group of almost 85,000 patients from the All-Japan Utstein Registry from January 1, 2013 to December 31, 2015. They examined the rates and outcomes associated with bystander CPR as a function of a patient's sex. The analysis included adult patients aged 18 years and older with OHCA of medical origin in public or residential locations, witnessed by bystanders. As in earlier studies, women had lower rates of shockable arrest rhythms and were less likely to receive advanced life support interventions.

During the study period, 373,359 OHCAs were registered and 84,734 cases were eligible for analysis. Overall, around 54 percent of women and 57 percent of men received bystander CPR in a public location and 46.5 percent of women and 44 percent of men received bystander CPR in residential locations. Women had a higher likelihood of receiving bystander CPR in a residential location. In public locations, women aged 18-64 years were less likely to receive bystander CPR. When witnessed by a non-family member, women were less likely to receive bystander CPR regardless of age.

Reasons for lower rates of bystander CPR among certain subgroups of women in this study remain uncertain, but the investigators speculate that in Japan, bystander CPR including use of an automated external defibrillator on a woman has the potential to result in being accused of sexual assault. "Cultural factors, specific to Japan, may influence bystander attitude toward patients of a different sex. Therefore, it may be difficult to increase the rates of CPR on non-family, young victims unless laypersons have confidence in legal protections in Japan," commented Dr. Matsuyama. "While we acknowledge that our findings may not be generalizable to other patient populations or countries, similar findings were reported in a recent North American study."

Their data show that younger women may miss the opportunity to receive one of the most important treatments for cardiac arrest because of some obstacles unique to young women. Correct knowledge of cardiopulmonary resuscitation may improve the chances for more young women, therefore it is important to disseminate the importance of bystander CPR particularly for young women.

In an accompanying editorial, Jacob C. Jentzer, MD, FACC, Assistant Professor of Medicine, Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA, and colleagues point out that similar findings were reported in the International Cardiac Arrest Registry. They agree these may relate to inherent biases and differences in social norms. In addition, they note lower utilization of other potentially-beneficial therapies in women after OHCA in several studies, with worse survival in women compared to men.

"This study highlights the importance of bystander CPR as a key component of the 'chain of survival' for OHCA victims, emphasizing the need for public heath interventions to ensure adequate CPR training among laypeople," commented Dr Jentzer. "Additional studies are needed to determine why these sex-based differences occur, to ensure that all patients with a witnessed OHCA can receive this crucial therapy, which can increase the likelihood of neurologically-intact survival."

http://bit.ly/2HHTWup

Can you 'catch' cancer?

Parasitic worms cause cancer -- and could help cure it

Billions worldwide are infected with tropical worms. Unsurprisingly, most of these people live in poor countries, kept poor by the effects of worm-related malnourishment.

What may surprise many is that worms also cause the majority of cases of some cancers in these countries.

Published in *Frontiers in Medicine* as a special article collection on parasite-associated malignancy, new research aims to inform prevention and treatment - and perhaps even turn worms against cancer.

Worms cause cancer

Over a million worm species are classified as helminths. A single characteristic unites them: parasitism.

"Helminths take many forms, but all of them harm their host in some way. In humans, they can live in the intestinal tract, urinary tract or bloodstream, causing a variety of illness from malnutrition to organ failure" explains co-editor of the research Dr. Monica Botelho of Portugal's National Institute of Health.

In 2015 a more bizarre case of infection put helminths into the headlines: a man with HIV-AIDS died after his tapeworm contracted cancer and spread around his body. This remains the only such case ever recorded. Meanwhile, scientists have known for decades that helminths can turn human cells into cancers.

"Three species of helminth are classified as class 1 carcinogens by the WHO," adds Botelho. "These are all designated trematodes - after the Latin name for the grisly feeding cavity with which they latch onto their host's insides."

Worm-related cancer is not just a fluke - it's three

Trematodes are known informally as 'flukes'. In this case however, they're anything but.

"In endemic regions - predominantly sub-saharan Africa and Southeast Asia - flukes are responsible for the majority of all bladder and liver cancer cases," says Dr. Joachim Richter, Associate Professor at Charité Berlin and co-editor with Botelho. "Cancers arise in sites of fluke infection including the bladder wall and the bile ducts of the liver."

But how does a worm cause cancer? According to the research collection, their feeding - and breeding - habits might be to blame.

"Flukes constantly wound and re-wound their host as they latch on with their feeding cavity, burrow through organs, and deposit eggs in the bladder wall. This leads to chronic inflammation as the body tries endlessly to heal, meaning lots of cell division and so lots of opportunities for cancer-causing mutations to accumulate over years of infection." The flukes' toxic toilet habits then add insult to injury. "Worms and their eggs also excrete proteins that exacerbate this chronic inflammation, further promoting cell division as well as the blood vessel growth required to feed it," adds Richter.

Hyper tapeworms protect hosts from cancer

Fluke infections and early stage cancers are often asymptomatic, so despite availability of anthelminthic drugs patients often present too late for curative treatment. Fortunately, flukes have an Achilles' heel: they require freshwater snails as a first host before infecting humans. "Flukes have been successfully eliminated in Japan by economic development and the filling and drainage of snail habitats," says Richter. "Eradication efforts are underway in Thailand, which has the world's highest rates of liver fluke infection and bile duct cancer - but some high-risk countries like Ethiopia lack a coordinated monitoring or prevention program for fluke-related cancer and need more help."

Beyond eradication efforts lies another twist in the bizarre world of worms and cancer: helminths as a cure for malignancy.

"Many parasites, including some helminths like the liver fluke Fasciola hepatica, inhibit cancer growth in vitro. Another of these - the ominously named 'hyper tapeworm' - is associated with a significantly lower rate of cancer in human hosts," reports Botelho.

"In fact, there is evidence that proteins produced by hyper tapeworms as well as F. hepatica not only kill cancer cells directly - but might also enhance their host's immune response to tumors."

"Even cancer-promoting fluke proteins might be repurposed as treatments for other conditions: for example, those that promote new blood vessel growth could help resolve chronic non-healing wounds in diabetics, tobacco users, and the elderly."

https://www.frontiersin.org/articles/10.3389/fmed.2019.00055/full

The full research collection: https://www.frontiersin.org/research-topics/5865/parasites-and-cancer

http://bit.ly/2I3ec9l

Ancient Garbage Heaps Show Fading Byzantine Empire Was 'Plagued' By Disease and Climate Change

About a century before the fall of the Byzantine Empire — the eastern portion of the vast Roman Empire — signs of its impending doom were written in garbage.

By Mindy Weisberger, Senior Writer | March 25, 2019 03:59pm ET

Archaeologists recently investigated accumulated refuse in trash mounds at a Byzantine settlement called Elusa in Israel's Negev Desert. They found that the age of the trash introduced an intriguing new timeline for the Byzantine decline, scientists reported in a new study.

Climate change trashed the Byzantine Empire, ancient garbage mounds revealed. **Credit: Shutterstock**

The researchers discovered that trash disposal — once a well-organized and reliable service in outpost cities like Elusa — ceased around the middle of the sixth century, about 100 years prior to the empire's collapse. At that time, a climate event known as the Late Antique Little Ice Age was taking hold in the Northern Hemisphere, and an epidemic known as the Justinian plague raged through the Roman Empire, eventually killing over 100 million people.

Together, disease and climate change took a devastating economic toll and loosened Rome's grip on its lands to the east a century earlier than once thought, according to the study.

Finding treasure in trash

Elusa was already partly excavated, but the new investigation was the first to explore the site's long-ignored trash heaps, lead study author Guy Bar-Oz, a professor of archaeology at the University of Haifa in Israel, told Live Science in an email.

Unlike the architecture of an ancient city, which could be repeatedly destroyed and rebuilt, landfills steadily accumulated over time, creating continuous records of human activity. Clues found in preserved garbage dumps could thereby reveal if a city was thriving or in trouble.

"For me, it was clear that the true gold mine of data about daily life and what urban existence in the past really looked like was in the garbage," Bar-Oz said.

In the dump sites, the scientists found a variety of objects: ceramic pot sherds, seeds, olive pits, charcoal from burned wood and even evidence of discarded "gourmet foods" imported from the Red Sea and the Nile, the study authors reported.

The scientists carbon-dated organic material such as seeds and charcoal in layers of trash mounds located near the city. They found that trash had built up in that location over a period of about 150 years and that the accumulation terminated in the middle of the sixth century. This suggested there was a failure of infrastructure, which happens when a city is about to collapse, the researchers noted.

Based on the new evidence, researchers concluded that Elusa's decline began at least a century before Islamic rule wrested control of the region from the Romans. In fact, Elusa was struggling during a period that was relatively peaceful and stable; it was during this time that the Roman Emperor Justinian was expanding the empire's boundaries across Europe, Africa and Asia, Bar-Oz said.

With the empire enjoying "a period of glorious success," it would seem logical to expect that its outposts would be financially secure, Bar-Oz said. Yet the data the researchers collected suggested the opposite.

"Instead, we are seeing a signal for what was really going on at that time and which has long been nearly invisible to most archaeologists — that the empire was being plagued by climatic disaster and disease," Bar-Oz explained.

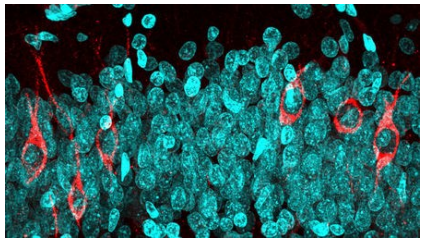
The findings were published online today (March 25) in the journal Proceedings of the National Academy of Sciences.

http://bit.ly/2WslmHR

New neurons for life? Old people can still make fresh brain cells, study finds

Study finds that even people long past middle age can make fresh brain cells

By Emily Underwood



Young neurons glow red in this brain tissue from a 68-year-old. **LlorensLab**

One of the thorniest debates in neuroscience is whether people can make new neurons after their brains stop developing in adolescence—a process known as neurogenesis.

Now, a new study finds that even people long past middle age can make fresh brain cells, and that past studies that failed to spot these newcomers may have used flawed methods.

The work "provides clear, definitive evidence that neurogenesis persists throughout life," says Paul Frankland, a neuroscientist at the Hospital for Sick Children in Toronto, Canada. "For me, this puts the issue to bed."

Researchers have long hoped that neurogenesis could help treat brain disorders like depression and Alzheimer's disease. But last year, a study in *Nature* reported that the process peters out by adolescence, contradicting previous work that had found newborn neurons in older people using a variety of methods. The finding was deflating for neuroscientists like Frankland, who studies adult neurogenesis in the rodent hippocampus, a brain region involved in learning and memory. It "raised questions about the relevance of our work," he says.

But there may have been problems with some of this earlier research. Last year's *Nature* study, for example, looked for new neurons in 59 samples of human brain tissue, some of which came from brain banks where samples are often immersed in the fixative paraformaldehyde for months or even years. Over time, paraformaldehyde forms bonds between the components that make up neurons, turning the cells into a gel, says neuroscientist María Llorens-Martín of the Severo Ochoa Molecular Biology Center in Madrid. This makes it difficult for fluorescent antibodies to bind to the doublecortin (DCX) protein, which many scientists consider the "gold standard" marker of immature neurons, she says.

The number of cells that test positive for DCX in brain tissue declines sharply after just 48 hours in a paraformaldehyde bath, Llorens-Martín and her colleagues report today in *Nature Medicine*. After 6 months, detecting new neurons "is almost impossible," she says.

When the researchers used a shorter fixation time—24 hours—to preserve donated brain tissue from 13 deceased adults, ranging in age from 43 to 87, they found tens of thousands of DCX-positive cells in the dentate gyrus, a curled sliver of tissue within the hippocampus that encodes memories of events. Under a microscope, the neurons had hallmarks of youth, Llorens-Martín says: smooth and plump, with simple, undeveloped branches.

In the sample from the youngest donor, who died at 43, the team found roughly 42,000 immature neurons per square millimeter of brain tissue. From the youngest to oldest donors, the number of apparent new neurons decreased by 30%—a trend that fits with previous studies in humans showing that adult neurogenesis declines with age. The team also showed that people with Alzheimer's disease had 30% fewer immature neurons than healthy donors of the same age, and the more advanced the dementia, the fewer such cells.

Some scientists remain skeptical, including the authors of last year's *Nature* paper. "While this study contains valuable data, we did not find the evidence for ongoing production of new neurons in the adult human hippocampus convincing," says Shawn Sorrells, a neuroscientist at the University of Pittsburgh in Pennsylvania who co-authored the 2018 paper. One critique hinges on the DCX stain, which Sorrells says isn't an adequate measure of young neurons

because the DCX protein is also expressed in mature cells. That suggests the “new” neurons the team found were actually present since childhood, he says. The new study also found no evidence of pools of stem cells that could supply fresh neurons, he notes. What’s more, Sorrells says two of the brain samples he and his colleagues looked at were only fixed for 5 hours, yet they still couldn’t find evidence of young neurons in the hippocampus.

Llorens-Martín says her team used multiple other proteins associated with neuronal development to confirm that the DCX-positive cells were actually young, and were “very strict,” in their criteria for identifying young neurons.

Heather Cameron, a neuroscientist at the National Institute of Mental Health in Bethesda, Maryland, remains persuaded by the new work. Based on the “beauty of the data” in the new study, “I think we can all move forward pretty confidently in the knowledge that what we see in animals will be applicable in humans, she says. “Will this settle the debate? I’m not sure. Should it? Yes.”

http://bit.ly/2JKUxgI

Study finds no causal link between smoking and dementia

Recent study demonstrates smoking is not associated with a higher risk of dementia

LEXINGTON, Ky. -- It's an irrefutable fact that smoking is bad for you. Study after study has proven that smoking increases your risk for cancer, heart disease, diabetes -- even blindness.

But dementia? Not so fast. A recent study has demonstrated that smoking is not associated with a higher risk of dementia.

Many previous studies have found a correlation between smoking and dementia. However, Erin Abner of the University of Kentucky's Sanders-Brown Center on Aging (SBCoA) and colleagues wanted to explore outcomes using a different method of data analysis.

"The underlying data (in those studies) was solid, but the analysis didn't take into account the idea of competing risk of mortality, which we felt was an important factor to consider in this case since smoking is so strongly associated with earlier death," Abner said.

Competing risk is a complicated concept which can change how data is "counted" in a study and ultimately change study conclusions.

"If, for example, we were studying cancer deaths and smoking, and one of the people in the study died from heart disease, what do we do with that person's data?" Abner said. "That person can't possibly die from cancer since a competing event (death from heart disease) has occurred. If we ignore that information, the data are not telling the right story"

"In the case of our study, if smoking kills someone before they show signs of dementia, how can you accurately count that person? "we think that those deaths should be accounted for when predicting dementia risk."

To answer that question, Abner et al examined longitudinal data from 531 initially cognitively-normal people who were part of the SBCoA BRAiNS study, which has followed hundreds of volunteers an average of more than 11 years to explore the effects of aging on cognition. They used a statistical method called Competing Risk Analysis to determine whether there was a connection between smoking and dementia once the competing risk of death was included.

The data demonstrated that smoking was associated with a risk of earlier death -- but not for dementia. Interestingly, said Abner, their conclusions support several earlier neuropathological studies, which did not find that AD pathology was more prevalent in smokers.

"To be clear, we are absolutely not promoting smoking in any way," said Abner. "We're saying that smoking doesn't appear to cause dementia in this population."

Abner also noted that while Competing Risk Analysis is well-known and has been adapted successfully in other areas of research, it is not

the standard approach in the field of dementia research, where the competing risk of death is ever-present.

"While our study results could influence smoking cessation policy and practice, we feel that the most important consequence of our work is to demonstrate how this method could change the way we approach dementia research and to advocate for its adoption in the appropriate areas of study."

Abner notes that this is not a population-based study, which means that the results don't necessarily apply to all groups of people in the same way.

"However, the lack of neuropathological data, which is the gold-standard diagnosis for confirming correlations in a large population-based study, is a significant and ever-present barrier for dementia researchers."

The data was published in the March 26, 2019 issue of the *Journal of Alzheimer's Disease* (JAD-68 (2)).

http://bit.ly/2HXPOFK

Red Yeast Rice Supplements Likely Damaged This Woman's Liver

Natural supplements may seem benign, but as highlighted in a new case report, that's not always the case.

By Rachael Rettner, Senior Writer

A woman in Michigan developed sudden liver damage after taking a red yeast rice supplement, doctors reported.

The 64-year-old woman had recently been to the doctor and was told she had high cholesterol levels. But she was hesitant to start taking statins — the common drugs prescribed to lower cholesterol. So instead, she turned to a supplement called red yeast rice, a type of fermented rice that's marketed to lower cholesterol.

However, many patients and doctors may not be aware that red yeast rice can naturally contain a compound called monacolin K, which is identical to the active ingredient in the statin drug lovastatin, the report said. Red yeast rice supplements with monacolin K come with the same risks as drugs containing lovastatin, which can include liver damage.

Credit: Shutterstock

Indeed, six weeks after she started taking the supplement, the woman went to the emergency room with signs of liver injury, including fatigue, dark urine and jaundice, which is a yellowing of the skin and eyes.

After a battery of tests, including a liver biopsy, the woman was diagnosed with "acute drug-induced liver injury," or liver damage due to a drug or supplement. In this case, red yeast rice supplements were the most likely cause of the woman's illness, given the sudden onset of her symptoms and her recent use of the supplement, according to the report, published today (March 25) in the journal BMJ Case Reports.

Doctors issue warning

The woman's case prompted the doctors who treated her to issue a warning about the potential harm of red yeast rice supplements.

"Physicians and patients should be made aware that red yeast rice is not a harmless supplement, and those choosing to use it should watch for symptoms of hepatotoxicity [liver damage]," the authors, from Henry Ford Health System in Detroit, wrote in their report.

The woman also reported drinking two glasses of red wine a day, which may have contributed to her disease, the report said. Drinking alcohol while taking red yeast rice supplements may increase the risk of liver damage, according to Mayo Clinic.

But the woman's case isn't the first instance of this supplement causing liver problems; indeed, there have been multiple reports that have linked the use of red yeast rice supplements to such problems.

For example, a recent study in Italy found 10 cases of liver damage tied to the supplement over a 13-year period.

The National Center for Complementary and Integrative Health (NCCIH) warns that red yeast rice supplements may not be safe and may have the same side effects as lovastatin.

Technically, the U.S. Food and Drug Administration (FDA) doesn't allow products to be sold as dietary supplements if they contain more than trace amounts of monacolin K, according to NCCIH. But despite FDA actions, some red yeast rice supplements may still contain the compound. A 2017 study found that levels of monacolin K in red yeast rice supplements sold in the U.S. ranged from undetectable to nearly 11 milligrams per daily recommended dose, which is on a par with dosages of lovastatin.

"Consumers have no way of knowing how much monacolin K is present in most red yeast rice products, and therefore have no way of knowing whether a particular product is safe, effective, or legal," the NCCIH says on its website. People should not use red yeast rice to replace standard medical care or to postpone going to the doctor; and they should tell their doctor about any supplements they are taking, the NCCIH says.

The woman was treated with steroids, which helped improve her liver function, and she was monitored weekly after she left the hospital. The report notes it can take months to fully recover from liver damage tied to red yeast rice supplements.

http://bit.ly/2CERLn8

Protein 'spat out' by cancer cells promotes tumor growth

Prostate cancer cells change the behaviour of other cells around them, including normal cells, by 'spitting out' a protein from their nucleus, new research has found.

The tiny pieces of protein are taken up by the other cells, provoking changes that promote tumour growth and - the researchers believe - help the cancer hide from the body's immune system.

The process has been captured for the first time on video by researchers at the University of Bradford and University of Surrey. The research is published today [26 March] in Scientific Reports.

Lead researcher, Professor Richard Morgan from the University of Bradford, said: "For tumours to survive, grow bigger and spread they need to control the behaviour of cancer cells and the normal cells around them and we've found a means by which they do this. Blocking this process could be a potential target for future cancer therapy."

The research focused on a protein called EN2 that has a role in early development of the brain but has also been found at high levels in many types of cancer cells.

The team highlighted the protein using a green florescent tag. The researchers then studied its activity in human prostate cancer cells, normal prostate cells and in bladder cancer, melanoma and leukaemia cells. They found that both cancer and normal cells took up the protein from other cells.

They also did time lapse photography of prostate cancer cells, taking pictures every five minutes for 24 hours. The resulting video shows the cells eject small parts of themselves containing the green florescent protein that are then taken up by otherwise dormant cancer cells, causing them to reactivate, changing shape or fusing together.

Professor Morgan explains: "We think this is significant because cell fusion in cancer is relatively unusual and is associated with very aggressive disease. It can lead to new and unpredictable hybrid cells that are frequently better at spreading to different sites and surviving chemotherapy and radiotherapy."

Molecular analysis of the normal prostate cells showed that take up of EN2 caused them to express a gene called MX2 that generates an anti-viral response.

"We believe the cancer is trying to minimise the chances of the cells around it being infected by a virus, to avoid scrutiny by the immune system," says Professor Morgan.

"This could undermine the effectiveness of immunotherapy treatments, which try to use viruses to kill cancer by stimulating the immune system to attack it."

The researchers were also surprised to find the EN2 protein in the cell membrane as well as in the nucleus - which is very unusual for this type of protein. This provides an opportunity to block its action, and the team were able to identify that part of the protein that was accessible at the cell surface to be a potential target for treatment.

Hardev Pandha, Professor of Medical Oncology at the University of Surrey, says: "This work follows on from earlier studies at Surrey where detection of EN2 in urine, after secretion from prostate cancer cells, was shown to be a robust diagnostic biomarker of prostate cancer. The more we learn about prostate cancer the more that can be done to identify and treat this devastating disease."

https://bbc.in/2Os6rL0

Climate change: Drilling in 'Iceberg Alley'

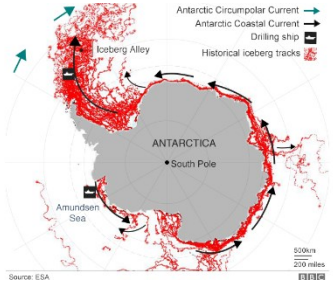
It sounds a bit like sitting in the middle of the road when there's a queue of juggernauts coming straight at you.

By Jonathan Amos BBC Science Correspondent

This is a little overplayed but it's kind of what an international group of scientists has just set out to do.

The researchers want to position themselves in the centre of "Iceberg Alley" off the tip of the Antarctic Peninsula and drill into the seafloor. Huge blocks of ice are likely to come drifting by in the process.

It's hoped the sediments the researchers recover will tell us something of how the White Continent has changed in the past and how its kilometres-thick ice sheet might react in the future in what's projected to be a much warmer world.



Expedition 382 of the International Ocean Discovery Program (IODP) left Punta Arenas in Chile on Monday. Using the drill ship, the Joides Resolution (JR), the team will core a number of seafloor locations right in the middle of Iceberg Alley.

The scientists are looking for the "rafted debris" that's been dropped by giant bergs as they head north from the Peninsula towards the South Atlantic.

This detritus of dust, dirt, and rock was originally scraped off the continent by the ice when it was part of a glacier, before it broke away to become an iceberg.

And through the wonder of modern geochemistry, it's possible to date this material and even to tie it to the specific locations in Antarctica.

The really helpful thing from the scientists' point of view is that they only need go to the alley to get a very broad view of past Antarctic behaviour.

It works like this: Bergs when they calve will bump anti-clockwise around the coast in the direction taken by near-shore currents. But when they reach the Peninsula - that's when they encounter the big clockwise flow of water known as the Antarctic Circumpolar Current. The bergs are then entrained and head north.

And just standing in the middle of this busy highway, as the JR now intends to do, means you get to sample the widest range of material dropped from historical bergs on their slow drift up into the South Atlantic.

In very simple terms: the more ice blocks that passed through the alley in any particular period in the past, the more unstable the Antarctic was likely to have been during that time.

In other words, the thickest layers of dropped stones and dust deposited on the ocean floor should relate to the warmest phases of ancient Antarctica.

There's quite a bit of oversimplification in this story, not least the recognition that the alley is dominated by bergs from the East of the continent - but the general picture holds.

The JR expects to pull up hundreds of metres of sediment core covering the past 20 million years. "A key interval of interest will be the Late Pliocene Warm Period (about 3-4 million years ago)," said expedition co-lead investigator Prof Maureen Raymo from the Lamont-Doherty Earth Observatory of Columbia University, US.

"This was when carbon dioxide was 400 parts per million (ppm) in the atmosphere - approximately similar to what it is today. I've spent a lot of time trying to work out what global sea-level was doing at that time because obviously that would speak directly to the question of whether East Antarctica loses mass or gains mass in a slightly warmer climate." The latter is possible if a warmer atmosphere triggers more snowfall.

Another period of keen interest is that of the Early Pleistocene - from 2.5 million to 800,000 years ago. It's a phase in Earth history when Ice Ages on the planet are known to have come and gone on roughly 41,000-year cycles.

This had something to do with the shifting nature of the Earth's orbit around the Sun, but has yet to be fully explained.

"I've proposed that Antarctica didn't transition to the ice sheet we see today until about 800,000 years ago, and prior to that there were maybe many sectors of the ice sheet that looked like modern Greenland with the ice margin on land," Prof Raymo told BBC News. Today's Antarctica has its glaciers terminating in the sea.

"We'll definitely get sediments from this time," she added.

If the current cruise is focussed on past behaviour in East Antarctica, a complementary drilling effort should fill in much of the narrative in the West of the continent.

Many blocks on Iceberg Alley eventually arrive at the British territory of South Georgia **Pete Bucktrout/BAS**

The JR has only recently finished drilling sediment cores in the Amundsen Sea area. IODP Expedition 379 cored to a depth of 800m, which likely gets back to the Late Miocene, or about 6 million year ago.

"This is the sector of the Antarctic Ice Sheet - more than any other area - that is changing before our eyes," explained 379's co chief scientist, Dr Julia Wellner from the University of Houston.

"While we have some ideas on why this is happening, it's not well understood yet; we've only been watching it for a few decades.

"So that's why we need these longer-term records, to get a real insight on what's occurring now and how things could change in the future.

"But it's not easy. There were times on our cruise when we thought we were in Iceberg Alley because there were so many bergs about, and every time one approaches you have to abandon your hole, wait for the berg to pass, and then return to resume drilling."

https://nyti.ms/2OH30R3

Advanced paternal age increases risk of early-onset schizophrenia in offspring

The effect of advanced paternal age on offspring risk is not explained by parental predisposition for schizophrenia, according to a study in Biological Psychiatry

Philadelphia - Advanced paternal age increases the risk in offspring of early-onset schizophrenia, a severe form of the disorder, according to a study in *Biological Psychiatry*, published by Elsevier. The

association between paternal age and risk in children remained after accounting for the contributions of the fathers' and mothers' genetic predispositions for schizophrenia, indicating that advanced paternal age itself contributes to risk.

Advanced paternal age has been associated with increased schizophrenia risk in offspring before, but it has been difficult to disentangle the effects of age versus factors related to age. "The paternal age association could be spurious if it was explained by selection into late fatherhood, which reflects fathers' own predisposition to schizophrenia," said senior author Wei J. Chen, MD, National Taiwan University in Taipei.

Maternal predisposition could also lead to late parenthood and increased risk in offspring. Recent advances in technology have allowed for schizophrenia predisposition to be estimated through genotyping--combining the individual contribution of genetic variations associated with schizophrenia across the entire genome provides a polygenic risk score, which helps predict the risk of developing the disorder.

Dr. Chen and colleagues determined the polygenic risk scores for the parents of over 1,600 people with schizophrenia to estimate the maternal and paternal predispositions to the disorder. Men who had their first child later in life tended to have increased polygenic risk for schizophrenia.

"After controlling for parental polygenic risk scores, every 10-year delay in paternal age increased the risk of early-onset schizophrenia in offspring by about 30 percent," said lead author Shi-Heng Wang, PhD, China Medical University in Taichung. Maternal age was not associated with risk of early onset in offspring. This finding supports that paternal age itself plays an independent role in the increased psychiatric risk in offspring, rather than being associated with increased risk through other factors related to late parenthood.

The authors defined early-onset schizophrenia as occurring before 18-years old, which tends to be a more severe form of the disorder and associated with more genetic abnormalities. Patients included in the study had healthy parents and no apparent family history of schizophrenia. These cases, referred to as sporadic, are thought to arise mainly from increased genetic mutations.

"Presumably, advanced paternal age increases risk for early-onset schizophrenia because advancing age is associated with an accumulation of mutations. These age-related mutations appear to be distinct from those more commonly associated with the risk for schizophrenia. It would be important to understand the distinct neural mechanisms through which advanced paternal age influenced the age of onset," said John Krystal, MD, Editor of *Biological Psychiatry*.

Identifying these mechanisms is of particular concern with the increasing age of fathers. The findings that the association with risk of early-onset schizophrenia exists after accounting for paternal and maternal polygenic risk provides an important advance in understanding the advanced paternal age effect on schizophrenia.

Notes for editors

The article is "Advanced paternal age and early-onset of schizophrenia in sporadic cases: not confounded by parental polygenic risk to schizophrenia," by Shi-Heng Wang, Po-Chang Hsiao, Ling-Ling Yeh, Chih-Min Liu, Chen-Chung Liu, Tzung-Jeng Hwang, Ming H. Hsieh, Yi-Ling Chien, Yi-Ting Lin, Yen-Tsung Huang, Chia-Yen Chen, Sharon D. Chandler, Stephen V. Faraone, Benjamin Neale, Stephen J. Glatt, Ming T. Tsuang, Hai-Gwo Hwu, and Wei J. Chen (https://doi.org/10.1016/j.biopsych.2019.01.023). It appears in Biological Psychiatry, *published by Elsevier.*

https://s.nikkei.com/2U79deU

Japan's drugmakers look to orphan drugs to vie with Western rivals

Technology and government aid are improving viability of rare disease cures

Nikkei staff writers March 25, 2019 15:32 JST

TOKYO -- Japanese pharmaceutical companies are ramping up efforts to develop cures for rare diseases. Progress in digital technology and

generous government financial support are making such drugs increasingly lucrative.

Fujifilm Holdings and Takeda Pharmaceutical are two of the drugmakers that are seeking to grow their business of selling costly drugs for rare conditions. The market for these so-called orphan drugs will be worth $200 billion in 2022, according to an estimate by a British research company.

These companies are betting that a successful product could bring in more than 100 billion yen ($911 million) in annual sales, making orphan drugs a profitable source of revenue. The new treatments will also help them hone their technological edge and become more competitive in a market dominated by Western giants.

There are nearly 7,000 globally recognized rare diseases. These conditions affect only a fraction of the population, so their markets are not large enough to justify the huge research and development costs required to develop treatments.

Major pharmaceutical companies in the U.S. and Europe have generally disregarded rare diseases, preferring to develop drugs for more common ailments like cancer and lifestyle diseases like diabetes and high cholesterol.

But market prospects for rare disease treatments are changing due to recent progress in artificial intelligence and data analysis, which has drastically improved the efficiency of drug development.

In Japan, the government is trying to encourage businesses to develop orphan drugs domestically.

Companies that develop drugs for rare diseases can receive subsidies and a tax break to cover half the research costs. The approval process for these drugs takes about six months compared with the one year typically required for other medicines.

The government also provides more generous financial aid to rare disease patients than in the U.S. or Europe. Patients are required to pay only about 10,000 yen per month for treatment, and children can receive treatment mostly free. The support creates a better business environment for medicines for diseases that affect 50,000 people or fewer.

Japan is also said to be uniquely competitive in developing drugs for rare diseases because of its history as an island nation that has been relatively less open to inflows of people from other parts of the world. That makes it easier to track down genes that cause rare diseases, most of which are genetic, among Japanese.

Fujifilm and Takeda are taking advantage of this environment. Fujifilm is planning to devote more resources to developing cures for lysosomal storage disorders -- rare inherited metabolic diseases that prevent cells from properly breaking down substances like proteins, carbohydrates and old cell parts.

The company has used regenerative medicine technology in experiments on mice to develop a new treatment that has reduced the accumulation of materials that cause these disorders.

Meanwhile, Takeda has acquired Shire, an Irish drugmaker with a large portfolio of treatments for rare diseases, for $58.3 billion. Takeda is using Shire technologies to develop potential drugs for 12 rare diseases, including hemophilia and hereditary angioedema, a very rare genetic disorder characterized by severe swelling in various parts of the body.

Takeda CEO Christophe Weber has pledged to put the company on the leading edge of rare disease drug development. The company is seeking to create new revenue sources that rival drugs for cancers and central nervous system diseases.

Fujifilm and Takeda also hope that technologies developed in creating new drugs can also be used for more common chronic conditions.

JCR Pharmaceuticals, a midsize Japanese drug manufacturer, has developed a technology to deliver therapeutic substances to the brain

by penetrating the blood-brain barrier, a huge obstacle for rare disease treatments.

The technology can be applied to treatments for chronic nervous system conditions, like Parkinson's disease and Alzheimer's disease. Global pharmaceutical giants have proposed tie-ups with the company.

Japanese pharmaceutical companies, which trail their Western rivals in the markets for drugs to treat lifestyle diseases and anticancer agents, need to find new sources of revenue as global competition becomes tougher. They can carve out a more profitable future in the treatment of rare diseases.

https://bbc.in/2HWZosG

Mumps outbreak at Nottingham universities

More than 220 suspected cases of mumps have been reported at two universities, Public Health England (PHE) has said.

Students are being urged to ensure they are vaccinated due to an outbreak at Nottingham Trent University and the University of Nottingham.

A total of 40 cases have been confirmed so far.

PHE, which confirmed the cases, said it was working with the universities to persuade unprotected students to get the MMR jab.

Dr Vanessa MacGregor said: "We have seen a rise in the figures recently and teenagers and young adults who have not had two doses of MMR vaccine are particularly vulnerable.

"School leavers and other young adults who have not received the MMR or only received one dose should ensure that they take up the offer of MMR vaccination."

PHE said latest figures showed cases of mumps in England had decreased in 2018, with 1,024 confirmed cases compared to 1,796 in 2017.

A spokesman for Nottingham Trent University said it was offering support to those affected. "If any students have any symptoms of the illness we would encourage them to visit their GP as they would do normally and inform a relevant member of staff on their course if it has an impact on their studies," he said.

The University of Nottingham said it has been alerted to a number of suspected cases by colleagues at the Cripps Health Centre on University Park campus. "We are working closely with Public Health England to monitor the situation," a spokeswoman said.

Mumps

Mumps is a contagious viral infection which causes swelling of the parotid glands.

General symptoms can include headache, joint pain, feeling sick, tiredness, loss of appetite and a high temperature.

It is spread in the same way as colds and flu - through infected droplets of saliva that can be inhaled or picked up from surfaces and transferred into the mouth or nose.

A person is most contagious a few days before the symptoms develop and for a few days afterwards.

Source: Public Health England

In 1998, a study by Andrew Wakefield linked the MMR vaccine to autism, and although he was struck off the UK medical register and his research has been completely discredited, it had an impact on the coverage of the vaccine, with rates dropping to about 80% in the late 1990s and a low of 79% in 2003.

Numerous public health campaigns have increased uptake in the years since, but health bosses have warned social media has been fuelling fear over vaccines based on misinformation.

On Tuesday, Health Secretary Matt Hancock called for new legislation to force social media companies to remove content promoting false information about vaccines.

According to World Health Organisation figures, measles cases tripled in Europe between 2017 and 2018, with concerns also raised about a global rise in recent years.

http://bit.ly/2HNaqS6

Vitamin C can shorten the length of stay in the ICU

Administering vitamin C shortened average ICU stay by 7.8%.

The biochemistry of vitamin C is complex. For example, it is involved in the synthesis of norepinephrine and vasopressin, both of which influence the cardiovascular system, and carnitine, which is involved in energy metabolism.

Through its epigenetic effects, vitamin C may influence hundreds of genes. In controlled trials, vitamin C has lowered blood pressure, decreased the incidence of atrial fibrillation, decreased bronchoconstriction, decreased pain, decreased glucose levels in patients with type 2 diabetes, and it has shortened the duration of colds.

Very low vitamin C plasma levels are not uncommon in hospitals. Furthermore, vitamin C metabolism is changed in many conditions that involve physiological stress, such as infections, surgery, traumas, and burns, in which case vitamin C levels can decline dramatically. Although 0.1 grams per day of vitamin C can maintain a normal plasma level in healthy persons, much higher doses, up to 4 grams per day, are needed for critically ill patients to increase their plasma vitamin C levels to the range of normal healthy people.

Therefore, high vitamin C doses may be needed to compensate for the increased metabolism in critically ill patients.

Given that vitamin C has shown diverse effects on medical conditions, and the accumulated evidence for low vitamin C levels and increased metabolism of vitamin C in critically ill patients, vitamin C might influence practical outcomes such as the length of ICU stay, without any restrictions on the specific medical conditions that cause the stay in the ICU.

Dr. Harri Hemilä from the University of Helsinki, Finland, and Dr. Elizabeth Chalker from the University of Sydney, Australia, carried out a systematic review of vitamin C for ICU patients. They identified 18 relevant controlled trials, and 12 of them were included in the meta-analysis on the length of stay.

On average, vitamin C administration shortened ICU stay by 7.8%. In six trials, orally administered vitamin C with an average dose of 2 grams per day reduced the length of ICU stay on average by 8.6%.

According to Hemilä and Chalker, "Vitamin C is a safe, low-cost essential nutrient. Given the consistent evidence from the trials published so far, vitamin C might be administered to ICU patients, although further studies are needed to find out optimal protocols for its administration. A few common cold studies have indicated that there may be a linear dose response for vitamin C on common cold duration for up to 6 and 8 grams per day. Evidently the dose response for doses higher than 2 grams per day should also be investigated for ICU patients."

http://bit.ly/2YCnZsE

Exercise helps prevent cartilage damage caused by arthritis

Exercise helps to prevent the degradation of cartilage caused by osteoarthritis, according to a new study from Queen Mary University of London.

The researchers show for the first time how mechanical forces experienced by cells in joints during exercise prevent cartilage degradation by suppressing the action of inflammatory molecules which cause osteoarthritis.

The study, published in the journal *Osteoarthritis and Cartilage*, demonstrates the benefits of exercise on the tissues that form our joints and how this is down to tiny hair-like structures called primary cilia found on living cells.

During exercise the cartilage in joints such as the hip and knee is squashed.

This mechanical distortion is detected by the living cells in the cartilage which then block the action of inflammatory molecules associated with conditions such as arthritis.

The researchers show that this anti-inflammatory effect of physical activity is caused by activation of a particular protein, called HDAC6, which triggers changes in the proteins that form primary cilia.

Pharmaceutical drugs that blocked HDAC6 activation prevented the anti-inflammatory effects of physical activity, whilst other drug treatments were able to mimic the benefits of exercise.

Changes in length of the primary cilia, which are only a few 1000th of a millimetre, provided a biomarker of the level of inflammation. Cilia got longer during inflammation, but treatments that prevented this elongation successfully prevented inflammation.

Mr Su Fu, PhD student at Queen Mary University of London and study author, said: "We have known for some time that healthy exercise is good for you - now we know the process through which exercise prevents cartilage degradation."

Professor Martin Knight, lead researcher of the study added: "These findings may also explain the anti-inflammatory effects of normal blood flow in arteries which is important for preventing arterial disease such as atherosclerosis and aneurism."

The researchers hope that these findings will help in the search for treatments for arthritis which affects over three million people in the UK causing stiff and painful joints.

The researchers suggest the results may lead to a whole new therapeutic approach known as mechano-medicine in which drugs simulate the effect of mechanical forces to prevent the damaging effects of inflammation and treat conditions such as arthritis.

** Research paper: 'Mechanical loading inhibits cartilage inflammatory signalling via an HDAC6 and IFT-dependent mechanism regulating primary cilia elongation'. Su Fu, Clare L Thompson, Ahmed Ali, Wen Wang, Paul Chapple, Hannah M Mitchison, Phil L Beales, Angus K Wann, Martin M Knight.* Osteoarthritis and Cartilage.

** Link to the paper: https://doi.org/10.1016/j.joca.2019.03.003*

http://bit.ly/2JRjNC0

Kids store 1.5 megabytes of information to master their native language

New research suggests language acquisition between birth and 18 is a remarkable feat of cognition rather than something humans are just hardwired to do

Learning one's native language may seem effortless. One minute, we're babbling babies. The next we're in school reciting Martin Luther King Jr.'s "I Have a Dream" speech or Robert Frost's poem "Fire and Ice."

But new research from the University of California, Berkeley, suggests that language acquisition between birth and 18 is a remarkable feat of cognition, rather than something humans are just hardwired to do.

Researchers calculated that, from infancy to young adulthood, learners absorb approximately 12.5 million bits of information about language -- about two bits per minute -- to fully acquire linguistic knowledge. If converted into binary code, the data would fill a 1.5 MB floppy disk, the study found.

The findings, published today in the Royal Society Open Science journal, challenge assumptions that human language acquisition happens effortlessly, and that robots would have an easy time mastering it.

"Ours is the first study to put a number on the amount you have to learn to acquire language," said study senior author Steven Piantadosi, an assistant professor of psychology at UC Berkeley. "It highlights that children and teens are remarkable learners, absorbing upwards of 1,000 bits of information each day."

For example, when presented with the word "turkey," a young learner typically gathers bits of information by asking, "Is a turkey a bird? Yes, or no? Does a turkey fly? Yes, or no?" and so on, until grasping the full meaning of the word "turkey."

A bit, or binary digit, is a basic unit of data in computing, and computers store information and calculate using only zeroes and ones. The study uses the standard definition of eight bits to a byte.

"When you think about a child having to remember millions of zeroes and ones (in language), that says they must have really pretty impressive learning mechanisms."

Piantadosi and study lead author Frank Mollica, a Ph.D. candidate in cognitive science at the University of Rochester, sought to gauge the amounts and different kinds of information that English speakers need to learn their native language.

They arrived at their results by running various calculations about language semantics and syntax through computational models. Notably, the study found that linguistic knowledge focuses mostly on the meaning of words, as opposed to the grammar of language.

"A lot of research on language learning focuses on syntax, like word order," Piantadosi said. "But our study shows that syntax represents just a tiny piece of language learning, and that the main difficulty has got to be in learning what so many words mean."

That focus on semantics versus syntax distinguishes humans from robots, including voice-controlled digital helpers such as Alexa, Siri and Google Assistant.

"This really highlights a difference between machine learners and human learners," Piantadosi said. "Machines know what words go together and where they go in sentences, but know very little about the meaning of words."

As for the question of whether bilingual people must store twice as many bits of information, Piantadosi said this is unlikely in the case of word meanings, many of which are shared across languages.

"The meanings of many common nouns like 'mother' will be similar across languages, and so you won't need to learn all of the bits of information about their meanings twice," he said.

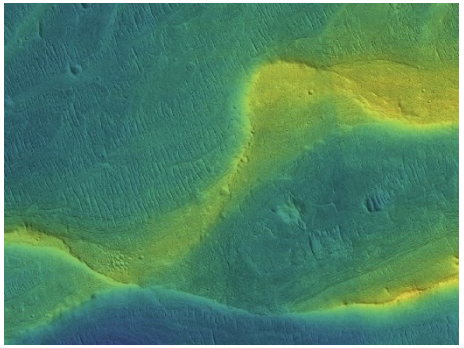
http://bit.ly/2OyEscO

Mars Was Once Covered in Wide, Raging Rivers

Mars was wet, until suddenly it wasn't.

By Rafi Letzter, Staff Writer | March 27, 2019 02:01pm ET

Scientists have long seen dry riverbeds slashed across the surface of Mars as evidence that water once flowed freely on the planet. And in 2012, NASA's Curiosity space rover sent back images of smooth, round pebbles from the bottom of one such riverbed, their lack of rough edges evidence that water had once flowed over them.



This NASA image shows a preserved river channel on Mars, with color overlaid to indicate elevation (blue is low, yellow is high). The range of elevation in the snapshot is about 115 feet (35 meters). **NASA/JPL/Univ. Arizona/UChicago**

Now, a new study published today (March 27) in the journal Science Advances catalogs those rivers and reports that their waters likely flowed heavily well into the last epoch, before Mars entirely dried up.

"It's already hard to explain rivers or lakes based on the information we have," Edwin Kite, a planetary scientist at the University of Chicago and lead author of the study, said in a statement. "This makes a difficult problem even more difficult."

If the rivers had been brief or flowed only part of the time, it still would have been challenging to explain their existence. But scientists just don't know where all the liquid water came from to form these heavy flows.

Mars today is frigid and mostly dry, with just a thin atmosphere on its surface. In the distant past, it seems that the weather should have been even colder, because the sunlight reaching the planet's surface

would have been dimmer. And yet, billions of years ago, water seems to have flowed heavily and freely across Mars, in rivers that were sometimes wider than those on Earth. These waters appear to have flowed so heavily that they would have been in motion all day, not just at peak sunlight hours or in thin trickles.

Scientists just don't know what sort of weather on the Red Planet would have produced these rivers, but the study showed that the heavily flowing water existed for more than a billion years, in early Martian history.

That implies, at a minimum, that Mars had a strong greenhouse effect back then to trap the energy of limited sunlight on the planet and melt its water — which then ran off into river channels.

Kite said that this work implies that something in the current science of planets and the early solar system is wrong, because everything scientists know suggests that the rivers on Mars should have been small and temporary, if they existed at all. The long-term, heavy flows lasting for millions of years, just don't fit into current scientific knowledge.

The research also shows that as the Red Planet got colder, it didn't slowly dry up. Instead, at the end of the Martian wet epoch, rivers became shorter, but still carried heavy runoff before — almost immediately — disappearing.

https://bbc.in/2CIt9Ks

Take over pharma to create new medicines, says top adviser

Part of the drugs industry should be taken over to make new antibiotics, an influential economist has argued.

By James Gallagher Health and science correspondent, BBC News

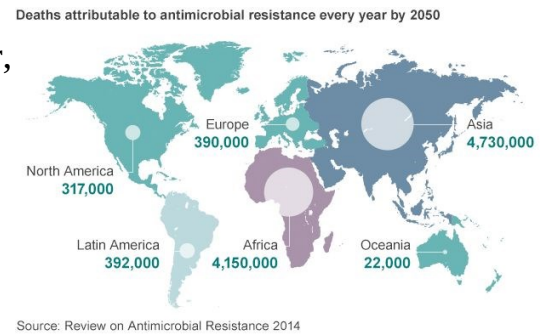
Lord Jim O'Neill, who advised the government on antibiotic resistance, said he was shocked by pharmaceutical companies failing to tackle drug-resistant infections. He said the solution may be to "just take it away from them and take it over".

The pharmaceutical industry said it was not standing still on the issue.

Bacteria evolving resistance to antibiotics threatens to take medicine back to the dark ages. Some infections could become untreatable and losing the drugs would make surgery and cancer therapy far more risky. It is known as the antibiotic apocalypse.

Part of the solution is developing new drugs, however, there has not been a new class of antibiotic since the 1980s.

The problem is there is simply no money in it - any new drug would need to be cheap and used rarely to minimise the risk of resistance.



Projections of deaths from drug-resistant infections by 2050

Three years ago, Lord O'Neill proposed solutions in his Review on Antimicrobial Resistance, including giving pharmaceutical companies around a billion dollars for each novel antibiotic they developed.

Lord O'Neill said that since then there had been empty words from global policy makers and that he was coming round to the idea of, in effect, nationalising part of the pharmaceutical industry.

He told the BBC: "If you had asked me three years ago, I would have thought that would have been a bit crazy.

"But nearly three years after our review came out, there's endless talk but there's no progress in waking up the pharmaceutical industry to want to do this. "So, by default, I find my mind thinking why not explore the idea of some public utility that's got public-purpose ownership of it, just take it away from them and take it over."

He said that companies ditching antibiotic research would be an opportunity for a new public body to acquire those assets.

The Association of the British Pharmaceutical Industry (ABPI) said it was "hardly standing still" in the fight against antimicrobial resistance.

Dr Sheuli Porkess, the deputy chief scientific officer at the ABPI, said: "Nationalising antibiotic development simply won't get us the antibiotics we need. "In 2016 the private sector invested around $2bn in research and development of new antibiotics, roughly four times as much as all government and foundations combined."

The ABPI said it had been working closely with government for the past two years and companies were "ready and waiting" to test a new model for supporting antibiotic. "We shouldn't write off this plan before we've tried it," Dr Porkess said.

However, there is wide agreement that developing new drugs will only ever be part of the antimicrobial resistance solution.

The practice of handing antibiotics out like sweets will continue to fuel the rise of drug-resistant infections.

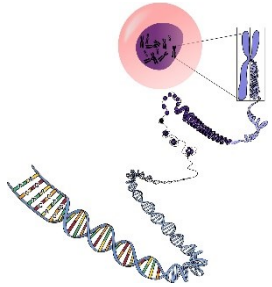
http://bit.ly/2FMSzsk

Interest in RNA editing heats up

RNA editing, which could offer advantages over CRISPR, has been gaining ground

by American Chemical Society

The gene-editing technology known as CRISPR has attracted much excitement and investor interest with its potential to someday treat diseases by fixing faulty copies of genes. But recently, a different approach called RNA editing, which could offer advantages over CRISPR, has been gaining ground in academic labs and start-ups, according to an article in *Chemical & Engineering News (C&EN)*.



Credit: CC0 Public Domain

RNA editing uses an enzyme called ADAR to make precise edits to RNA, the shorter-lived cousin to DNA that acts as a blueprint for proteins. Researchers direct ADAR to specific RNAs with a guide sequence attached to the enzyme. Unlike CRISPR gene editing, the effects of RNA editing are reversible because cells are constantly making new copies of RNA. Therefore, RNA editing avoids the risks of permanent gene editing with CRISPR, writes Assistant Editor Ryan Cross, and could also be used to treat temporary conditions, such as pain or inflammation.

However, finding an easy way to control how ADAR makes its edits has been challenging. Researchers have tried chemically attaching ADAR to a guide RNA, adding an RNA-binding protein or even linking the catalytic portion of ADAR to the bacterial Cas9 enzyme used in CRISPR. However, these approaches require getting the modified enzymes into human cells. Some researchers are working on using human cells' own ADAR for RNA editing, by introducing chemically modified guide RNAs that recruit the editing enzyme and direct it to specific RNAs. With researchers and investors becoming increasingly interested in this approach, RNA editing could someday give CRISPR a run for its money, Cross writes.

http://bit.ly/2WBk7X6

Chinese Women Once Had to Point Out Their Medical Troubles on Ivory Dolls

For centuries, miniature ivory women helped real women seek medical help.

by Sabrina Imbler

Often when a woman saw a doctor in 18th-century China, she wasn't allowed to actually see him. Instead, she sat behind a curtain or bamboo screen, where she had to map out her pain on a body that wasn't her own. Her hand, or that of a close female attendant, would poke through the drapes or screen, and gesture toward the naked body of an ivory doll. If the patient had difficulty breathing, she might run a finger along the doll's curved chest. For menstrual pain, the smooth abdomen. For a headache, the bump of a bun. After

studying these cryptic communications, the doctor would issue his diagnosis.

In the final centuries of China's Qing Dynasty, these intricately carved medicine dolls were an ailing woman's only option, writes medical historian Howard Dittrick in his 1952 paper in the *Bulletin of the History of Medicine*, "Chinese Medicine Dolls."

A jade diagnostic doll rests on a tiny embroidered throw. **Jamie Rees/Courtesy Clendening History of Medicine Library & Museum, University of Kansas Medical Center**

From the 1300s to the late 19th century, China's Ming and Qing Dynasties had ushered in a cult of chastity that made it impossible for a doctor to physically examine a female patient, or for her to undress before him. And at the time, China only allowed men to be doctors. In 1879, the Canton Missionary Hospital became the first medical institution to admit women to their medical class, according to a Columbia University dissertation on Chinese medical care for women in the late-19th and early-20th centuries, by Shing-ting Lin. This decision was made not out of some feminist ideal, but rather in reaction to the belief that male physicians should not be touching female patients.

Chinese diagnostic dolls depict a reclining woman, usually naked save for a pair of bangles around her wrists and the occasional fan. Though most dolls were carved out of ivory, they could also be sculpted of jade, amber, bronze, wood, or even lapis lazuli. Dittrick notes the dolls all strike the same pose: propped up on the left arm, with the other draped across the body. Carvers did distinguish adult women, with hair tied up in a bun, from girls with braids or twin ponytails. Early carvings also often depict Chinese women with shrunken lotus feet, a pretty term for the painful and eroticized practice of footbinding. To retain a degree of modesty, the dolls' feet were always shod in shoes or constricting bandages.

Upper-class women might bring their own beautiful, customized dolls to doctors, whereas poorer women had to make do with the doctor's own, more rudimentary, model. The more luxurious dolls—such as the intricate Ming Dynasty doll shown above on a blue blanket—reclined on miniature couches, some of which even featured silk cushions or embroidered throws. To remove the final layer of interpersonal contact, wealthier ladies simply marked the afflicted parts of the doll with India ink or charcoal, and then sent the doll to the doctor via messenger.

The physicians of late imperial China saw no issue with diagnosing and treating patients on the basis of pointing and words alone (or even less). In fact, it was close to the primary practice at the time for male patients as well (though men had no issues with disrobing before a doctor), as scholarly doctors found physical contact to be beneath them, writes Shing-ting Lin. Unsurprisingly, the smooth, polished surfaces of an ivory doll proved insufficient for certain female medical concerns. Midwives and other lower-class female workers would have had to take charge of anything gynecological or obstetric, such as period management or childbirth.

http://bit.ly/2U4rIk9

The bigger the evolutionary jump, the more lethal cross-species diseases could be

The bigger the evolutionary jump between species, the more likely the disease could be lethal in its new host

Some diseases which are fatal in one species can cause only mild discomfort in another--but it's hard for scientists to predict how lethal a disease will be if it leaps across species.

However, a new paper published this week in the Proceedings of the National Academy of Sciences indicates that the evolutionary relationship between infected hosts can predict the impact of diseases. Canadian researchers used data from the World Organisation for Animal Health to track diseases in domesticated mammals, tracing their paths and outcomes across the world.

"The bigger the evolutionary jump between species, the more likely the disease could be lethal in its new host," says Jonathan Davies, a University of British Columbia biologist and senior researcher on the paper.

A disease jumping from a buffalo to a cow is making a short evolutionary jump, and is less likely to be fatal. A disease jumping from a buffalo to a cat involves a larger evolutionary jump and a higher chance of death. Luckily, this lethality may cause the disease to spread poorly amongst its new hosts.

Nevertheless, such infections are a concern. Many diseases are transmitted between domesticated animals, wildlife and humans. A disease that is less lethal, but easy to spread, could be even more problematic than one with a high mortality rate.

"With the world's ecosystems undergoing rapid transformations and climate change altering species' ranges, different animals are coming in contact for the first time. This may promote the emergence of diseases in new hosts," says Maxwell Farrell, the lead author of the study who conducted the research while at McGill University. "Predicting the outcome of these interactions will pose a major challenge."

The biologists hope to expand their research, looking at more species, including humans, to create a database of infection outcomes.

"We shouldn't worry about the number of diseases we have, we should be worried about how virulent they are--whether they are in wildlife, domesticated animals or humans," concludes Davies.

http://bit.ly/2WBfqN2

For Cancer Risk, a Bottle of Wine Equals This Many Cigarettes

Drinking a bottle of wine per week may be like smoking five to 10 cigarettes in the same time period, in terms of cancer risk, according to a new study from the United Kingdom.

By Rachael Rettner, Senior Writer

The study, published today (March 28) in the journal BMC Public Health, is the first to estimate the "cigarette equivalent" of alcohol, with regard to cancer risk.

The researchers found that the increase in cancer risk tied to drinking one bottle of wine per week is equivalent to smoking five cigarettes per week for men and 10 cigarettes per week for women.

The goal of the research is to better convey the cancer risks that are tied to moderate alcohol consumption, which is generally thought to be less harmful than smoking cigarettes. Indeed, studies in both the U.S. and U.K. have found that many people aren't aware of alcohol's link to cancer. For example, a 2017 survey from the American Society of Clinical Oncology found that 70 percent of Americans didn't know that drinking alcohol is a risk factor for cancer.

"Our estimation of a cigarette equivalent for alcohol provides a useful measure for communicating possible cancer risks that exploits successful historical messaging on smoking," lead study author Dr. Theresa Hydes, of the Department of Gastroenterology and Hepatology at the University Hospital Southampton NHS Foundation Trust, said in a statement. "We hope that by using cigarettes as the comparator we could communicate this message more effectively to help individuals make more informed lifestyle choices."

Dr. Richard Saitz, an addiction medicine specialist and chair of the Department of Community Health Sciences at Boston University

School of Public Health, said that the study's comparison makes sense.

"I think it's about time that we communicate the cancer risks of alcohol — it's really been under the radar [and] this way is a good way to do it," said Saitz, who wasn't involved with the study.

Still, the researchers stress that the study isn't saying that moderate alcohol consumption is the same thing as smoking. The study only considered cancer risk, and not the risks of other health conditions, such as heart disease. In addition, the study looked at the lifetime risk of cancer in the general population, which might differ from an individual's cancer risk from either smoking or alcohol, the authors said.

Alcohol vs. cigarettes

To put alcohol's cancer risks in perspective, the study aimed to answer the question: In terms of cancer risk, how many cigarettes are in a bottle of wine? One bottle contains about 80 grams (2.5 ounces) of pure alcohol.

The researchers used national data from the U.K. on the lifetime risk of cancer in the general population as well as previously published research on the relationship between alcohol, smoking and cancer.

They estimated that, among nonsmokers, drinking one bottle of wine per week is tied to a 1.0 percent increase in lifetime cancer risk for men; and a 1.4 percent increase in lifetime cancer risk for women. In other words, if 1,000 men and 1,000 women each drank one bottle of wine per week, about 10 extra men and 14 extra women would develop cancer at some point in their lives, the researchers said. The higher risk among women is mainly due to the link between alcohol consumption and breast cancer. This risk was comparable to smoking five cigarettes per week for men and 10 for women.

A "known carcinogen"

"Everybody knows that cigarettes cause cancer," Saitz told Live Science. "Hearing that some amount of alcohol is the equivalent of some amount of cigarettes" in terms of cancer risk, is helpful for the general public, he said.

Saitz noted that there's been little discussion of the cancer risks tied to alcohol, even though alcohol is a known carcinogen. Even dietary guidelines discuss the recommended number of alcoholic drinks per day.

"If I didn't call it alcohol or wine or beer or cocktails, and I just called it a carcinogen, no one would be talking about how many glasses of a carcinogen you could have," Saitz said.

The study authors noted that because the study only considered cancer risk, it didn't take into account other diseases tied to smoking or alcohol use, such as respiratory, cardiovascular or liver diseases.

The authors also pointed out that smokers typically consume far more than five to 10 cigarettes per week — the average smoker in the U.K. consumes around 80 cigarettes per week, and the average smoker in the U.S. consumes around 100 cigarettes per week.

Still, "these findings highlight moderate levels of drinking as an important public health issue," the authors concluded.

http://bit.ly/2CKKn9K

Bacteria partners with virus to cause chronic wounds, Stanford study finds

A common bacterial pathogen called* Pseudomonas aeruginosa *produces a virus that substantially increases the pathogen's ability to infect us, according to a study by investigators at the Stanford University School of Medicine.

P. aeruginosa weaponizes its resident virus to exploit the immune system's distinct responses to bacterial versus viral infections.

This marks the first time a bacteria-infecting virus, otherwise known as a bacteriophage or just phage, has been observed inducing the immune system to mount an antiviral response and, in doing so, causing it to ignore the bacterial infection. When the scientists

generated a vaccine directed at the virus, they showed that it dramatically lowered the bacteria's ability to infect wounds in mice.

Detailed in a study to be published March 29 in Science, the findings could fuel new ways of preventing chronic, intractable infections by keeping antibiotic-resistant bacteria from getting a foothold in the first place. The discovery that phages foster bacterial infections also adds a previously unexpected layer of complexity to the relationship between us and the billions of bacteria inhabiting our gut and other organs.

Paul Bollyky, MD, PhD, assistant professor of infectious diseases and of microbiology and immunology, is the study's senior author. The lead author is former graduate student Johanna Sweere, PhD.

Quadrillions of phages in body

"We've long known that you've got up to 10 quadrillion phages in your body, but we just figured whatever they were doing was strictly between them and your commensal bacteria," Bollyky said. "Now we know that phages can get inside your cells, too, and make you sick."

There's currently no approved vaccine targeting *P. aeruginosa*, an increasingly drug-resistant pathogen that infects the lungs of most adults with cystic fibrosis and accounts for a sizable percentage of all infections of diabetic ulcers, bedsores and burn wounds.

In 2017, the World Health Association named *P. aeruginosa* one of the "critical priority" pathogens posing the greatest threat to human health.

"I see this every day in my clinical practice," Bollyky said. "What starts off as a little cut can't heal as a result of a persistent, drug-resistant bacterial infection. The toll in terms of sickness, death and dollars is enormous." Infected diabetic foot ulcers are the single biggest cause of amputation, he said.

P. aeruginosa is itself frequently infected with a phage called Pf. This phage lives inside the bacteria but can be shed from the bacterial surface into the surrounding environment (such as a wound), much like the virus herpes lives in our cells and is shed from cold sores. In the study, Bollyky's team showed Pf was common in wounds infected with *P. aeruginosa*. The researchers examined 111 patients with microbially infected, non-healing wounds and found that 37 of them were infected with *P. aeruginosa*. Two-thirds of those wounds infected with *P. aeruginosa* were carrying Pf -- a fraction that grew the longer a wound persisted.

To prove Pf actually promotes *P. aeruginosa* infections rather than merely co-exists with them, the scientists inoculated small wounds in the skin of mice with *P. aeruginosa* strains that either did or didn't contain Pf. They observed that the two strains differed greatly in their ability to establish wound infections. The inoculation dose necessary to result in a reliable *P. aeruginosa* infection was 50 times larger if it lacked Pf.

Next, the scientists looked to see what Pf might be doing to immune cells that could affect *P. aeruginosa*'s ability to sustain an infection. In a lab dish, they found that the presence of the phage in *P. aeruginosa* reduced by 10-fold the number of invading bacteria that were engulfed by either mouse or human phagocytes -- immune cells that ingest, then digest, invading bacteria.

"The phagocytes lost their appetite," Bollyky said.

Tripping molecular detectors

Bollyky's team determined that stretches of the phage's genomic material trigger molecular detectors in the phagocytes, steering the immune system's response from an antibacterial to an antiviral one.

When a phagocyte encounters bacteria, the appropriate response is to gobble them up, chew them up and call in more troops. But phagocytes' response to a virus is different, Bollyky said. "If you're an immune cell, ingesting a virus is absolutely the worst thing you can do, because now you've let it get inside of you -- you're infected by it."

So it's only sensible for a phagocyte that comes in contact with a virus to shut down phagocytosis. The appropriate antiviral immune response involves the generation of antibodies to tag virally infected cells and to signal other types of immune cells to home in on and destroy any virus-carrying cell they come across.

What Pf does inside phagocytes, Bollyky said, is like somebody pulling the fire alarm when they should have called the police. "If 20 fire engines pull up to the scene of the crime, it makes it easier for the thief to get away," he said.

The investigators generated a vaccine containing a component of a Pf protein and noted that it cut the incidence of wounds infected with Pf-positive *P. aeruginosa* by half. They also generated antibodies that specifically target the same protein component and showed that they worked at least as well as the vaccine.

Bollyky and his colleagues have filed for a patent on intellectual property associated with the vaccine, and they plan to test it in large animals as a step toward eventual clinical trials.

Bollyky's vision is to vaccinate people against Pf when they're first diagnosed with cystic fibrosis or diabetes, as well as people in nursing homes and hospitals, in order to protect them from *P. aeruginosa* infections. Since a vaccine takes time to arouse the immune system, he suggested that Pf-targeting antibodies (which can be produced in bulk and stored for long periods) could be useful in burn cases, when there's no advance warning.

The Pf vaccine might turn out to be effective against other pathogenic bacteria, such as E. coli and Klebsiella pneumoniae, which can also carry Pf and tend to co-infect wounds colonized by *P. aeruginosa*, Bollyky said.

Other Stanford co-authors of the study are postdoctoral scholar Jonas Belleghem, PhD; former postdoctoral scholars Vivekananda Sunkari, PhD, Xiou Cao, PhD, and Christiaan de Vries, MD; research scientists Gernot Kaber, PhD, and Robert Manasherob, PhD; Stanford Health Care affiliate physician Gina Suh, MD; technician Dung Lam; lab manager Heather Ishak; graduate students Michelle Bach and Medeea Popescu; medical student Payton Marshall; the late MD-PhD student Maria Birukova; former undergraduate Ethan Katznelson; and former medical student Daniel Lazzareschi, MD.

Researchers at Baylor College of Medicine in Houston, the University of Washington and the University of Montana also contributed to the study.

Bollyky is a member of Stanford's Bio-X, Maternal & Child Health Research Institute and Wu Tsai Neurosciences Institute.

The work was funded by the National Institutes of Health (grants R21AI133370, R21AI133240, R01AI12492093, K22AI125282, R01AI138981, P20GM103546, P30DK116074 and R01GM111808), Stanford SPARK, the Falk Medical Research Trust and the Cystic Fibrosis Foundation.

Stanford's departments of Medicine and of Microbiology and Immunology also supported the work.

http://bit.ly/2FDjnKe

Cancer prevention drug also disables H. pylori bacterium

A medicine currently being tested as a chemoprevention agent for multiple types of cancer has more than one trick in its bag when it comes to preventing stomach cancer, Vanderbilt researchers have discovered.

The investigators found that in addition to its known ability to block the production of cell growth compounds, the drug DFMO (difluoromethylornithine) acts directly on the bacterium Helicobacter pylori to reduce its virulence. *H. pylori* infection is the primary cause of gastric cancer.

The findings, reported in the March 12 issue of *Proceedings of the National Academy of Sciences*, support further studies of DFMO for the prevention of stomach cancer, the third leading cause of cancer deaths worldwide.

H. pylori infects the stomachs of half of the human population, but only about 1 percent of infected individuals develop stomach cancer. Although it's possible to treat the infection to prevent stomach cancer, it's not clear whom to treat. Plus, the bug may be conferring beneficial effects -- esophageal reflux diseases, asthma and other allergic disorders occur more frequently in people who are not infected with *H. pylori*.

"*H. pylori* has co-evolved with humans for at least 60,000 years, probably longer, and attempting to prevent stomach cancer by eliminating the infection with widespread use of antibiotics is not necessarily a good idea," said Keith Wilson, MD, Thomas F. Frist Sr. Professor of Medicine and professor of Pathology, Microbiology and Immunology.

"Our study suggests that it might be possible to reduce the virulence of the bacteria, without having to eliminate it. It's a speculative and unusual way to think about an infection, but it could be an interesting strategy."

Wilson, who also directs the Vanderbilt Center for Mucosal Inflammation and Cancer, and his team previously linked the production of cell growth compounds called polyamines to the development of stomach cancer in an *H. pylori*-infected animal model. They demonstrated that treatment of the animals with DFMO, which inhibits an enzyme that is key to the production of polyamines, prevents stomach cancer.

Their findings are the basis for an ongoing clinical trial of DFMO for stomach cancer prevention in Honduras and Puerto Rico.

Patients with pre-malignant lesions in the stomach, as determined by endoscopy, are enrolled in the trial of DFMO and will be studied for disease progression.

To further explore how DFMO works, J. Carolina Sierra, PhD, research instructor in Medicine, collected *H. pylori*bacteria from infected animals that had been treated (or not) with DFMO. Using an in vitro test, she assessed the activity of one of the main *H. pylori* virulence factors, a protein called CagA. CagA is "injected" into stomach epithelial cells, where it contributes to oncogenic signaling pathways.

"What we noticed is that bacterial strains coming from DFMO-treated animals have reduced ability to move this virulence factor into epithelial cells," Sierra said.

The researchers discovered that DFMO treatment -- in animals or in vitro -- caused mutations in the *H. pylori* gene that encodes CagY, part of the translocation machinery that injects CagA into cells.

They demonstrated that animals infected with *H. pylori* strains containing mutations in the CagY gene did not develop stomach cancer.

This finding, Wilson said, supports using DFMO or other tools to reduce *H. pylori* virulence for cancer prevention.

"This drug (DFMO), which inhibits a very specific enzymatic pathway, also has what some might call 'off target' effects: it causes mutations in an *H. pylori* gene that affects the translocation of CagA," Wilson said. "The vast majority of gastric cancer is associated with strains that are CagA-positive. If this drug interferes with CagA activity, that's an added bonus."

The investigators will analyze *H. pylori* strains isolated from the DFMO trial participants in Honduras and Puerto Rico to determine if there is a similar reduction of bacterial virulence in people.

This research was supported by the National Institutes of Health (grants CA190612, CA116087, CA028842, AT004821, AT006896), a Veterans Affairs Merit Review Award, the American Heart Association, the Thomas F. Frist Sr. Endowment and the Vanderbilt Center for Mucosal Inflammation and Cancer.

http://bit.ly/2V3vJlm

Dogs Detect the Scent of Seizures

These very good dogs are very good at what they do—taking a whiff of a chemical during an attack

By Emily Willingham

Although most of us don't know it, humans emit hundreds of odor compounds that waft into the air around us. As our bodies change with age, disease and reproductive status, this cloud of volatile chemicals changes, too. What we sweat, secrete and exhale documents the ever-changing landscape inside of us.

As far back as 400 B.C., Hippocrates took note of how some of these odors, especially in urine, reflected disease. But the human olfactory

sense—even that of Hippocrates—has nothing on the capacity of the canine nose for detecting smells. And of course, once humans figured that out, we sought to co-opt it for our own uses.

Some dogs have undergone training to detect significant blood sugar changes in people with diabetes or even identify melanoma or prostate cancer with a quick whiff of skin or urine. And then there are the SADs, or seizure-alerting dogs. Their anecdotal ability to detect an oncoming seizure in a beloved human and alert their owners set off a flurry of investigations into the secrets behind their skill. Among the candidates: seizure-specific scent detection.

Now a quintet of canines—Casey, Dodger, Lana, Zooey and Roo—have answered the question of whether or not seizures have odors. It turns out that they do, and these five dogs can detect that smell in a sample swabbed from a human having an episode. Some of the trained detector dogs are better than others—we're looking at you, Lana and Roo—but they all did well, according to findings published March 28 in *Scientific Reports*. "The obtained accuracy is very high," says Tim Edwards, behavioral analyst and senior lecturer at the University of Waikato in Hamilton, New Zealand, who was not involved in the study. "As far as implications go, the results are very exciting."

Craig Angle, co-director of the Canine Performance Sciences Program in the College of Veterinary Medicine at Auburn University, isn't surprised by the dogs' ability to suss out seizure from non-seizure samples. "The dog is a natural bio sensor, preprogramed with 30,000 years of evolutionary algorithms, and 300 million sensory receptors," says Angle, who also was not involved in the study. A dog brain can detect "massive amounts" of chemical information at thresholds that are much lower than any machines.

To establish whether or not seizures have a smell, Amélie Catala, a doctoral student at Ethos, a center studying animal and human ethology at the Universtity of Rennes, and her colleagues trained Casey, Dodger, Lana, Zooey and Roo as SADs. Learning to be a SAD is a three-step process, starting with positive detection of a seizure scent in association with something pleasant, like a treat or praise. The dogs then learn to discriminate a lab sample of a scent from other potentially confounding odors added in. Their final challenge was to detect a seizure scent placed on a person—one signal out of those hundreds of chemical odors wafting from the human body.

The five SADs then evaluated a series of samples from people they'd never met—or smelled—some taken during a seizure, some after physical exercise, and some just during random moments of the day. After participants wiped their foreheads, hands and necks with cotton pads, they dropped the pad in a ziplock bag, exhaled into the bag and sealed it. These samples were placed in steel cans in groups of seven, and the SAD team went about the work of detecting which ones were taken during a seizure.

Casey, Dodger and Zooey were superstars, getting it right 100 percent of the time and in under five minutes. The other dogs were correct at least 67 percent of the time, and the entire SAD team performed well even with multiple trials. Catala says that the slightly reduced accuracy of Lana and Roo might trace to their having joined the team later and having a little less training.

Because the seizure samples were from patients having different kinds of seizures, the findings suggest that the odor the dogs detected is something common among all seizure episodes, says Edwards. Catala's team noted that being able to generalize across different types of epilepsy was an unexpected but welcome finding.

How does a seizure go from the brain to an odor the body emits? Angle says that the body produces signature odor chemicals that pass into the bloodstream and then into our breath, sweat and urine. The seizure scent that the SADs detected might reflect a change in cell

processes during a seizure that in turn alters the odors the person emits, he says.

The next step for Catala and her team is to use human skills to figure out what exactly is in those emissions. Chemical analyses can separate the various compounds to pinpoint what might differ between seizure- and non–seizure-related samples. Whether or not technology can match a dog remains in question. Dogs can smell in the parts per trillion range, says Angle, which might far exceed what even the most sophisticated machines can detect. Edwards agrees. “It’s likely that dogs are still more sensitive than our most sensitive analytical devices,” he says.

Nevertheless, if dogs can detect seizure odors, Edwards is hopeful that eventually, humans can sub in artificial intelligence (AI) to do the job. Angle and other researchers at Auburn have been imaging the canine olfactory system with the same goal in mind. “If you want to build an AI-based chemical detection system, why not study the most sensitive and advanced real-time chemical detection system on the planet, the dog,” says Angle.

http://bit.ly/2FHCRqu

Could dogs be the source of a new flu?

Results from a 10-year study suggest two strains of influenza that could mix and form a dangerous new strain of influenza spread by dogs.

by Microbiology Society

Dr. Daesub Song, Associate Professor (Korea University, Republic of Korea) has called for closer monitoring of dogs and other companion animals as they could be a source of novel human influenza strains. He said, "Until now, dogs were considered neglected hosts in the field of flu research. However, after the first report of interspecies transmission, surveillance of flu viruses from companion animals should be further strengthened."

In the 2000s, several cases of viruses crossing the host barrier were recorded. Most notably, H3N2 bird flu crossed over to dogs and developed into Canine Influenza virus (CIV). Dr. Song's research has found that this H3N2 CIV could combine with H1N1/2009 and form a new influenza virus, called CIVmv.

The emergence of new species of influenza such as this is concerning. Those infected will have not come into contact with a virus like this before, meaning they would not have immunity to the disease. If the virus could be carried and spread to humans from companion animals, it could have the potential to spread throughout the population extremely quickly.

H1N1/2009 is known for causing the 2009-2010 global 'swine flu' pandemic. When this strain of influenza combines with CIV in dogs, some of the viruses recombine to form CIVmv. Although CIVmv is very similar to CIV, researchers have calculated there is a much higher risk of the disease spreading to humans due to its high infection rates in ferrets.

Viruses bind to host cells and cause infection via sialic acid (SA) receptors, which differ between species. Ferrets have very similar SA receptors to humans. Because of this, ferrets are considered themost reliable experimental model for predicting and evaluating the risk of novel human influenza viruses.

During their studies of the new CIVmv strain, Dr. Song noted that infected dogs and ferrets displayed typical symptoms of respiratory disease, including congestion, breathing difficulties, coughing, runny eyes, sneezing, lethargy, and appetite loss. As well as these symptoms, Dr. Song reported the new strain spread between ferrets more quickly than other influenza viruses and replicated quickly.

Researchers are trying to develop a vaccine for the virus. However, due to the high level of mutations, vaccines are very difficult to develop.

Despite being named Canine Influenza Virus, it is not just dogs that can be infected by CIV. During the ten-year study, researchers found that cats were also susceptible to the virus. Dr. Song investigated an outbreak of CIV in an animal shelter, during which 100% of the cats were infected and 40% died.

The development of susceptibility in cats is worrying as it shows that CIV can spread amongst different animal species. Researchers have raised concerns as there is a potential for the virus to become endemic in companion animals. As both dogs and cats are in frequent contact with humans, much more frequently than pigs or chickens, the potential risk for a new strain to develop and infect humans is even higher.

Since being first identified in South Korea, CIV has spread to China, Thailand and USA. A case of CIVmv infection was identified in a dog in 2012 following an epidemic of H1N1. Dr. Song used this strain in ferrets to determine whether it had the potential to spread from canines to humans. From there, a novel human influenza strain could emerge. Dr. Song said, "Pre-existing CIV may recombine or reassort with human influenza viruses and give rise to novel viruses that could in turn lead to unique pandemics."

http://bit.ly/2U4vrOF

The Worst Disease Ever Recorded

A doomsday fungus known as Bd has condemned more species to extinction than any other pathogen.

Ed Yong

A century ago, a strain of pandemic flu killed up to 100 million people—5 percent of the world's population. In 2013, a new mystery illness swept the western coast of North America, causing starfish to disintegrate. In 2015, a big-nosed Asian antelope known as the saiga lost two-thirds of its population—some 200,000 individuals—to what now looks to be a bacterial infection. But none of these devastating infections comes close to the destructive power of Bd—a singularly apocalyptic fungus that's unrivaled in its ability not only to kill animals, but to delete entire species from existence.

Bd—*Batrachochytrium dendrobatidis* in full—kills frogs and other amphibians by eating away at their skin and triggering fatal heart attacks. It's often said that the fungus has caused the decline or extinction of 200 amphibian species, but that figure is almost two decades out-of-date. New figures, compiled by a team led by Ben Scheele from the Australian National University, are much worse.

Scheele's team estimates that the fungus has caused the decline of 501 amphibian species—about 6.5 percent of the known total. Of these, 90 have been wiped out entirely. Another 124 have fallen by more than 90 percent, and their odds of recovery are slim. Never in recorded history has a single disease burned down so much of the tree of life. "It rewrote our understanding of what disease could do to wildlife," Scheele says.

"It's a terrifying summary," says Jodi Rowley from the Australian Museum. "We knew it was bad, but this really confirms how bad. And these are just the declines we know about."

The Toad Mountain harlequin frog is endangered and at risk from the Bd fungus. **B. Gratwicke / Smithsonian Conservation Biology Institute**

The scale of these losses can be hard to appreciate, especially if you think that a frog is a frog is a frog. But amphibians are ancient survivors that have been diversifying for 370 million years, and in just five decades, *one disease* has nearly decimated their ranks. Imagine if a new disease started wiping out 6.5 percent of all *mammal* species—that would be roughly everything with hooves and everything with flippers. The world would freak out.

And amphibian experts "have been freaking out a long time," says Karen Lips from the University of Maryland, who was involved in

the new study. “Despite all the attention, I don’t think we fully appreciate what was lost.”

In the 1970s and ’80s, amphibian experts began sharing ominous anecdotes about once-plentiful populations that had mysteriously disappeared. Streams once full of eggs were clear. Nights once resonant with *ribbit*s were silent. Nothing about the habitats had changed, save for their sudden, inexplicable froglessness. No one knew what the problem was, let alone the culprit. “It was more than a search for a needle in a haystack—we were still debating the existence of the haystack,” Lips wrote recently. Steele’s analysis shows that by the point the fungus was finally identified, in 1998, it had already done the brunt of its lethal work. At least 60 species were already extinct, and hundreds more were going south.

Bd is perhaps the perfect frog killer. It kills with gusto and without fuss. While some diseases affect only specific hosts, Bd covets nutrients found across amphibian skins, and so targets the entire group indiscriminately. It spreads easily through the water, and it persists outside its hosts.

The fungus hasn’t acted alone; humans have been its unwitting accomplice. A genetic study led by Matthew Fisher from Imperial College London suggested that Bd had originated somewhere in Asia. From there, one especially virulent and transmissible strain spread around the world in the early 20th century—a time when international trade was booming. Infected animals could have stowed away aboard ships, or been deliberately transported as food, pets, or pregnancy tests. Either way, the killer strain eventually spread to five other continents.

In the new study, Scheele’s team compares the modern world to Pangaea—the single, epic supercontinent that existed at the dawn of the dinosaurs. It has long split up, but humans have effectively re-created it. For wildlife diseases, all the world is once again a single connected mass, easily traversed. For that reason, new fungal diseases seem to be emerging at an ever-increasing pace, affecting bats, snakes, salamanders, and more. “These fungi would normally have fried on a sailing craft across the Atlantic, but now they’re viable,” Scheele says. “We’re just able to move things around at higher speed and volume than we used to.”

Humans have also repeatedly sown islands with introduced hunters such as cats, rats, and mongooses, to the detriment of local fauna. In many ways, it’s more fitting to think about Bd as one of these introduced predators—and perhaps the most destructive that people have ever unleashed. “Cats have been a plague on biodiversity over generations, and they eat everything,” Scheele says. “And yet Bd, whose impact we have only been able to measure for decades, already far outstrips the cats and rats in terms of the species affected.”

The comparison is especially apt because once in a new place, Bd is hard to dislodge. A typical disease might cause an epidemic and burn out, only to be later reintroduced from a reservoir. But once Bd arrives, it doesn’t fade out, and it cannot be removed. Like rats on islands, it becomes a nigh-permanent fixture of the areas it invades.

Limiting its movements remains the best strategy, and that means curbing the wildlife trade. “Moving wildlife around the globe can and does have devastating consequences,”Rowley says. “There’s more awareness of the impact of invasive species like cane toads and rabbits, but this paper highlights that it may be the inadvertent hitchhikers—the parasites and pathogens we don’t see—that cause the most biodiversity loss.”

Encouragingly, the pace of decline has eased. Better still, 60 species have begun to show glimmers of recovery. But no one knows whether this means that frogs have managed to eke out an evolutionary truce with Bd, or whether further outbreaks are to come. That’s possible if the fungus makes it to Papua New Guinea—a thus far Bd-free stronghold that is heaving with amphibians. The virulent,

globe-hopping strain has also hybridized with indigenous varieties, raising concerns that hybrids could behave unpredictably.

"There's no obvious way to deal with this," Lips says. Some researchers have set up captive-breeding programs to buy time for species in contaminated habitats. Others are looking at ways of manipulating the fungus, or breeding more tolerant frogs, or pairing the frogs with defensive bacteria, or relocating frogs to sites that are inhospitable to the fungus. None of these solutions is a silver bullet, and none is close to readiness. "It says a lot about the scary nature of the disease that even after intense, long-term collaborations we haven't come up with a viable solution," Lips adds.

https://bbc.in/2I24SlN

Chicxulub asteroid impact: Stunning fossils record dinosaurs' demise

Scientists have found an extraordinary snapshot of the fallout from the asteroid impact that wiped out the dinosaurs 66 million years ago.

By Jonathan Amos BBC Science Correspondent

Excavations in North Dakota reveal fossils of fish and trees that were sprayed with rocky, glassy fragments that fell from the sky.

The deposits show evidence also of having been swamped with water - the consequence of the colossal sea surge that was generated by the impact. The detail is reported in PNAS journal.

The seismic shockwave would have triggered a water surge, known as a seiche **Robert DePalma**

Robert DePalma, from the University of Kansas, and colleagues say the dig site, at a place called Tanis, gives an amazing glimpse into events that probably occurred perhaps only tens of minutes to a couple of hours after the giant asteroid hit the Earth.

When this 12km-wide object slammed into what is now the Gulf of Mexico, it would have hurled billions of tonnes of molten and vaporised rock into the sky in all directions - and across thousands of kilometres. And at Tanis, the fossils record the moment this bead-sized material fell back down and strafed everything in its path.

Fish are found with the impact-induced debris embedded in their gills. They would have breathed in the fragments that filled the water around them.

There are also particles caught in amber, which is the preserved remnant of tree resin. It is even possible to discern the wake left by these tiny, glassy tektites, to use the technical term, as they entered the resin.

Geochemists have managed to link the fallout material directly to the so-called Chicxulub impact site in the Gulf. They have also dated the debris to 65.76 million years ago, which is in very good agreement with the timing for the event worked out from evidence at other sites around the world.

Fossilised fish piled one atop another as they were flung ashore by the seiche **Robert DePalma**

From the way the Tanis deposits are arranged, the scientists can see that the area was hit by a massive surge of water.

Although the impact is understood to have generated a huge tsunami, it would have taken many hours for this wave to travel the 3,000km from the Gulf to North Dakota, despite the likely presence back then of a seaway cutting directly across the American landmass.

Instead, the researchers believe local water could have been displaced much more quickly by the seismic shockwave - equivalent to a Magnitude 10 or 11 earthquake - that would have rippled around the Earth. It is a type of surge described as a seiche, which would have picked up everything in its path and dumped it into the jumbled collection of specimens now being reported by the team.

Dating the tektites gives an age for the impact - 65.76 million years ago

Robert DePalma

"A tangled mass of freshwater fish, terrestrial vertebrates, trees, branches, logs, marine ammonites and other marine creatures was all packed into this layer by the inland-directed surge," said Mr DePalma.

"A tsunami would have taken at least 17 or more hours to reach the site from the crater, but seismic waves - and a subsequent surge - would have reached it in tens of minutes," he added.

By The New York Times | Sources: PNAS; Geological Society of America

The PNAS paper, which will go online on Monday, includes among its authors Walter Alvarez, the Californian geologist who, with his father Luis Alvarez, is credited with helping to develop the impact theory for the demise of the dinosaurs.

The Alvarez pair identified a layer of sediment at the boundary of the Cretaceous and Palaeogene geological periods that was enriched with iridium, an element commonly found in asteroids and meteorites.

Iridium traces are also found to be capping the Tanis deposits.

"When we proposed the impact hypothesis to explain the great extinction, it was based just on finding an anomalous concentration of iridium - the fingerprint of an asteroid or comet," said Prof Alvarez. "Since then, the evidence has gradually built up. But it never crossed my mind that we would find a deathbed like this."

Phil Manning, from the University of Manchester, the only British author on the paper, commented: "It's one of the most important sites in the globe now. You know, if you truly wanted to understand the last day of the dinosaurs - this is it," he told BBC News.

https://bbc.in/2V9bwdU

Tasmanian devils 'adapting to coexist with cancer'

There's fresh hope for the survival of endangered Tasmanian devils after large numbers were killed off by facial tumours.

By Beth Timmins BBC News

The world's largest carnivorous marsupials have been battling Devil Facial Tumour Disease (DFTD) for over 20 years.

But researchers have found the animals' immune system to be modifying to combat the assault.

And according to an international team of scientists from Australia, UK, US and France, the future for the devils is now looking brighter.

"In the past, we were managing devil populations to avoid extinction. Now, we are progressively moving to an adaptive management strategy, enhancing those selective adaptations for the evolution of devil/DFTD coexistence," explains Dr Rodrigo Hamede, from the University of Tasmania.

First discovered in north-eastern Tasmania in 1996, the disease has since spread across 95% of the species' range, with local population losses of over 90%.

Dr Hamede's team has been collecting epidemiological evidence over the past 10 years. The group has plotted scenarios based on current infection rates in the wild, and in their forecast for the next 100 years, 57% of scenarios see DFTD fading out and 22% predict coexistence.

How does the disease spread?

The disease is transmitted when devils bite each other's faces during fights. The biting behaviour is a way to socialise and assert dominance which, alongside the growl-like screams, helped earn the devils their nickname.

"Our current hypothesis is that the biting doesn't only lead to the spread of tumours but it might be the starting point," explains Max Stammnitz, from the University of Cambridge, UK, who sequences tumour genomes. "If the scarring processes for the recurring wounds are interrupted by a mutation, this might become cancerous. It fails to heal and starts to grow out into an external tissue that may then become transmissible," Mr Stammnitz says.

After the bite, a solid tumour then grows around the face or neck, with the power to break bones in the jaw - killing the animal after 6 to 24 months. To worsen the crisis, in 2014, a second transmissible cancer (DFT2) was discovered in wild populations in the south of the island. "A second transmissible tumour in devils was extremely surprising, like lightning striking the devils twice," says Dr Hamede. But in the last 5-6 years, some devils have developed higher tolerance to infection and even resistance without human intervention, meaning that while population numbers have not recovered to pre-DFTD numbers, the decline has at least now levelled out.

How is natural selection helping?

"Natural selection is trying to fix the problem on its own by favouring those who can survive the tumour, so we're more hopeful these days than ever before," explains Dr Hamede.

The international team monitors eight sites across the east, south and west of the island every three months, observing multiple generations of devils. "We have witnessed how these tumours shape the ecology of devils and how they have been evolving with their hosts in real time," Dr Hamede says.

Devils can now adapt to the transmissible cancer at the genetic and phenotypic levels - meaning the DNA and characteristics of the gene traits. This is due to their phenotypic plasticity - the capacity of an individual organism to alter its physiology or gene expression in response to changing environmental conditions. And what's even more unique is how rapidly this has happened - in a matter of 16 years, over just eight devil generations.

"It's a constant arms race of adaptation between animals and diseases. We develop mechanisms of resistance which put pressure on pathogens to improve infection," Mr Stammnitz says. The first of these mechanisms is tolerance and the second is resistance.

The team has found devils that have lived for up to two years with the disease, allowing for two more litters to serve as population recruitment for the disease. In addition, 23 cases of tumour regression have been found so far - showing devils also have the capacity to fight and recover from DFTD.

What is the future for the devils?

The second largest threat to devils is roadkill, with a minimum of 350-450 devils killed each year according to Dr Fox from Save the Tasmanian Devil Programme (STDP).

Targeting hotspots, the STDP has installed fencing which sounds an alarm and warns wildlife of approaching cars. The current trial has led to a 50% reduction in roadkill since 2015.

The number of devils hit has dropped by a quarter and Tasmanian pademelons and Bennett's wallabies have also benefited. The government has also been trialling a new app since July that members of the public can use to report sightings to help monitor populations.

So far, the app has been downloaded by over 2,000 users who have entered 6,000 reports.

"When we tracked the start of DFTD in 2003, road kill reports by the public informed our knowledge of where it had spread showing the power of citizen science to help the devils," Dr Fox adds.

In the curious case of the Tasmanian devil, there is much still to be learned about cancer biology and the evolutionary arms-race between malignant cells and their hosts.

The sheer speed of the decline has created a strong selective pressure on the world's largest remaining carnivorous marsupial but it now seems hope could lie in co-existence.

http://bit.ly/2UlLPJM

Fat, Not Meat, May Have Led to Bigger Hominin Brains

A new theory challenges assumptions about when and how our ancestors altered their behaviors to boost brainpower.

Richard Kemeny

Northern Ethiopia was once home to a vast, ancient lake. Saber-toothed cats prowled around it, giant crocodiles swam within. The streams and rivers that fed it—over 3 million years ago, during the Pliocene—left behind trails of sediment that have now hardened into sandstone.

Deposited within these layers are fossils: some of early hominins, along with the bones of hippos, antelope, and elephants. Anthropologist Jessica Thompson encountered two of these specimens, from an area named Dikika, in 2010.

At the time, she was a visiting researcher at the Institute of Human Origins at Arizona State University. Given no explanation as to their history, she analyzed the bones and found signs of butchery. Percussion marks suggested someone may have accessed the marrow; cut marks hinted that flesh was stripped from bone. To her surprise, the specimens were 3.4 million years old, putting the butcher's behaviors back 800,000 years earlier than conventional estimates would suggest. That fact got Thompson, now an assistant professor in the department of anthropology at Yale University, thinking there might be more traces of tool use from those early times.

In a wide-ranging review published in February's issue of *Current Anthropology*, Thompson joins a team of researchers to weave together several strands of recent evidence and propose a new theory about the transition to large animal consumption by our ancestors.

The prevailing view, supported by a confluence of fossil evidence from sites in Ethiopia, is that the emergence of flaked tool use and meat consumption led to the cerebral expansion that kickstarted human evolution more than 2 million years ago. Thompson and her colleagues disagree: Rather than using sharpened stones to hunt and scrape meat from animals, they suggest, earlier hominins may have first bashed bones to harvest fatty nutrients from marrow and brains.

Humans are the only primate to regularly consume animals larger than themselves. This nutritional exploitation, something Thompson and her colleagues call the "human predatory pattern," has long been synonymous with the flesh-eating, man-the-hunter view of human origins.

Because large animals such as antelope pack a serious micro-and-macro-nutrient punch, scientists have thought their meat contributed to humanity's outsized brains. A consensus arose in the 1950s that our ancestors first hunted small animals before moving on to larger beasts around 2.6 million years ago. Flaked tool use and meat eating became defining characteristics of the *Homo* genus.

"It's a very appealing story," says Thompson. "Right around that time there appeared to be the first stone tools and butchery marks. You have the origins of our *Homo* genus. A lot of people like to associate that with what it means to be human."

Then, starting in the mid-1980s, an opposing theory arose in which *Homo*'s emergence wasn't so tightly coupled with the origins of

hunting and predatory dominance. Rather, early hominins first accessed brain-feeding nutrients through scavenging large animal carcasses. The debate has rolled on through the decades, with evidence for the scavenging theory gradually building.

The new paper goes further: Harvesting outer-bone meat would have come at significant costs, the authors argue. The chance of encountering predators is high when scraping raw flesh from a carcass. Chewing raw meat without specialized teeth doesn't give much energetic benefit, studies have shown. In addition, meat exposed to the elements will quickly rot.

In pursuit of nutrients from marrow and brain, early hominins likely smashed animal bones with percussive tools, such as the flint hammerstones in the top row. Flaked stone tools, such as the ax-head fragment in the lower photo, may have been crafted for other tasks. **Frank Basford/Wikimedia Commons (Top/Bottom)**

Marrow and brains, meanwhile, are locked inside bones and stay fresh longer. These highly nutritional parts are also a precursor to the fatty acids involved with brain and eye development. And more easily than flesh-meat, bones could be carried away from carcass sites, safe from predators.

Conventional thinking has been that the behavioral package of early hominins was to go after meat and marrow together, explains Briana Pobiner, a paleoanthropologist at the Smithsonian Institution, who did not contribute to the new paper. But in the new paper, she says, "This team has shown that marrow may have in fact been more important. It's a nuance, but an important nuance."

The Pliocene—between 5.3 and 2.6 million years ago—was an era of dramatic change. An intensely variable and cooling climate transformed vast swaths of rainforest into mosaics of grassland and savanna. Large clearings spawned ecological niches for opportunistic and versatile hominins like *Australopithecus*, a likely contender for the *Homo* ancestor, and *Kenyanthropus* to fill in. Larger predators may well have left carcasses for them to scavenge.

Evidence suggests hominins shifted their diet around 3.76 million years ago as they took advantage of the open spaces. By around 3.5 million years ago, some species of *Australopithecus* already showed increased brain sizes, up to 30 percent larger than chimpanzees of comparable body size. Canines had shrunk to proportions later seen in the genus *Homo*, and hand morphology was already more human than ape, with potential both for terrestrial travel and tool use.

Percussive tools, the authors argue, were the key to the transition to large animal exploitation. Rocks could bash open bones, exposing the marrow inside. The alternative—that humans sharpened stone against stone, creating a flaked tool to carve meat from bone—seems more onerous, they say. They argue that such meat carving and the associated tool creation would likely come later.

As to who wielded these percussive instruments, the timeline presents a puzzle. The earliest *Homo* specimen is now dated to 2.8 million years. The Dikika fossils suggest butchery behaviors at 3.4 million years ago. *Homo* may have emerged earlier than scientists suspected—a theory that would need more fossil evidence to support it—or another hominin, such as *Australopithecus*, may have created tools before *Homo*.

Some scholars aren't convinced by the study's arguments, however. For example, Craig Stanford, an anthropologist at the University of Southern California, questions the emphasis on hominin scavenging behavior appearing before hunting. "We have no examples today of animals that scavenge but don't hunt," he adds.

To test the new theory, the review authors suggest seeking out further evidence of percussive tools that predate flaked tools. Researchers could, they note, broaden the search for the signatures of such instruments within both the existing fossil record and at dig sites.

Thompson's graduate students, for example, are using 3D scanning and artificial intelligence techniques to improve the identification of marks on fossils—whether they were created by early hominins, saber-toothed cats, hyenas, or other types of creatures.

What they uncover could deal a blow to their theory, but it will also, undoubtedly, enrich our understanding of how our ancestors evolved.