http://bit.ly/2q3zG5F

# Stronger gun laws tied to decreased firearm homicides

***Review of 34 studies finds strongest evidence for laws that strengthen background checks and require a permit to purchase a firearm***

Stronger firearm laws are associated with reductions in firearm homicide rates, concludes a narrative review published in the November 14 issue of JAMA Internal Medicine.

Researchers at Boston Children's Hospital reviewed all available articles published in peer-reviewed journals from January 1970 to August 2016 that focused specifically on the connection between firearm homicide and firearm laws. Of the 582 abstracts found, only 34 met the criteria for inclusion. These 34 studies were weighted for quality and divided into five general categories: those that strengthened background checks, those that curbed firearm trafficking, those that improved child safety, those banning military-style assault weapons and those restricting firearms in public places.

"Overall, we found evidence that stronger firearm laws are associated with decreased homicides due to firearms," says lead author Lois Lee, MD, MPH, of Boston Children's Hospital's Division of Emergency Medicine and Harvard Medical School. "Specifically, the laws that seemed to have the most effect were those that strengthened background checks and those that required a permit to purchase a firearm."

Laws that banned assault weapons, improved child safety or aimed to limit firearm trafficking had no clear effect on firearm homicide rates. Laws that aimed to restrict guns in public places had mixed results, with some studies showing such laws reduce homicides and others not finding this result. However, the researchers point to the need for larger, longer-term studies to draw conclusive results.

"One of our most important findings is the lack of high-quality research on this topic, especially in relation to the major health impact gun violence has had in this country," says co- author Eric Fleegler, MD, MPH, also of Boston Children's Division of Emergency Medicine and Harvard Medical School. "Much of the research really didn't have access to or use the highest quality data or analysis. The quality, number and time frame of these studies is very limited; many didn't study the laws over a long enough time to see the full effects of these types of laws."

Despite these limitations, the findings are consistent with a study the team conducted in 2013, which found that states with stronger firearm legislation had decreased deaths, from both homicides and suicides, compared to states with weaker firearm laws.

"Gun legislation is a very important and controversial issue right now, but our findings show that some laws, specifically those to strengthen background checks and require a permit to purchase a firearm, will not deny people the right to bear arms, but will help protect the public," says Lee. "We hope our findings will help states draft legislation that is useful and sensible to both sides of the gun issue." The researchers also call for more federal support for gun-related research.

"When you look at other areas of injury prevention, such as motor vehicle safety, there are streams of data," says Fleegler. "There is no funding in health care for serious researchers who are trying to look at firearm data."

*This study was conducted without any specific funding.*

*Other authors of the study include Caitlin Farrell, MD, Elorm Avakame, BS, and Michael C. Monuteaux, ScD, of Harvard Medical School; David Hemenway, PhD, of Harvard School of Public Health; and Saranya Srinivasan, MD, of Texas Children's Hospital, Houston.*

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# Homicide rates rise after introduction of 'Stand Your Ground' self-defense law

***A change in self-defense laws in Florida which gave citizens the right to use lethal force to protect themselves in public has been linked with the state's homicide rates going up by nearly a quarter***

A change in self-defence laws in Florida which gave citizens the right to use lethal force to protect themselves in public has been linked with

the state's homicide rates going up by nearly a quarter, according to a new study published in JAMA Internal Medicine.

The research, led by the University of Oxford with the London School of Hygiene & Tropical Medicine and the University of Pennsylvania, looked at homicide rates before and after the enactment of State Bill 436, known as the Stand Your Ground law, which was signed by Governor Jeb Bush in 2005.

Before 2005, Florida's so-called 'Castle doctrine' allowed the use of lethal force in situations where individuals believed there was an imminent threat of death or serious physical harm from an intruder within their own home. The 2005 Bill extended the 'no duty to retreat' clause of the Castle doctrine, giving individuals immunity for using lethal force to defend themselves in public places, as well as on private property.

Prior to the introduction of the law, Florida (pop. 19.8 million) had on average 82 homicides per month, of which 49 deaths per month on average resulted from firearm-related injuries. The study says this change in the law is associated with homicide rates in Florida rising by 24% over 2005-2014 (compared with 1999-2004). Rates of homicide involving firearms specifically, went up even more- by 31%. Meanwhile, elsewhere in the United States, homicide rates in general have been declining since the 1990s, says the paper.

The researchers examined publicly available data showing monthly totals of homicides - in total and for firearm-related cases only - for January 1999 to December 2014. Increases in homicide rates in Florida affected all the demographic groups examined, with the largest proportional rises in the 20-34 age group (which went up by 31%) and among the white population (which rose by 28%). A 20% increase was also found among African-Americans, says the paper.

The researchers considered a number of explanations: Firstly, they examined and found no significant changes in homicide rates with or without the involvement of guns in four US states that had not enacted a Stand Your Ground law over the same period of time (1999-2014) - New York, New Jersey, Ohio and Virginia. Secondly, they tested whether the global recession of 2008-09 could have contributed to the observed rise in violence, examining outcomes known to be sensitive to economic shocks but unlikely to be affected by changes in self-defence laws. However, they found suicide rates in Florida between 2005 and 2014 did not rise significantly, so the research concludes that the recession was not the major factor associated with the rise in homicides in Florida.

Lead author Dr David Humphreys, Associate Professor of Evidence-Based Social Intervention and Policy at the University of Oxford, said: 'For some time, critics of Stand Your Ground laws have been concerned that laws extending the rights of citizens to use lethal force are likely to result in increased homicide and injury rates. Given Florida was the first state to extend the use of lethal force in this way, it is an important test case that many other states have since followed. Our study shows that the enactment of the law is linked with a sudden reversal in the decline in homicide rates and homicide rates have risen particularly where guns are involved. We hope these findings will inform the ongoing debates about the implications that Stand Your Ground laws may have for public safety in Florida and other US states.'

Co-author Dr Antonio Gasparrini at the London School of Hygiene & Tropical Medicine added: 'Stand Your Ground laws have been implemented across US states since 2005. Surprisingly, in spite of controversy surrounding guns and gun law in the US, very little research analysing its introduction has been conducted. This study highlights how Stand Your Ground is likely to be a cause of the rise in Florida homicides, and provides crucial information which may influence future decision-making that affects wellbeing in the US and abroad.'

Dr Douglas Wiebe at the University of Pennsylvania, also a study co-author, commented: 'The findings are strong evidence that by extending the "no duty to retreat clause", this change to the law in

Florida led to deaths that otherwise would not have occurred. We need to think about the implications of these findings and Florida should consider reversing this decision that appears to have increased the use of lethal force.'

*The paper, 'Evaluating the impact of Florida's 'Stand Your Ground' self-defense law on homicide and homicide by firearm: an interrupted time series study', will be published in the journal, JAMA Internal Medicine.*

*Florida's stand-your-ground law increases the scope of self-defence claims by creating a 'no duty to retreat' rule when individuals 'reasonably believed' that force was necessary to prevent harm to themselves or others. It was extended to public places as well as private property, and created a series of conditions to strengthen the defence of anyone who used lethal force to protect their private property and who initiated the confrontation. It also entitled defendants to pre-trial immunity hearings, allowing judges to sanction immunity prior to jury trial and provide defendants with immunity from ensuing civil lawsuits.*

*The research team accessed data relating to homicides through the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research web portal. It provides access to public health information for state and local health departments, the Public Health Service, and the academic public health community. The researchers categorised the data according to whether deaths occurred within or outside the State of Florida, by cause of death (homicide or suicide), mode of death (firearms or other means), and month.*

***https://www.eurekalert.org/pub_releases/2016-11/jj-ici111316.php***

## Heater-cooler devices blamed for global Mycobacterium chimaera outbreak

### *Cardiac surgery patients in various countries have been infected by M. chimaera*

NEW YORK - A global outbreak of Mycobacterium chimaera, an invasive, slow-growing bacterium, is linked to heater-cooler devices (HCD) used in cardiac surgery, according to a study published today in Infection Control & Hospital Epidemiology, the journal of the Society for Healthcare Epidemiology of America. This study adds interim guidance to recent field reports on the outbreak, providing precautionary recommendations to hospitals and health systems to reduce the risk of infections.

"It is surprising that a global outbreak like this could go unnoticed for years. This dangerous infection has put many patients at risk all over the world," said Rami Sommerstein, MD, of Inselspital, Bern University Hospital in Switzerland, the lead author of the study. "Now that we know HCDs are the source, individual action from the different players (healthcare institutions, manufacturers, etc.) is needed to contain the ongoing patient risk. The most important action a hospital can take is to remove contaminated HCDs from the operating room and other critical areas. That is the only way to ensure that patients are protected from this infection moving forward."

HCDs are stand-alone devices needed for heat exchange in heart-lung machines used in some 250,000 surgeries annually in the U.S., according to the Centers for Disease Control and Prevention. In response to an increasing number of infections, investigators looked into hospital water sources and found M. chimaera in HCD water circuits - specifically, in the LivaNova 3T HCD used in most hospitals around the world. They also found the bacteria in air samples during surgeries with LivaNova HCDs, suggesting transmission through air particles.

To prevent future cases of invasive M. chimaera infections, the researchers made the following recommendations for hospitals and health systems, as well as public health authorities, based on their personal experience with the outbreak:

***Ensure strict separation of contaminated HCDs from air of critical medical areas***

***Educate clinicians on the risks for and dangers associated with M. chimaera***

***Screen patients who had open heart surgery, heart transplantation or those who were exposed to ventricular assist devices and demonstrate prolonged and unexplained fevers.***

M. chimaera is a non-tuberculous mycobacterium that was previously known to cause lung infections. Invasive M. chimaera in cardiac surgery patients is particularly difficult to treat because it requires surgery and prolonged antibiotic therapy.

"While our understanding of the causes and the extent of the M. chimaera outbreak is growing, several aspects of patient management, device handling and risk mitigation still require clarification," said Sommerstein.

*Rami Sommerstein, Peter Schreiber, Daniel Diekema, Michael Edmond, Barbara Hasse, Jonas Marschall, Hugo Sax. "Mycobacterium chimaera Outbreak Associated with Heater-Cooler Devices - Piecing the Puzzle Together." Web (November 14, 2016).*

***http://bit.ly/2fE12Bj***

## Study reveals 82 percent of the core ecological processes are now affected by climate change

### *Global changes in climate have already impacted every aspect of life on Earth*

Most studies of global climate change attempt to predict what might happen to the Earth as temperatures rise in future. A new study representing an international collaboration by ecologists and conservation biologists shows that global changes in climate have already impacted every aspect of life on Earth, from genes to entire ecosystems. It was published in the prestigious journal Science on November 10, 2016.

The research team, led by the University of Florida and with participation from the University of Hong Kong, showed that of a total of 94 ecological processes evaluated globally, 82% of them showed evidence of impact from climate change. Land, freshwater and marine ecosystems and species have all been all affected, and consequential impacts on people could range from increased pests and disease outbreaks, to unpredictable changes in fisheries and decreasing agriculture yields.

This study is released at an important moment as it helps shed light on the need to plan practically for the implementation of the Paris agreement on climate change which entered into force last Friday (November 4, 2016). The Paris agreement marked the first time that governments have agreed binding limits to keep global warming well-below two degrees Celsius above pre-industrial levels. That agreement was overdue: the World Meteorological Organization announced on Wednesday (November 9, 2016) that the 2011-15 had been the five hottest years on record, with temperatures peaking in 2015.

"We now have evidence that, with only a ~1 degree Celsius of warming globally, major impacts are already being felt in natural systems," said study lead author Dr Brett Scheffers of the University of Florida. "Genes are changing, species' physiology and physical features such as body size are changing, species are moving and we see clear signs of entire ecosystems under stress, all in response to changes in climate on land and in the ocean".

"Some people didn't expect this level of change for decades," said co-author Dr James Watson, of the University of Queensland in Australia. "The impacts of climate change are being felt with no ecosystem on Earth being spared. It is no longer sensible to consider climate change as a concern just for the future."

"The paper shows that there are winners and losers under global warming: the geographic ranges of some species have expanded while others have contracted, and timing of breeding and other seasonal events have shifted," said co-author, Professor David Dudgeon, Chair of Ecology & Biodiversity and Director of the School of Biological Sciences at the University of Hong Kong.

This study has significant implications for Hong Kong. According to Professor Dudgeon, we can envisage that endemic species - found nowhere else but Hong Kong - will have little chance to make compensatory range shifts in response to climate change. The Hong Kong paradise fish and the short-legged toad are examples of species that would be unable to adjust their ranges due to intense urbanization around the sites they occupy currently. If conditions change, they must adapt or perish.

The Hong Kong newt, which breeds only during the coolest months of the year, would also likely fall victim to warming since, in future, winter temperatures might not fall sufficiently to permit reproduction by this species which is, already, globally near-threatened. Mountain-top animals such as the giant spiny frog, already mainly confined to

streams near the summit of Tai Mo Shan and globally vulnerable to extinction, would have nowhere to go as the climate warms.

"The new paper shows a pervasive ecological finger print of only 1 degree Celsius of global warming. This will not be beneficial for local species of conservation concern." On a global scale, Dudgeon added, "we face an uncertain ecological future as the temperature continues to rise, especially if warming exceeds the 1.5-degree boundary incorporated in the Paris climate-change agreements that came into force last week. Such warming would put at risk biodiversity and the ecosystem services delivered by nature that benefit humans".

Dudgeon concluded: "To put it bluntly, climate change is already happening, and it is altering ecological process and natural systems everywhere. We must to do more to limit carbon emissions and prevent further warming."

*DOI for this paper, The broad footprint of climate change from genes to biomes to people, is 10.1126/science.aaf7671*

***http://bit.ly/2q4GT8e***

## Dan Rather: Now, More Than Ever, We Must Stand Up for Science

***The Trump administration is outlining policies that put our response to climate change in deep jeopardy and threaten to change the fundamental direction of science in the U.S.***

**By Dan Rather on November 14, 2016**

When historians look back at the presidential election of 2016 they will certainly have many questions, but perhaps the biggest one isn't getting enough attention today. "What the (insert the popular profanity of the future)?" they will likely ask. "Why was there hardly any mention of climate change?" Or will the future inhabitants of Earth be so distracted by survival that they won't even care what happened in 2016 when the greatest country on the planet at that time denied this problem existed?

With just a few mentions in speeches—and, jaw-droppingly, no questions at the presidential debates—this omission marks a singular failure of the press and the political class. But it is indicative of a much broader systemic rot. Make no mistake; science was on the ballot this fall. And almost nobody took notice. But they should now because the Trump Administration is outlining an aggressive policy portfolio that not only puts our global response to climate change in deep jeopardy but that also threatens to radically change the fundamental direction of science in the United States.

The political press treats science as a niche issue. But I would argue that it is central to America's military and economic might, that it shapes the health and welfare of our citizenry, and that our governmental support of the pure pursuit of knowledge through basic research is one of the defining symbols of American excellence. Science bolsters our global stature by its institutionalized respect for the truth, its evidence-based decision-making, and its willingness to accept differing opinions when the facts dictate them.

This is why we need to radically rethink how the press, scientists and politicians place science in the national discourse. And we can't afford to wait. The top priority must be for scientists to try to engage the incoming administration. While the early indications of how a President Trump may approach issues of science are concerning, we cannot afford not to try. I would suggest that a group of Nobel Prize winners, members of the National Academy of Sciences and other scientific leaders who may get his attention, offer to meet with the President-elect to lay out what they think the biggest issues are. Top of the list is to assert the special role of science in planning for our future, especially, of course, when it comes to climate change.

Polling suggests that the public is not as rigid on issues of science as our recent political divide might suggest. Historically a strong science policy has been a place of bipartisan cooperation. Perhaps, with a President who owes little political capital to a national party, we can embrace a form of decision-making that has traditionally been apolitical and begin to base more of our policies on science. Perhaps our new President can be persuaded to listen to topics on which he

hasn't thought deeply. Perhaps he can see this as a way to rebuild America's agriculture, manufacturing, and technology sector for the benefit of all. Of course this outreach effort may go nowhere. But we would be foolhardy not to try. Now is not the time for the scientific community and the new political leadership to withdraw from each other. If they do, each of them, and the rest of the country as well, will be damaged.

But scientists need an ally in making their case, and that must come from an active and involved press. The press can build bridges between the scientific community, the public, and elected officials. It can raise awareness of important issues and put pressure on obfuscating politicians. This posture for the press has been its role throughout the history of our democracy, and it must extend to a robust coverage of science. If science fails to engage with the leadership and with the people, the press will share a large part of the responsibility.

I would suggest that contrary to the general view in newsrooms, science stories are often very popular and could be a way to expand audience and reach. The problem I have long worried about is that there are not nearly enough editors and reporters with scientific training reporting and writing the news in America. The importance of this training isn't only a matter of getting the facts right about science, it's about understanding the spirit and process of discovery, the culture of the research enterprise and the relevance of science to so many other stories. The newsrooms that do cover science often turn to medical doctors. There is nothing wrong with that, but looking at almost all of at least the life sciences through the lens of human health is too limiting. It makes science seem reductive and constrained, rather than focusing on the exciting, innovative, and widespread applications of scientific research in improving our everyday lives.

What we need is sustained and improved partnerships between the press and the scientific community. We need more cross-pollination and engagement. We need experimentation on form, tone, content, and distribution. We cannot allow science content to be relegated to echo chambers or elite distribution outlets. We need to try to find a way to take the message to where the people are, through digital promotion, distribution and social media engagement.

I firmly believe science to be of the utmost importance to the world that I want my children and grandchildren to inherit. I believe it is a way to connect different groups, nations, and generations. I believe that scientists have more power in the public marketplace of ideas than they may realize. I refuse to believe that the moral weight of fact-based research has no place in what can seem like a post-truth era. All it takes is a Zika virus or the discovery of a new cancer treatment and the world comes pounding on the doors of the academy demanding relief.

I do not have much training in science. When I learned biology in school, Watson and Crick still hadn't discovered the structure of DNA. But as a journalist, I have realized that science is one of the biggest and most important stories of our age. Don't get me wrong, there is some wonderful science journalism being done, especially in new forms emerging online and in such things as podcasts. But there needs to be much more of it and it must be more prominently distributed. At this point in my life, I am determined to make a contribution. I have teamed up with researchers and science-minded storytellers to try to shift this dynamic. I hope to have more news on that in the months ahead. But this is a cause that must be bigger than any one single effort. I am eager to lend my name and voice, as well as organizational support, reporting, production, promotion, and any other contribution I can make. But we will need as much help as possible.

In the end, science is about hope; it's about expanding our horizons, and endeavoring to understand more. It is an instinct so deeply human, and an instinct we need now more than ever. An enterprise this core to our national future must enlist all who can help from the world of journalism and science. The public and the policymakers need to hear

this message. Science creates self-evident truths that everyone can own. I believe the world is ready to listen if we can only find a better way to speak.

The views expressed are those of the author(s) and are not necessarily those of Scientific American.

***ABOUT THE AUTHOR(S)***

*Dan Rather spent 24 years as Anchor and Managing Editor for CBS News, and served as a correspondent for 60 Minutes. He has interviewed every President since Eisenhower, and covered major stories from Kennedy Assassination and Civil Rights movement to 9/11 and the invasion of Iraq. He is the founder of News and Guts, production company committed to bringing important stories to life across a variety of media and genres.*

***http://bbc.in/2q4MP0Z***

## Dementia now leading cause of death

***Dementia, including Alzheimer's disease, has overtaken heart disease as the leading cause of death in England and Wales, latest figures reveal.***

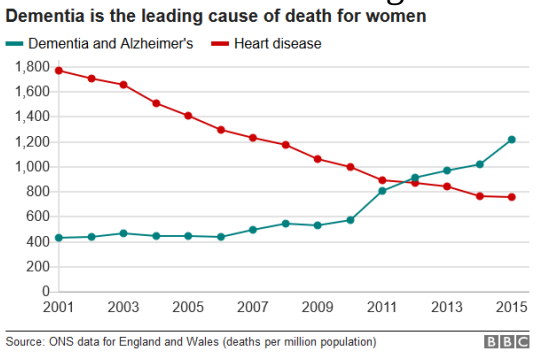
Last year, more than 61,000 people died of dementia - 11.6% of all recorded deaths. The Office for National Statistics says the change is largely due to an ageing population.

People are living for longer and deaths from some other causes, including heart disease, have gone down. Also, doctors have got better at diagnosing dementia and the condition is now given more weight on death certificates.

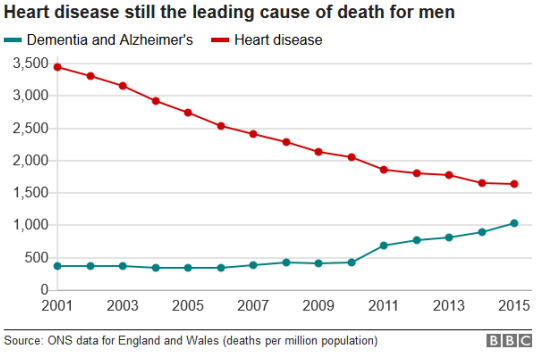
The bulk of the dementia deaths seen were among women - 41,283, compared to 20,403 dementia deaths in men in 2015. Dementia, including Alzheimer's disease, accounted for 15.2% of all female deaths, up from 13.4% in 2014. For men, however, heart disease remained the leading cause of death in 2015.

All types of cancer as a group was still the most common cause of death overall. In the youngest age group, aged five to 19, suicide was the leading cause of death. Among women aged 35 to 49, breast cancer was the biggest killer.

Hilary Evans of Alzheimer's Research UK said: "These figures once again call attention to the uncomfortable reality that currently, no-one survives a diagnosis of dementia.




"Dementia is not an inevitable part of ageing, it's caused by diseases that can be fought through research, and we must bring all our efforts to bear on what is now our greatest medical challenge."




Martina Kane of the Alzheimer's Society said: "It is essential that people have access to the right support and services to help them live well with dementia and that research into better care, treatments and eventually a cure remain high on the agenda."

There are around 850,000 people living with dementia in the UK.

### Warning signs of dementia

Seek medical advice if your memory loss is affecting daily life and especially if you:

***struggle to remember recent events, although you can easily recall things that happened in the past***

***find it hard to follow conversations or programmes on TV***

***forget the names of friends or everyday objects***

***cannot recall things you have heard, seen or read***

***lose the thread of what you are saying***

***have problems thinking and reasoning***

***feel anxious, depressed or angry***

***feel confused even when in a familiar environment or get lost on familiar journeys***

***find that other people start to notice or comment on your memory loss***

Linda Trueman, 67 and from Hertfordshire, lost her mother, father and grandmother to dementia. She says attitudes about the disease have changed, but some taboos remain.

"It was the 1970s when my grandmother died from dementia and really, at that time, most people didn't know the term Alzheimer's.

"And when my father died in 1987 there were several instances where I was explaining to the doctors about his Alzheimer's.

"Since then there's been a big change in knowledge and expertise. My mother died from dementia last Christmas and I was really impressed with the level of care she received. It was really touching and respectful the way she was treated.

"But it's still a condition that everyone is frightened of. People can find it difficult to be around those with dementia. I understand that. It can be really difficult to handle, particularly if they behave badly in public. But it's the disease, not the person."

***http://bit.ly/2fOQZal***

## Hearing with your eyes -- a Western style of speech perception

***Japanese people influenced less by lip movements when listening to another speaker: Evidence from neuroimaging study***

Which parts of a person's face do you look at when you listen them speak? Lip movements affect the perception of voice information from the ears when listening to someone speak, but native Japanese speakers are mostly unaffected by that part of the face. Recent research from Japan has revealed a clear difference in the brain network activation between two groups of people, native English speakers and native Japanese speakers, during face-to-face vocal communication.

It is known that visual speech information, such as lip movement, affects the perception of voice information from the ears when speaking to someone face-to-face. For example, lip movement can help a person to hear better under noisy conditions. On the contrary, dubbed movie content, where the lip movement conflicts with a speaker's voice, gives a listener the illusion of hearing another sound. This illusion is called the "McGurk effect."

According to an analysis of previous behavioral studies, native Japanese speakers are not influenced by visual lip movements as much as native English speakers. To examine this phenomenon further, researchers from Kumamoto University measured and analyzed gaze patterns, brain waves, and reaction times for speech identification between two groups of 20 native Japanese speakers and 20 native English speakers.

The difference was clear. When natural speech is paired with lip movement, native English speakers focus their gaze on a speaker's lips before the emergence of any sound. The gaze of native Japanese speakers, however, is not as fixed. Furthermore, native English speakers were able to understand speech faster by combining the audio and visual cues, whereas native Japanese speakers showed delayed speech understanding when lip motion was in view.

"Native English speakers attempt to narrow down candidates for incoming sounds by using information from the lips which start moving a few hundreds of milliseconds before vocalizations begin. Native Japanese speakers, on the other hand, place their emphasis only on hearing, and visual information seems to require extra processing," explained Kumamoto University's Professor Kaoru Sekiyama, who lead the research.

Kumamoto University researchers then teamed up with researchers from Sapporo Medical University and Japan's Advanced Telecommunications Research Institute International (ATR) to measure and analyze brain activation patterns using functional magnetic resonance imaging (fMRI). Their goal was to elucidate differences in brain activity between the two languages.

The functional connectivity in the brain between the area that deals with hearing and the area that deals with visual motion information, the primary auditory and middle temporal areas respectively, was stronger in native English speakers than in native Japanese speakers.

This result strongly suggests that auditory and visual information are associated with each other at an early stage of information processing in an English speaker's brain, whereas the association is made at a later stage in a Japanese speaker's brain. The functional connectivity between auditory and visual information, and the manner in which the two types of information are processed together was shown to be clearly different between the two different language speakers.

"It has been said that video materials produce better results when studying a foreign language. However, it has also been reported that video materials do not have a very positive effect for native Japanese speakers," said Professor Sekiyama. "It may be that there are unique ways in which Japanese people process audio information, which are related to what we have shown in our recent research, that are behind this phenomenon."

These findings were published in the nature.com journal Scientific Reports on August 11th and October 13th, 2016.

*J. Shinozaki, N. Hiroe, M. Sato, T. Nagamine, K. Sekiyama et al, "Impact of language on functional connectivity for audiovisual speech integration," Sci. Rep., vol. 6, no. August, p. 31388, Aug. 2016. DOI: 10.1038/srep31388.*

*S. Hisanaga, K. Sekiyama, T. Igasaki, and N. Murayama, "Language/Culture Modulates Brain and Gaze Processes in Audiovisual Speech Perception," Sci. Rep., vol. 6, p. 35265, Oct. 2016. DOI: 10.1038/srep35265.*

***http://bit.ly/2faCyvC***

## After decades of research, science is no better able to predict suicidal behaviors

### *Future research needs to look at combinations of risk factors, study says*

Experts' ability to predict if someone will attempt to take his or her own life is no better than chance and has not significantly improved over the last 50 years, according to a comprehensive review of suicide research published by the American Psychological Association.

"Suicidal thoughts and behaviors are among the most common, deadly and potentially preventable public health problems. Despite major advances in medical and psychological science, the devastating impact of this problem has remained constant for at least several decades," said Joseph Franklin, PhD, of Harvard University, lead author on the study, which appeared in the journal Psychological Bulletin.

A proper understanding of risk factors for suicidal thoughts and behaviors is essential in crafting scientific theories, accurate risk assessments and effective treatments, according to Franklin.

"Each day, thousands of clinicians rely on a half century of risk factor research to inform critical decisions about suicide risk and treatment," he said. "The primary purpose of this study was to estimate the power and accuracy of these risk factors."

Franklin and his colleagues conducted a meta-analysis of 365 studies conducted over the last 50 years looking at risk factors (e.g., depression, previous suicide attempts, stressful life events, substance abuse) and their ability to predict suicidal thoughts and behaviors over long periods of time.

"Our analyses showed that science could only predict future suicidal thoughts and behaviors about as well as random guessing. In other words, a suicide expert who conducted an in-depth assessment of risk factors would predict a patient's future suicidal thoughts and behaviors with the same degree of accuracy as someone with no knowledge of the patient who predicted based on a coin flip," said Franklin. "This was extremely humbling -- after decades of research science had produced no meaningful advances in suicide prediction."

The findings do not necessarily mean that widely used risk guidelines are invalid or useless, or that therapists should abandon them, warns Franklin. "As most of these guidelines were produced by expert consensus, there is reason to believe that they may be useful and effective. We recommend that these guidelines remain in use but emphasize that there is an urgent need to evaluate these guidelines within longitudinal studies."

The problem with the past research analyzed in this study is that the methodologies used were extremely narrow (most only looked at a

single risk factor) and may not have taken into account the complexity of the roles of these risks in the real world, suggested Franklin.

"Few scientists believe that a single factor, such as hopelessness, measured at one point in time will accurately predict suicide over the next 10 years," he said. "Instead, most would propose something like the following: a rapid elevation in hopelessness in an elderly man who just lost his wife, owns guns, has a history of suicidal behavior and has multiple physical health problems may increase risk for suicidal behaviors for a few hours, days or weeks. But the studies have not been testing these kinds of ideas."

There is good news on the horizon, according to Franklin. In the past two years, multiple groups have begun working on developing "machine learning algorithms" (the same things that drive the Google Search algorithm, make your email spam filter effective and show you relevant advertisements) to combine tens or even hundreds of risk factors together to predict suicidal behaviors.

"The preliminary results are promising, with algorithms predicting suicidal behaviors with greater than 80 percent accuracy, but this work is just in its initial phases," said Franklin. "However, in the very near future, this work may produce accurate prediction of suicidal behaviors on a large scale."

*Article: "Risk Factors for Suicidal Thoughts and Behaviors: A Meta-Analysis of 50 Years of Research," by Joseph Franklin, PhD, and Jessica Ribeiro, PhD, Vanderbilt University and Harvard University; Kathryn Fox, AM, Evan Kleinman, PhD, Adam Jaroszewski, AM, and Matthew Nock, PhD, Harvard University; Kate Bentley, MA, Boston University; Xieyining Huang, BA, and Katherine Musacchio, MEd, Vanderbilt University; and Bernard Chang, MD, Columbia University. Psychological Bulletin, published online Nov. 14, 2016.*

*Full text of the article is available from the APA Public Affairs Office and at http://www.apa.org/pubs/journals/releases/bul-bul0000084.pdf.*

***http://bit.ly/2fehYO6***

## Drinking red wine before smoking can prevent short term vascular damage

***Occasional smokers can avoid some harmful effects, according to a new report in The American Journal of Medicine***

Philadelphia, PA, Nov.15, 2016 - Drinking red wine is widely regarded as protective against cardiovascular disease. A new report in The American Journal of Medicine found that a glass or two of red wine before lighting up a cigarette can counteract some of the short-term negative effects of smoking on blood vessels.

Cigarette smoke causes acute endothelial damage, vascular and systemic inflammation, and cellular aging. Red wine stimulates the formation of endothelium-dependent relaxation factors such as nitric oxide, which improve endothelial function in coronary arteries possibly because of the high phenol concentration in red wine.

"However, sparse data exist on the short term potential vasoprotective effects of red wine in smoking-healthy individuals," explained lead investigator Viktoria Schwarz, MD, of the University of Saarland, Homburg, Germany. "The aim of our study was to investigate the acute vascular effects of red wine consumption prior to 'occasional lifestyle smoking' in healthy individuals. We found evidence that preconsumption of red wine prevented most of the vascular injury caused by smoking."

The study examined the effects of smoking on various biochemical processes in the blood and vessels of 20 healthy non-smokers who volunteered to smoke three cigarettes. Half of the subjects drank red wine one hour before smoking, in an amount calculated to result in 0.075% blood alcohol content. Blood and urine were collected before and after drinking and smoking and continued until 18 hours after smoking.

Smoking is known to cause microparticles to be released into the bloodstream. These particles come from endothelial cells, platelets, and monocytes and indicate that cells in the blood vessels are being damaged. Researchers found that in subjects who consumed red wine before smoking, these cellular changes did not occur.

Another biochemical process affected by smoking is telomerase activity. Telomeres can be thought of as "protective caps" on chromosomes. During aging, these caps can shorten and lose their

protective ability. By measuring telomerase activity, investigators determined that the group that smoked without drinking red wine showed a 56% decrease in telomerase activity while the drinking group showed only a 20% decrease.

Inflammation puts stress on cells due to an imbalance in reactive oxygen species production and the body's antioxidant defenses. According to Dr. Schwarz, "We observed acute proinflammatory changes, namely, leukocytosis, neutrophilia, upregulated levels of IL-6 in serum, and enhanced messenger RNA expression of IL-6 and tumor necrosis factor alpha. Our study adds to the present evidence that the proinflammatory effects in nonsmokers with 'occasional lifestyle smoking' could be prevented by red wine consumption."

Since the study was limited to young, healthy nonsmokers, it is not clear whether these findings apply to the elderly, the ill, or chronic smokers. There was no comparison to different alcoholic and non-alcoholic beverages or whether the results would apply to more than just occasional smokers and drinkers.

These findings underscore the magnitude of acute damage exerted by cigarette smoking in "occasional lifestyle smokers" and demonstrate the potential of red wine as a protective strategy to avert markers of vascular injury. Dr. Schwarz and co-investigators emphasized that they do not intend to motivate occasional smokers to drink or occasional drinkers to smoke. "Nevertheless, this study identified mechanisms suitable to explore damage and protection on the vasculature in humans, paving the way for future clinical studies."

***http://bit.ly/2g675iD***

## Once inside a tumor, our immune cells become traitors

### *T cells are are particularly good at suppressing the anticancer immune response*

New research has found a subset of our immune cells (called regulatory T cells) that are highly abundant in the tumor microenvironment and are particularly good at suppressing the anticancer immune response. In two independent studies, published November 15 in Immunity, scientists describe the distinct features and differences in molecules expressed by regulatory T cells inside of human breast, colon, and lung tumors compared to normal tissue that could be potential biomarkers or therapeutic targets.

Both sets of researchers hope to use what they've learned about the unique properties of regulatory T cells in tumor sites to improve cancer immunotherapies--drugs that stimulate immune cells to attack cancer cells. While these treatments have been successful for some types of tumors, such as melanoma, up to 40% of patients report serious adverse events.

"Our working hypothesis is that most of the adverse effects that patients experience with these immunotherapy treatments is because they are targeting molecules that are present both on regulatory T cells in the tumor and regulatory T cells outside of the tumor," says Sergio Abrignani, co-lead author on one of the studies with Massimiliano Pagani, both of the Istituto Nazionale Genetica Molecolare "Romeo ed Enrica Invernizzi" and Università degli Studi di Milano in Italy.

"If we target molecules that are selectively present in the tumors, then we would have comparable efficacy and fewer adverse events," adds Pagani. "We are discovering a lot of new markers for these cells that can be used to make future therapies safer."

Their study, part of the International Human Epigenetics Consortium, specifically analyzed tissue samples collected from nearly 200 patients with colon and lung cancer and compared them to normal tissue and peripheral blood. The researchers identified specific signature molecules and genes not previously associated with regulatory T cells that could be detected in both primary and metastatic tumors. Certain molecules may even be potential biomarkers for poor prognosis.

"We know that tumors that are highly infiltrated with regulatory T cells are bad, but our paper also shows that tumors with the highest expression of signature molecules on intratumoral regulatory T cells had the worst outcomes," Abrignani says, noting that clinical trials on new biomarkers and immunotherapies inspired by this study could

begin in as soon as two years. "We've set the stage for a bunch of important studies that must be done as soon as possible."

The other Immunity study, led by Alexander Rudensky of the Ludwig Center at Memorial Sloan Kettering Cancer Center, looked specifically at the distinct feature of regulatory T cells from over 100 human breast tumors removed during surgery. His group found that compared to normal tissue and peripheral blood, breast tumors possess an increased presence of regulatory T cells and that the most aggressive breast cancers have the highest number of the cells.

In the analysis of the immune cells by Rudensky's team, the most notable contrast was increased expression of chemokine receptor protein CCR8 in the tumor-resident cells in breast and other cancers (also found to be overexpressed in colon and lung tumors in Abrignani and Pagani's study). Why CCR8 may be significant is still unknown, but it offers itself as another potential target for immunotherapy.

"What's remarkable is the differential expression of CCR8; it is a very clear and clean marker that distinguishes regulatory T cells in the tumor," says Rudensky, also of the Howard Hughes Medical Institute. "This suggests one path to a more selective strategy to deplete regulatory T cells present in breast and other types of cancer."

Many questions still remain about the relationship between regulatory T cells and cancer, as well as why some of their unique properties promote immunosuppression. It will be helpful to learn, for example, why more aggressive tumors have an increased number of regulatory T cells--are they better at recruiting the cells or are there more at the tumor to begin with?--as well as what triggers from the tumors are changing the regulatory T cells' behavior.

"It is a really exciting time for both basic researchers and cancer biologists as we reveal a more complete picture of the interactions between different immune cell types and the tumor microenvironment," Rudensky says.

*Immunity, De Simone, Arrigoni, Rossetti, and Gruarin et al.: "Transcriptional landscape of human tissue lymphocytes unveils uniqueness of tumor-infiltrating T regulatory cells" http://www.cell.com/immunity/fulltext/S1074-7613(16)30432-0 DOI: 10.1016/j.immuni.2016.10.021*

*Immunity, Plitas and Konopacki et al.: "Regulatory T cells exhibit distinct features in human breast cancer" http://www.cell.com/immunity/fulltext/S1074-7613(16)30443-5 DOI: 10.1016/j.immuni.2016.10.032*

***http://bit.ly/2fehoA6***

## Early evidence of dairying discovered

***A team of scientists and archaeologists have discovered widespread evidence of prehistoric milk production in southern Europe.***

The study, a collaboration between the University of York, the University of Bristol, and the Centre National de la Recherche Scientifique, uncovered evidence that humans have been utilising milk and dairy products across the northern Mediterranean region from the onset of agriculture - some 9,000 years ago.

The importance of meat and dairy production in the Neolithic Mediterranean area remains a topic of debate, with previous research showing that the attraction for milk may have been a driving force for the domestication of cud-chewing animals like cows, goats and sheep.

This study combined evidence of the presence of milk and carcass fats in more than 500 pottery vessels together with an examination of the ages at death of domesticated animals excavated from 82 sites dating from the 7th to 5th millennia BC.

The findings show varying intensities of dairying and non-dairying activities in the northern Mediterranean region, with the slaughter profiles of the animals mirroring the fats detected in cooking pots.

Dr Cynthianne Spiteri, Junior Professor of Archaeometry at the University of Tübingen, who conducted the residue analysis as part of her PhD at the University of York's Department of Archaeology, said: "At the onset of food production in the northern Mediterranean region, milk was an important resource to these early farming communities.

"It is likely to have played an important role in providing a nourishing and storable food product which was able to sustain early farmers, and consequently, the spread of farming in the western Mediterranean."

Dr Mélanie Roffet-Salque and Professor Richard Evershed, from the University of Bristol's School of Chemistry said: "In this work, we integrate for the first time the findings of the analyses of lipid fats extracted from hundreds of cooking pots with the reconstruction of the actual herds at tens of sites, based on the remains of sheep, goats and cattle.

"Some of our earlier work had demonstrated that milk use was highly regionalised in the Near East in the 7th millennium BC, and this new multidisciplinary study further emphasises the existence of diverse use of animal products in the northern Mediterranean Neolithic.

"Dairying was clearly practiced both in the east and west of the region, but surprisingly not in Northern Greece, where the lipids from pots and the animal bones tell the same story: meat production was the main activity not dairying."

Dr Rosalind Gillis and Dr Jean-Denis Vigne, archaeozoologists at the Centre National de la Recherche Scientifique in the National Museum of Natural History in Paris added: "The choice of raising certain domesticates for their milk would have been heavily influenced by the landscape around the Neolithic communities. For example, rugged terrains are more suitable for sheep and goats. And open well-watered landscapes are better suited for cattle."

Professor Oliver Craig from the University of York's Department of Archaeology said the findings were particularly relevant as much of the population in that region today can't digest milk.

He added: "We presume this was also true back in the early Neolithic period, although this is still to be confirmed through genetic testing of ancient skeletons. Despite this deficiency, our research shows that they certainly exploited milk because we have found organic remnants in the pots they were using. This implies they were transforming milk into dairy products, such as yogurt and cheese, to remove the lactose.

"Despite dairying being a multi-billion pound global industry, we know that much of the world's population today are still intolerant to lactose so it is very important to know at what point people in the past were exposed to it and how long they have had to adapt to it."

The study, which was partly funded by The Natural Environment Research Council (NERC) and the European Union, is published today in the Proceedings of the National Academy of Sciences of the United States of America.

***http://bit.ly/2q7xzxJ***

## NIH scientists identify potent antibody that neutralizes nearly all HIV strains

***Antibody from HIV-infected person potently neutralized 98% of HIV isolates tested***

Scientists from the National Institutes of Health have identified an antibody from an HIV-infected person that potently neutralized 98 percent of HIV isolates tested, including 16 of 20 strains resistant to other antibodies of the same class. The remarkable breadth and potency of this antibody, named N6, make it an attractive candidate for further development to potentially treat or prevent HIV infection, say the researchers.

The scientists, led by Mark Connors, M.D., of NIH's National Institute of Allergy and Infectious Diseases (NIAID), also tracked the evolution of N6 over time to understand how it developed the ability to potently neutralize nearly all HIV strains. This information will help inform the design of vaccines to elicit such broadly neutralizing antibodies.

Identifying broadly neutralizing antibodies against HIV has been difficult because the virus rapidly changes its surface proteins to evade recognition by the immune system. In 2010, scientists at NIAID's Vaccine Research Center (VRC) discovered an antibody called VRC01 that can stop up to 90 percent of HIV strains from infecting human cells. Like VRC01, N6 blocks infection by binding to a part of the HIV envelope called the CD4 binding site, preventing the virus from attaching itself to immune cells.

Findings from the current study showed that N6 evolved a unique mode of binding that depends less on a variable area of the HIV envelope known as the V5 region and focuses more on conserved regions, which change relatively little among HIV strains. This allows N6 to tolerate changes in the HIV envelope, including the attachment of sugars in the V5 region, a major mechanism by which HIV develops resistance to other VRC01-class antibodies.

The new findings suggest that N6 could pose advantages over VRC01, which currently is being assessed as intravenous infusions in clinical trials to see if it can safely prevent HIV infection in humans. Due to its potency, N6 may offer stronger and more durable prevention and treatment benefits, and researchers may be able to administer it subcutaneously (into the fat under the skin) rather than intravenously. In addition, its ability to neutralize nearly all HIV strains would be advantageous for both prevention and treatment strategies.

*J Huang, BH Kang, E Ishida, T Zhou et al. Identification of a CD4-binding site antibody to HIV that evolved near-pan neutralization breadth. Immunity DOI: 10.1016/j.immuni.2016.10.027 (2016).*

***http://bit.ly/2q7sYMb***

## Cough virus kills liver cancer cells and hepatitis virus

### *Reovirus stimulates the body's own immune system to kill off the cancerous cells*

A virus that causes childhood coughs and colds could help in the fight against primary liver cancer, according to a study.

Reovirus stimulates the body's own immune system to kill off the cancerous cells, the researchers at the University of Leeds found.

In addition, Reovirus is able to kill off the hepatitis C virus - a common cause of primary liver cancer - at the same time, the team discovered. These early-stage findings are important because primary liver cancer is the third highest cause of cancer deaths worldwide and, if surgery is not an option, the prognosis is poor.

Study co-leader Dr Stephen Griffin, Associate Professor of Viral Oncology at the University of Leeds, said: "Ultimately we hope that by simultaneously treating the tumour, and the hepatitis virus that is driving the growth of the tumour, we may provide a more effective therapy and improve the outcomes for patients.

"Current treatments for liver cancer that can't be removed by surgery are mainly palliative - with chemotherapy only tending to prolong life, rather than cure - and it can have significant side effects."

Reovirus can cause respiratory illnesses and stomach upsets in children but by adulthood most people have been exposed to it and therefore it does not cause illness.

The University of Leeds team, whose study is published today in the journal Gut, found that Reovirus was successful in treating both liver cancer cells grown in the laboratory and those taken directly from patients undergoing surgery.

When introduced into the body, Reovirus stimulates an immune system factor known as interferon, which in turn causes the activation of a specific white blood cell called a Natural Killer cell. These Natural Killer cells then kill both the tumour, and cells infected with the hepatitis C virus.

Stimulating the immune system to kill cancer cells is known as immunotherapy. It differs from chemotherapy, in which the actual drugs kill the cancer cells. The researchers are now hoping to start the first in-human clinical trials.

Study co-leader Professor Alan Melcher, now Professor of Translational Immunotherapy at the Institute of Cancer Research, London, said: "Our study establishes a completely new type of viral immunotherapy for the most common primary liver cancer type, hepatocellular carcinoma, which has a very poor prognosis in its advanced form. "Using a mixture of experiments in human cancer samples and mice, our research showed that the Reovirus therapy switches on the host immune system to attack cancer cells - as well as suppressing the replication of hepatitis C virus, which is linked to many hepatocellular cancers. "We also showed that Reovirus therapy could be used to treat a range of other cancer types associated with viral infection, including Epstein Barr Virus-associated lymphoma."

Primary liver cancer is cancer that starts in the liver. It is a separate condition from secondary liver cancer, where the cancer originally developed in another part of the body and then spread to the liver.

Most cases of primary liver cancer are associated with damage and scarring of the liver, most commonly from having a hepatitis B or hepatitis C viral infection. Less commonly it is caused by drinking excessive amounts of alcohol over many years. At least 130 million people globally have chronic hepatitis C infection, according to the World Health Organisation, and a significant proportion of these will develop liver cancer.

Co-researcher Dr Adel Samson from the University of Leeds said: "It is becoming increasingly clear that one of the most powerful weapons available to treat cancer is our own immune system.

"However, as cancers are formed from our own cells, the immune system frequently struggles to identify the subtle differences that differentiate cancerous cells from normal cells, without help.

"Immunotherapy involves various strategies - such as a virus, as in our study - to kick-start our immune system to better identify and fight cancer. "These 'oncolytic' viruses show great promise in clinical trials, and the first such virus has recently been licensed as a medicine for the treatment of skin cancer."

Dr Justine Alford, senior science information officer at Cancer Research UK which funded the research, said: "This study in cells and mice suggests the possibility of using a harmless oncolytic virus as an immune-boosting one-two punch against liver cancer and the cancer-causing hepatitis C virus. "These early results also suggest this oncolytic virus could be used more widely in the treatment of virus-driven cancers.

"In these cancers, the viruses can represent a major hurdle for treatment, so we urgently need new and effective ways to tackle the root of the problem. "The next step will be to see if this technique will work in patients."

***http://bit.ly/2fFEUX9***

## Marijuana could help treat drug addiction, mental health

***Using marijuana could help some alcoholics and people addicted to opioids kick their habits, a UBC study has found.***

"Research suggests that people may be using cannabis as an exit drug to reduce the use of substances that are potentially more harmful, such as opioid pain medication," says the study's lead investigator Zach Walsh, an associate professor of psychology at UBC's Okanagan campus.

This comprehensive systematic review of research on the medical cannabis use and mental health also found some evidence that cannabis may help with symptoms of depression, PTSD and social anxiety. However, the review concluded that cannabis use might not be recommended for conditions such as bipolar disorder and psychosis.

"In reviewing the limited evidence on medical cannabis, it appears that patients and others who have advocated for cannabis as a tool for harm reduction and mental health have some valid points," says Walsh.

Walsh and his team systematically reviewed all studies of medical cannabis and mental health, as well as reviews on non-medical cannabis use--making the review one of the most comprehensive reports to date on the effects of medical cannabis on mental health.

With legalization of marijuana possible as early as next year in Canada, its important to identify ways to help mental health professional move beyond stigma to better understand the risk and benefits of cannabis is increasingly important, adds Walsh.

"There is not currently a lot of clear guidance on how mental health professionals can best work with people who are using cannabis for medical purposes," says Walsh. "With the end of prohibition, telling people to simply stop using may no longer be as feasible an option. Knowing how to consider cannabis in the treatment equation will become a necessity."

*Walsh's research was conducted with UBC's Michelle Thiessen, Kim Crosby and Chris Carroll, Raul Gonzalez from Florida State University, and Marcel Bonn-Miller from the National Centre for PTSD and Center for Innovation and Implementation in California.*

*The study was recently published in the journal Clinical Psychology Review.*

***http://bit.ly/2eR4nhk***

# Napping before an exam is as good for your memory as cramming

***To sleep, per chance to learn?***

***By Jessica Hamzelou in San Diego***

You've got a spare hour before a big exam. How should you spend it? It seems napping is just as effective as revising, and could even have a longer-lasting impact.

Repeatedly revising information to learn it makes sense. "Any kind of reactivation of a memory trace will lead to it being strengthened and reconsolidated," says James Cousins at the Duke-NUS Medical School in Singapore. "With any memory, the more you recall it, the stronger the memory trace."

However, sleep is also thought to be vital for memory. A good night's sleep seems to help our brains consolidate what we've learned in the day, and learning anything when you're not well rested is tricky. Many people swear by a quick afternoon kip.

So if you've got an hour free, is it better to nap or revise? Cousins, along with Michael Chee and their colleagues, also at Duke-NUS Medical School, set out to compare the two options. The team mocked-up a real student experience, and had 72 volunteers sit through presentations of about 12 different species of ants and crabs. The participants were asked to learn all about these animals, including their diets and habitats, for example.

After 80 minutes of this, the students were given an hour to either watch a film, have a nap, or revise what they had just learned. After this hour, they had another 80 minutes of learning. Then they had to sit an exam in which they were asked 360 questions about the ants and the crabs.

**Long-term benefits**

"The napping group got the best scores," says Cousins, whose work was presented at the Society for Neuroscience annual meeting in San Diego, California on Tuesday.

Cousins and his colleagues called the volunteers back for another test a week later. The nappers scored the highest in this test, too. And while the crammers significantly outperformed the movie-viewers on the first test, they lost their edge in the second test – there was no significant difference in the two groups' scores a week later.

"It could indicate that cramming information might be good in the short term, but in the long run, the benefits might not be that great," says Cousins.

However, Cousins is holding back on drawing definitive conclusions from his work – while the nappers were significantly better than film watchers, and crammers and film-watchers were statistically as bad as each other, the difference between the nappers and crammers did not come out as statistically significant. So until the team has conducted bigger studies, the evidence suggests napping is at least as effective as cramming, and might be better.

**Napping in the lab**

Cousins's team isn't sure why napping might be so beneficial. It's possible that some memories are laid down in the brain during a short sleep, or more likely, a refreshing rest can leave you better able to learn. "It could be that what the nap is doing is making them more alert," says Gareth Gaskell at the University of York in the UK. "It's an interesting question, but we need more research," he says.

Either way, the team are embracing afternoon napping. "There's a natural dip in alertness at around 3 pm," says Cousins. "I would say take a nap then. We do it in our lab." Some members have futons in their offices, he says, while others nod off at their desks. "Napping is encouraged."

And Cousins has some advice for students: "Don't stress yourself out just cramming some information into your head," he says. "Taking a nap is just as good."

http://wb.md/2faLpxt

# The World Is Not Prepared for Pandemics

***Hi. I am Victor Dzau, president of the US National Academy of Medicine. I am very pleased to be speaking from the 2016 World Health Summit in Berlin, Germany.***

**Victor J. Dzau, MD|November 15, 2016**

More than a year ago and propelled by the Ebola outbreak, the US National Academy of Medicine was asked by several foundations to commission an international study to look at current disease response preparedness and to project future global response preparedness. We spent 6 months consulting with hundreds of experts. We conducted four workshops in different parts of the world to learn about the major global issues. The subsequent report[1] has implications for all sorts of emerging infectious outbreaks and pandemics.

We have learned that the world is not prepared for pandemics. There are failures at every level. At the international level, there is a lack of coordination and resources; at the national level, there is a lack of public health infrastructure, capacity, and workforce; and at the local level, there is a lack of community trust and engagement.

Our report asserts that pandemics and infectious outbreaks are national and global security problems. These events have an impact on the global economy and on global security. Within the past 100 years, more than 100 million people have died because of Spanish Flu, HIV, and other infections. Of equal importance is the financial impact of these diseases. We project that infectious disease outbreaks in the 21st century will cost the world $6 trillion. Governments must pay attention, invest in health systems, and strengthen the World Health Organization (WHO) so that the world will be much better prepared for these events.

The report talks about fundamental reform of WHO, but it also emphasizes that governments, world leaders, and every country must invest in public health and preparedness. We also affirm the importance of WHO in terms of its leadership and the importance of WHO member-states conforming to the international health regulations. This means that WHO must be more accountable and capable of tracking and evaluating its core competencies. The report also discusses research and development; the need for vaccine development, public/private partnerships, and mobilizing financial initiatives.

In summary, our comprehensive statement looks objectively at the issues of infectious disease outbreaks and pandemics, and affirms that the world needs to be prepared through enhanced coordination, more investment, and better infrastructure, such as improved systems for disease surveillance.

*Sands P, Mundaca-Shah C, Dzau VJ. The neglected dimension of global security--a framework for countering infectious-disease crises. N Engl J Med. 2016; 374:1281-1287.*

http://bit.ly/2q7Dmnd

# Some Heartburn Drugs May Increase Stroke Risk

***A popular type of heartburn medicine may raise a person's risk for a common type of stroke, a new study from Denmark finds.***

**By Sara G. Miller, Staff Writer | November 16, 2016 09:58am ET**

People in the study who took proton pump inhibitors (PPI) faced an increased risk of ischemic stroke, compared with people who did not take these medicines, according to the study, presented today (Nov. 15) at the American Heart Association's annual meeting, called the Scientific Sessions.

Ischemic strokes are the most common type of stroke, according to the American Stroke Association. They occur when a blood clot blocks the flow of blood to the brain, preventing a region of the brain from receiving oxygen and nutrients.In the study, the researchers examined data collected between 1997 and 2012 on more than 244,000 Danish adults who had never had a stroke. The average follow-up time was six years, the researchers said.

Nearly 9,500 people in the study had a stroke during the follow-up period, the researchers found. Overall, the people who took PPIs faced a 21 percent increase in risk of ischemic stroke, compared with nonusers.

However, the dose of the medicine mattered, the researchers also found. At the lowest doses, the increase in stroke risk was only slight, or there was no increase at all, depending on the specific drug, according to the study.

At the highest doses, however, the risk of ischemic stroke was much greater. For example, people who took a daily dose of more than 80 milligrams of a PPI called pantoprazole, which goes by the brand name Protonix, faced a 94 percent increase — in other words, a near doubling — in stroke risk, compared with people who not take a PPI, the researchers found. And those who took more than 40 mg a day of the PPI omeprazole (Prilosec) were associated with a 40 percent increased risk of stroke.

This is not the first study to suggest that PPIs should be used with caution, the authors said. "PPIs have been associated with unhealthy [blood vessel] function, including heart attacks, kidney disease and dementia," Dr. Thomas Sehested, a researcher at the Danish Heart Foundation in Copenhagen, and the lead author of the study, said in a statement. "At one time, PPIs were thought to be safe, without major side effects. This study further questions the cardiovascular safety of these drugs," Sehested said.

Although the study found an association between PPIs and stroke risk, it does not prove cause and effect. More studies are needed, and doctors should consider if and for how long patients should take these drugs, the researchers said.

PPIs are not the only medicines available to treat heartburn. The researchers noted that another type of heartburn medication, called a histamine H2 antagonist, was found to have no association with stroke risk in the study. Histamine H2 antagonists include famotidine (Pepcid) and ranitidine (Zantac).

The authors said that they couldn't conclude whether these drugs were better for people than PPIs, however. Histamine H2 agonists can also have side effects, although they are rare, according to information about the drugs from the Mayo Clinic.

The new findings have not been published in a peer-reviewed journal.

***http://bit.ly/2fflXqp***

## People with Ebola May Not Show Symptoms

***People who have Ebola may not always have symptoms, a new survey confirms.***

**By Stephanie Bucklin, Live Science Contributor | November 16, 2016**

Researchers who conducted the survey in a known Ebola "hotspot" in West Africa found 14 people who tested positive for Ebola antibodies, but who reported that they never had any significant symptoms. Two of these people said they had suffered a fever during the Ebola outbreak, which stretched from late 2014 until the spring of 2016. The other 12 said they had no symptoms at all.

The survey was "really one of the first to study the rate of minimally asymptomatic cases of Ebola in a 'hot zone,'" said Dr. Michele Barry, a professor of medicine at the Stanford University School of Medicine and a co-author of the new paper. Her team was surprised that they found so many people who were infected with Ebola virus but had few or no symptoms, Barry told Live Science.

The researchers conducted their survey in the village of Sukudu, in Sierra Leone, which has about 900 people. The survey was conducted from October 2015 to January 2016, which was approximately one year after the Ebola outbreak struck the village. During the outbreak, 34 cases of Ebola were reported in Sukudu, and six of those people who were infected survived.

The researchers tested the blood of 187 people who lived in Sukudu, and had not reported having Ebola during the outbreak, for antibodies to the Ebola virus. All of these people had been placed under quarantine during the outbreak, either because they lived with someone who did have Ebola, or because they had shared a public latrine with an infected person. The researchers also tested 30 people from the surrounding region who did have Ebola, as a "positive control" group, meaning a group that should definitely all have antibodies to Ebola.

The finding that 14 people had antibodies to the Ebola virus, despite reporting no Ebola-like symptoms, is further evidence that Ebola has "a spectrum of clinical manifestations, including minimally symptomatic infection," the researchers wrote in their paper, published Tuesday (Nov. 15) in the journal PLOS Neglected Tropical Diseases.

Moreover, the finding shows "that a significant portion of Ebola transmission events may have gone undetected during the outbreak." This could change how survivorship of Ebola is defined, and may have implications for future research on vaccine studies or the transmission of the disease, the researchers said.

The new study is not the first to find people who likely had Ebola but did not have any symptoms, the researchers noted. A 2010 studyof about 4,300 people living in Gabon, a country in Central Africa, found that 15.3 percent had antibodies against Ebola. Most of these, the authors believed, had suffered only a mild or asymptomatic infection.

The new study has some limitations: Given the stigma of admitting to having Ebola symptoms and the fear of being admitted to an Ebola Treatment Unit, some people who had symptoms may have been eager to downplay their symptoms or deny feeling sick. In addition, the researchers said that it is difficult to verify people's symptoms through interviews, and that they had to rely on the participants' memories of how they felt up to a year prior.

The researchers stressed that their findings were from one village, and may not apply to the entire region affected by the Ebola epidemic. However, more research on asymptomatic cases of Ebola could help improve understanding of the disease. "As a result, we may learn more about how efforts at containment can be improved," the researchers wrote in their study.

http://bit.ly/2fTkO9y

## Serious, highly drug-resistant infections increasing among US children

***Highly drug-resistant infections are on the rise among U.S. children, reports a new study published in the Journal of the Pediatric Infectious Diseases Society.***

Researchers found increasing rates of antibiotic resistance among samples of Pseudomonas aeruginosa, an important type of bacteria, collected from pediatric patients nationwide over the last decade. The findings provide more evidence that aggressive strategies to track, prevent, and treat these concerning infections in children are greatly needed.

"Infections with P. aeruginosa can be serious and are associated with significant morbidity and mortality," said study author Latania K. Logan, MD, of Rush University Medical Center. In children, these infections can result in prolonged illness, require longer hospital stays, and, ultimately, increase the risk of death. "Highly drug-resistant P. aeruginosa infections leave health care providers with limited--or sometimes no--antibiotic choices available, and these antibiotics are less safe and more toxic in children," said study author Sumanth Gandra, MD, MPH, of the Center for Disease Dynamics, Economics & Policy.

In the study, researchers analyzed information from a network of clinical microbiology laboratories serving approximately 300 hospitals across the country. Their analysis focused on data obtained by testing P. aeruginosa isolates for susceptibility to several different types of antibiotics. The samples were collected from patients between the ages of 1 and 17 who were in outpatient, inpatient, intensive care unit, and long-term care settings from 1999 to 2012.

The proportion of P. aeruginosa isolates resistant to at least three classes of antibiotics rose from 15.4 percent in 1999 to 26.0 percent in 2012. The proportion of bacterial strains resistant to carbapenems, a class of antibiotics considered one of the treatments of last resort for

highly resistant infections, increased from 9.4 percent in 1999 to 20.0 percent in 2012. Drug resistance was more common in pediatric patients in intensive care units, among those 13-17 years old, and in the Midwest (Iowa, Kansas, Minnesota, Missouri, Nebraska, and the Dakotas).

An estimated 51,000 health care-associated P. aeruginosa infections occur in adults and children in the U.S. each year, according to the Centers for Disease Control and Prevention. More than 6,000 (13 percent) of these infections are resistant to multiple classes of antibiotics, leading to about 400 deaths annually. Few studies have assessed trends of resistant P. aeruginosa infection specifically in children, despite rising rates of antibiotic resistance nationally overall.

The latest findings highlight the need for better tracking of antibiotic-resistant infections and for effective strategies to prevent these infections in children, in addition to antibiotic stewardship programs to address inappropriate antibiotic prescribing, the study authors concluded. Health care facilities should also consider using rapid molecular diagnostics to guide antibiotic treatment decisions.

***http://bit.ly/2q9WDqr***

## GW dermatologist publishes survey finding fungal skin infections commonly misdiagnosed

***Adam Friedman, M.D., highlights the challenge of distinguishing between various skin conditions, leading to common misdiagnosis of fungal infections***

WASHINGTON - Fungal skin infections may be commonly misdiagnosed, according to a survey published in the Journal of the American Academy of Dermatology by George Washington University (GW) dermatologist Adam Friedman, M.D.

With colleagues from GW and Therapeutics Clinical Research in San Diego, California, Friedman surveyed dermatologists at the 2016 Orlando Dermatology Aesthetic & Clinical Conference. The survey asked dermatologists to anonymously review 13 clinical images and determine whether or not the image was consistent with a fungal skin infection. The majority of cases were only appropriately classified by 50 percent of participants, with only one of the cases correctly identified by 90 percent of the audience.

Dermatophyte infections, the most common kind of fungal infection in the skin, hair, or nails, affect an estimated 25 percent of the world's population and have accounted for 51 million outpatient visits over the last 10 years in the U.S. Misdiagnosis of dermatomycosis can result in incorrect therapy selection, worsening of symptoms, and even additional skin and soft tissue infections.

"It is crucial to push for proper and continued medical education on dermatophyte and other fungal skin infections to minimize misdiagnoses and ultimately curb disease impact," said Friedman, associate professor, director of the residency program, and director of translational research in the Department of Dermatology at the GW School of Medicine and Health Sciences.

The survey highlights the challenge of distinguishing between certain fungal skin infections and primary inflammatory conditions, and the ease with which one may miss the correct diagnosis.

"Secondary syphilis, annular psoriasis, and pityriasis rosea are among a few inflammatory skin diseases that mimic dermatophyte infections," said Friedman. "However, knowledge and training of bedside diagnostic techniques like potassium hydroxide preps during residency and beyond can combat misdiagnosis." ***"Cutaneous fungal infections are commonly misdiagnosed: a survey-based study"*** is published in the Journal of the American Academy of Dermatology.

***http://bit.ly/2fiWsba***

## The Real Reason Life-Saving Drugs Are So Expensive (Op-Ed)

***Pharmaceutical companies put their ad dollars behind brand-name drugs, rather than generics.***

**By Mark Abramowicz, M.D., President, The Medical Letter**

Dr. Mark Abramowicz is president of The Medical Letter, a nonprofit publication that provides unbiased, rigorous drug evaluations for

physicians, pharmacists, libraries, hospitals and teaching institutions. Before joining the editorial staff of The Medical Letter, Abramowicz was a member of the Pediatrics Department at the Albert Einstein College of Medicine. Abramowicz contributed this article to Live Science's Expert Voices: Op-Ed & Insights.

Drug prices are in the headlines: inflated costs of life-saving EpiPens, the many thousands of dollars for drugs that can cure hepatitis C, and hundreds of thousands to save children with rare diseases such as lysosomal acid lipase deficiency — a life-threatening genetic disease in which an enzyme that breaks down certain lipids doesn't work properly, leading those lipids to accumulate and affect the functioning of organs and growth in general.

There are two simple reasons for these high costs: a lack of generic-drug competition, and pharmaceutical companies' success in marketing their brand-name drugs.

Yet one of the most effective classes of drugs — statins, which treat the leading cause of death in the U.S. — are hardly mentioned in pharmaceutical advertising. What's more, there are generic versions of these drugs that cost much less, and yet you won't see them in commercials. You also won't see them in as many medicine cabinets as you might expect. That's because many doctors prescribe the brand names and many people don't know that the generic versions are just as good.

Why is that? The generic versions of statins just don't cost enough to support an advertising budget. But here's what every consumer should know about them.

Heart disease remains the leading cause of death in the United States, according to the National Center for Health Statistics. In addition to the drug-free methods that have been shown to reduce the risk of heart disease and cardiovascular-related deaths — including low-fat diets, low-carb diets, stress tests, angiograms (an X-ray test that shows blood flow in a vein or artery), angioplasties (repairing blood vessels), coronary bypasses and heart transplants — there are also a litany of cardiovascular drugs to treat heart disease.

For many years, there has been general agreement in the medical community that statins (also called HMG-CoA reductase inhibitors) can decrease the incidence of heart attacks and death in patients with atherosclerotic cardiovascular disease, in which plaque — a semi-hardened accumulation of substances made up of fat and cholesterol — builds up inside the arteries, as well as for patients without heart disease who have risk factors such as high blood cholesterol levels or diabetes.

All drugs have side effects, but in controlled trials, statins have been shown to have very few side effects, and the number of heart attacks and strokes they have prevented is substantial. In a study published earlier this year in The New England Journal of Medicine, researchers examined the effect of a statin or a placebo on more than 12,000 men over age 55 and women over age 65 in 21 countries. These study participants did not have cardiovascular disease, and their annual risk of a major "cardiovascular event," such as a heart attack or stroke, was calculated to be about 1 percent.

After a median follow-up of 5.6 years, the people who had taken a statin had a 25 percent lower chance of dying due to cardiovascular causes or having a nonfatal heart attack or stroke compared with the people who had not taken the statin, the study found.

No drug class has a comparable impact on cardiovascular disease, yet statins are one class of drugs that pharmaceutical companies seem to downplay. They exaggerate the benefits and safety of many drugs, but not statins.

Is cost the problem?

All of the statins marketed in the United States (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin), with one exception (pitavastatin), are available as generics. But many physicians still shy away from generics, perhaps because they feel more comfortable with brand names that they have customarily

prescribed or perhaps because of the persuasiveness of the pharmaceutical industry.

For instance, Collette Dejong of the University of California, San Francisco School of Medicine and colleagues found that industry-sponsored meals were linked to an increased rate of prescribing the brand-name medication, including statins, that was being promoted, though they couldn't establish that one caused the other in the study, published in August 2016 in the medical journal JAMA.

If doctors aren't making the change, it will have to come from consumers. The next time you see an advertisement on television for a new anti-cancer drug that extends life by a month or two and costs hundreds of thousands of dollars (which the commercial probably will not mention), think about why we never see ads for the underused generic statins that can extend healthy lives by decades for just a few dollars a month.

So, the next time your doctor gives you a new prescription for a brand-name medication, be sure to ask if a generic equivalent is available.

***http://bit.ly/2fTnEeB***

## Older first-time mothers are also more likely to live longer

***Study finds that women giving birth for first time later in life increase chances of living to 90***

The average age of a woman giving birth for the first time has risen dramatically in the United States over the past 40 years, driven by factors like education or career. A new study by researchers at University of California San Diego School of Medicine found that women choosing to become first-time mothers later in life may increase their chances of living into their 90s.

The study, published online November 17 in American Journal of Public Health, is the first to look at age at first childbirth in relation to longevity. The researchers found an association between a woman's age at childbirth and parity (the number of times a woman has been pregnant) with survival to age 90.

"We found that women who had their first child at age 25 or older were more likely to live to age 90," said Aladdin Shadyab, PhD, lead author of the study with the Department of Family Medicine and Public Health at UC San Diego School of Medicine. "The findings indicate that women with two to four term pregnancies compared with a single term pregnancy were also more likely to live at least nine decades."

Of the approximately 20,000 participants in the study, 54 percent of women survived to 90 years old. The participants were part of the Women's Health Initiative (WHI), a national longitudinal investigation of women that began in 1991. The women were followed for up to 21 years.

The study also found that women who lived to age 90 were more likely to be college graduates, married, have a higher income and less likely to be obese or have a history of chronic disease.

"Our findings do not suggest that women should delay having a child, as the risk of obstetric complications, including gestational diabetes and hypertension, is higher with older maternal ages. It is possible that surviving a pregnancy at an older age may be an indicator of good overall health, and as a result, a higher likelihood of longevity," said Shadyab. "It is also possible that women who were older when they had their first child were of a higher social and economic status, and therefore, were more likely to live longer."

Shadyab said further research is needed to determine which social factors might explain associations of age at first childbirth and parity with longevity.

"Our findings have several public health implications," said Shadyab. "We hope this is a foundation to help identify targets for future interventions among women in the preconception and family planning phases of their lives, which may improve women's healthy longevity in the long term."

*Study co-authors include: Andrea LaCroix, Sonia Jain, UC San Diego; Caroline Macera, Richard Shaffer, Linda Gallo, San Diego State University; Margery Gass, The North American Menopause Society; Molly Waring, University of Massachusetts Medical School; and Marcia Stefanick, Stanford University School of Medicine.*

http://bit.ly/2ffqyZJ

# New research clarifies why wounds heal more slowly with age

## *Older bodies need longer to mend.*

This reality of aging has been documented since World War I, with the observation that wounds heal slower in older soldiers. Yet until now, researchers have not been able to tease out what age-related changes hinder the body's ability to repair itself.

Recent experiments at The Rockefeller University explored this physiological puzzle by examining molecular changes in aging mouse skin. The results, described November 17 in Cell, delineate a new aspect of how the body heals wounds.

"Within days of an injury, skin cells migrate in and close the wound, a process that requires coordination with nearby immune cells. Our experiments have shown that, with aging, disruptions to communication between skin cells and their immune cells slow down this step," says Elaine Fuchs, the Rebecca C. Lancefield Professor and head of the Robin Chemers Neustein Laboratory of Mammalian Cell Biology.

"This discovery suggests new approaches to developing treatments that could speed healing among older people," adds Fuchs, who is also a Howard Hughes Medical Institute investigator.

**Return of the skin cells**

Whenever a wound occurs, the body needs to repair it quickly to restore its protective skin barrier. "Wound healing is one of the most complex processes to occur in the human body," says Brice Keyes, a former postdoc in Fuch's lab and currently a researcher at Calico Life Sciences. "Numerous types of cells, molecular pathways, and signaling systems go to work over timescales that vary from seconds to months. Changes related to aging have been observed in every step of this process." Keyes and Siqi Liu, an immunology specialist and a current Jane Coffin Childs postdoctoral fellow in in the lab, are co-first authors of the Cell article.

Both skin cells and immune cells contribute to this elaborate process, which begins with the formation of a scab. New skin cells known as keratinocytes later travel in as a sheet to fill in the wound under the scab.

The team focused on this latter step in healing in two-month-old versus 24-month-old mice--roughly equivalent to 20- and 70-year-old humans. They found that among the older mice, keratinocytes were much slower to migrate into the skin gap under the scab, and, as a result, wounds often took days longer to close.

Wound healing is known to require specialized immune cells that reside in the skin. The researchers' new experiments showed that following an injury, the keratinocytes at the wound edge talk to these immune cells by producing proteins known as Skints that appear to tell the immune cells to stay around and assist in filling the gap. In older mice, the keratinocytes failed to produce these immune signals.

**Seeking a reversal**

To see if they could enhance Skint signaling in older skin, the researchers turned to a protein that resident immune cells normally release after injury. When they applied this protein to young and old mouse skin tissue in a petri dish, they saw an increase in keratinocyte migration, which was most pronounced in the older skin. In effect, the old keratinocytes behaved more youthfully.

The scientists hope the same principle could be applied to developing treatments for age-related delays in healing.

"Our work suggests it may be possible to develop drugs to activate pathways that help aging skin cells to communicate better with their immune cell neighbors, and so boost the signals that normally decline with age," Fuchs says.

http://bit.ly/2qcqNr3

# Donor lungs could be kept alive for substantially longer with new lung preservation technique

## *Donor lungs could be preserved for twice as long*

The length of time donor lungs could be preserved prior to transplant could be safely extended to more than 12 hours--more than double the average 5-6 hour standard time[1] - without jeopardising recipient outcomes, by using a combination of cold preservation and a new technique called ex-vivo lung perfusion (EVLP), whereby the lung is kept alive outside the body and supported by a supply of oxygen and nutrients.

The new study, published in The Lancet Respiratory Medicine, found that patients who received a donor lung preserved for more than 12 hours had similar survival at 1 year post transplant to those who received lungs preserved for less than 12 hours. The findings suggest that this new approach could increase the availability of donor organs by reducing geographical limitations on donors and recipients, and enabling organs to be transported over longer distances to recipients further away than previously viable.

Currently, about 200 adults are waiting for a lung transplant in Canada, and over 1500 in the USA [1]. About a quarter of those on the waiting list will die before they receive a transplant. Lung transplantation requires the donor organ to be stored and transported from the donor to the recipient. Traditionally, donor lungs have been flushed and preserved at cold temperatures to reduce tissue decomposition during transport. But the generally accepted maximum time from when an organ is removed from the donor, cooled, and then transplanted into the recipient is 6 to 8 hours.

The recent development and use of EVLP around the world has completely altered the basic theory of lung preservation from slowing tissue death to preserving life, in order to allow and enhance recovery. This new technique involves continuously perfusing or pumping a bloodless solution containing oxygen, proteins, and nutrients into donor lungs to give doctors the opportunity to protect, assess and treat the lungs while they are outside the body and make them suitable for transplantation.

"We have been using EVLP as standard practice to assess high-risk donor lungs for the last decade and almost 300 patients have benefited from this technology at our centre to date", explains lead author Dr Marcelo Cypel, Thoracic Surgeon at Toronto General Hospital, University of Toronto, Toronto, Canada. "Donor lungs are transported cold to the hospital where they are warmed, evaluated and then cooled again until they are transplanted into the recipient. Because assessing the lungs using EVLP takes at least 4 hours, total preservation times have regularly exceeded 8 hours."[2]

Intrigued by the technique's possibilities for extending overall preservation times, Cypel and his team retrospectively examined data on the outcomes of 906 patients (aged 18 or older) who received a lung transplant at Toronto General Hospital between 2006 and 2015. They compared patients who had received a lung that had been preserved (i.e. the sum of cold preservation and normal temperature EVLP) for more than 12 hours (97 patients; 95% donor organs underwent EVLP) with those who were given lungs preserved for less than 12 hours (809; 5% underwent EVLP).

They found that despite the use of higher-risk lungs in the more than 12-hour group, the average length of time recipients spent in the intensive care unit and in hospital post-transplant were similar in both groups (table 2). Additionally, the life-threatening complication of immediate graft dysfunction and survival at 1 year did not differ between the two groups (figure 2). Further analysis also showed that cold preservation and EVLP time did not affect survival (table 4). Older recipient age was the only factor that was linked with reduced survival.

"It is important to remember that the lungs preserved for more than 12 hours using EVLP started out as more injured lungs. In fact, many of them might have been turned down for transplantation in the past.

That they performed similar to conventional lungs with shorter preservation times suggests EVLP provides additional benefit over cold preservation", says first author Dr Jonathan Yeung, also from Toronto General Hospital [2].

The authors point to several limitations including the study's retrospective nature and the fact that it was conducted at a single institution. Additionally, the maximum safe preservation time for human lung transplantation remains unknown. They say that clinical trials are now needed to understand the optimum combination of cold and normal temperature EVLP lung preservation methods.

According to Dr Cypel, "At a time when there is a critical shortage of lungs available for transplantation, combining cold preservation and EVLP will hopefully make a lot more donor lungs available for successful transplantation. This approach has allowed our Toronto-based programme to essentially abolish any geographical boundaries to donor lung retrieval in North America. The safe extension of preservation time not only has the potential to give clinicians extra time to evaluate, but also to treat and recondition donated organs that would otherwise not be used. Extra preservation time also allows additional flexibility in planning recipient surgery and gives more time to transport the donor lung from the EVLP site to the recipients' operating room."[2]

[1] *Data from United Network for Organ Sharing, USA* https://www.unos.org/

[2] *Quotes direct from authors and cannot be found in text of Article.*

http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(16)30323-X/abstract

***http://bit.ly/2fTrGUC***

# Dino-Killing Asteroid May Have Punctured Earth's Crust

***Could shed light on how impacts can reshape the faces of planets and how such collisions can generate new habitats for life***

**By Charles Q. Choi, Live Science Contributor | November 17, 2016**

After analyzing the crater from the cosmic impact that ended the age of dinosaurs, scientists now say the object that smacked into the planet may have punched nearly all the way through Earth's crust, according to a new study.

The finding could shed light on how impacts can reshape the faces of planets and how such collisions can generate new habitats for life, the researchers said.

Asteroids and comets occasionally pelt Earth's surface. Still, for the most part, changes to the planet's surface result largely from erosion due to rain and wind, "as well as plate tectonics, which generates mountains and ocean trenches," said study co-author Sean Gulick, a marine geophysicist at the University of Texas at Austin.

In contrast, on the solar system's other rocky planets, erosion and plate tectonics typically have little, if any, influence on the planetary surfaces. "The key driver of surface changes on those planets is constantly getting hit by stuff from space," Gulick told Live Science.

The researchers in the new study looked at Earth features to learn more about impact effects found on other solar system objects. Major craters sometimes possess rings of rocky hills in their centers. Most of these "peak rings" exist on extraterrestrial rocky bodies such as the moon or Venus, making it difficult to analyze these structures in detail and pin down their origins.

So to learn more about peak rings, scientists investigated a gargantuan crater on Earth that measures more than 110 miles (180 kilometers) across, located near the town of Chicxulub (CHEEK-sheh-loob) in Mexico's Yucatán Peninsula. This crater likely resulted from the epic crash of an object about 6 miles (10 km) wide, and the resulting impact is thought to have ended the age of dinosaurs about 65 million years ago.

The researchers focused on the Chicxulub crater because it has the only intact peak ring on Earth. In contrast, larger craters on Earth, such as Sudbury in Canada or Vredefort in South Africa, "have [been] heavily eroded — neither one has peak rings anymore," Gulick said. "On the other hand, Chicxulub's peak ring is completely preserved."

The structures that the researchers wanted to examine were under about 60 feet (18 meters) of water in the Gulf of Mexico. To collect samples from these structures, the scientists traveled to the site in the

spring of 2016 in a "liftboat" that could lower three pillars into the seafloor and lift the boat off the water by about 50 feet (15 m). The liftboat then lowered drills into the seafloor and "drilled into the crater for two months, to as low as 1,335 meters [4,380 feet] below the seafloor," Gulick said. (Lifting the boat from the water helps it avoid waves that can rock the vessel and snap the drill pipe.)

In the peak ring samples, the scientists discovered granite that likely once was deeply buried for about 500 million years, Gulick said. "These deeply buried rocks rose up to the surface of the Earth within the first few minutes of the impact," Gulick said. "They showed evidence they experienced a high degree of shock from the impact."

After the impact, "the earth there would have temporarily behaved like a slow-moving fluid," Gulick said. "The stony asteroid would have opened up a hole probably almost the thickness of Earth's crust, almost 30 km [18 miles] deep, and on the order of 80 to 100 km [50 to 62 miles] wide."

And similar to how fluids behave, the earth would immediately flow to fill in the hole, meaning the sides of the crater would collapse inward, he added.

"At the same time, the center of this hole starts reaching upwards, like when you throw a rock in a pond and you get a water droplet rising in the middle," Gulick said. "The center would have risen up from the surface of the Earth as much as 15 km [9 miles], and then become gravitationally unstable, collapsing downwards and outwards."

The end result of this dynamic process is a ring of mountains, or the peak ring, the researchers said.

The study's findings support one of the two main hypotheses that describe peak ring formation, the researchers said. One explanation suggested that peak rings originate closer to the surface: As an impact causes a peak to form in the middle of the crater, the uppermost part of this peak melts, causing the material to disperse into a ring of peaks. The other hypothesis suggested that peak rings formed because impacts dug deep into their targets.

"It turns out the models based on the deeper origins seemed to have gotten it right," Gulick said. "The model these findings support is based on what are known as hydrocode models, which are used for simulating nuclear bomb blasts. Those models simulate an asteroid impacting a target at close to about 20 km per second [44,740 mph], which can get the crust to flow."

Unexpectedly, the researchers noted that rocks from peak rings "got fundamentally altered by their journey upward during the impact," Gulick said. "They end up lower in density by a lot, with their porosity increasing from 1 to 2 percent to 10 percent."

These changes may have proven critical for the evolution of life on Earth, and perhaps on other planets, Gulick said. "When you get rocks with 10 percent more pore space, microbial life living below the surface may find new habitats on the surface," he said. "Our next area of research involves looking at whether ecosystems can get started by craters."

The scientists detailed their findings online today (Nov. 17) in the journal Science.

***http://bit.ly/2ffEbIx***

## Age of First Stroke Is Getting Younger, Study Finds

***Strokes are striking people in the U.S. at younger ages, a new study finds.***

**By Sara G. Miller, Staff Writer | November 17, 2016 11:29am ET**

NEW ORLEANS — The average age of people having a first stroke decreased from 71.7 in 2000 to 69.3 in 2012, according to the study.

Overall, the rates of stroke in the U.S. have gone down in the past few decades, said Chengwei Li, an epidemiologist at the University of Michigan School of Public Health and the lead author of the study.

But the rates have not gone down in people under age 65, Li told Live Science. And in people under age 55, the rates of stroke have actually increased, Li said.

In the study, presented here Monday (Nov. 14) at the American Heart Association's Scientific Sessions annual meeting, Li and his

colleagues wanted to see whether these changes in stroke rates have affected the average age that strokes occur.

A decline in the average age of people having strokes can have big implications for public health, according to the study. For example, a person who has a stroke at a younger age may be disabled for a longer time afterward, compared with someone who was older when a stroke occurred.

Each year, about 795,000 people in the U.S. have a stroke, and about 610,000 of those are first-time strokes, according to the Centers for Disease Control and Prevention. Strokes are the leading cause of serious long-term disability, the CDC says.

The researchers studied data between 2000 and 2012 from patients in an ongoing stroke study called Brain Attack Surveillance in Corpus Christi Project. Patients who had had a stroke before the study began were excluded.

The researchers focused on a type of stroke called an ischemic stroke. Ischemic strokes are the most common type of stroke, and occur when a blood clot blocks the flow of blood to the brain, preventing a region of the brain from receiving oxygen and nutrients, according to the American Stroke Association.

More than 3,200 people had an ischemic stroke during the study period, according to the study. The researchers used the stroke patients' medical records to determine which, if any, risk factors for stroke the patients had.

The researchers found that the average age for someone to have a stroke decreased by about two years, Li said.

One possible explanation for this finding is that risk factors for stroke became more common during the study period, Li said. Conditions such as atrial fibrillation (a type of irregular heartbeat), Type 2 diabetes and high blood pressure all became more common among the study participants during the study period — and all of these conditions can raise a person's risk for stroke, he said.

People should learn about the risk factors for stroke, Li said. In addition, efforts to prevent stroke should be made when people are in middle age, the researchers said.

Li noted that the findings suggest only an association. More studies are needed to determine why the age that people have strokes is getting younger, he said.

***http://bit.ly/2fj9Uvx***

## Stopping brain protein from turning rogue prevents Alzheimer's

***Enzyme shields mice brains from the actions of a problem protein***

**By Alice Klein**

Alzheimer's disease can be prevented by stopping a crucial brain protein from turning rogue, a study in mice suggests.

Tau protein has long been suspected to play a role in causing the condition. In healthy brains, tau is essential for normal cell functioning. But during Alzheimer's disease, the protein goes haywire, clumping together to form twisted tangles and, it is thought, releasing toxic chemicals that harm the brain.

Now Lars Ittner at the University of New South Wales, Australia, and his colleagues have pinpointed a crucial enzyme that controls how tau proteins behave in the brain. The enzyme, called p38γ kinase, helps keep tau in a healthy, tangle-free state, preventing the onset of memory loss and other symptoms in mice that have been bred to develop Alzheimer's disease.

**Protective effect**

The enzyme seems to block Alzheimer's by interfering with the action of another problem protein, called beta-amyloid. Like tau, clumps of this protein accumulate in the brains of people with Alzheimer's, making it another suspected cause of the disease.

When beta-amyloid forms these sticky plaques, it can also modify the structure of tau proteins, causing them to form tangles and release toxic chemicals. But Ittner's team found that p38γ kinase makes a different kind of structural change to tau. If this change is made first,

it prevents beta-amyloid from being able to turn tau bad, and mice do not develop the disease.

In people, the levels of this enzyme decline significantly as Alzheimer's progresses, hinting that boosting this enzyme could help prevent or treat the disease.

**New approach**

Using an enzyme to stop tau from becoming toxic is novel because most existing research has focused on targeting beta-amyloid, says Ralph Martins at Edith Cowan University in Western Australia.

"We've got treatments now that decrease beta-amyloid levels, but they don't have much efficacy," he says. "Animal work is increasingly showing that beta-amyloid toxicity is mediated through tau, so it's an attractive target."

One reason why Alzheimer's treatments that have shown promise in mice have frequently failed in clinical trials is because earlier mouse models were designed to only mimic beta-amyloid plaque formation in humans, he says.

Ittner's study instead used mice that were engineered to recreate the beta-amyloid-tau relationship in humans, so the results should be more applicable to people, he says. "I think this is very, very exciting. Our focus has been on beta-amyloid but this gives the tau approach a really good kick."

*Journal reference: Science, DOI: 10.1126/science.aah6205*

***http://bit.ly/2fj4UqJ***

## U.S. Military Preps for Gene Drives Run Amok

***DARPA researchers are developing responses for accidental or malicious "genetic spills"***

**By Josie Garthwaite on November 18, 2016**

If a tanker splits its hull and dumps oil into the sea, trained teams show up with specialized gear to begin the process of stanching the flow and cleaning up the spill. Today, there's no equivalent team or tools for resolving a "spill" of genetic material into the environment, but that could soon change.

Over the next four years a new program in the Pentagon's Defense Advanced Research Projects Agency (DARPA) plans to cultivate, among other things, a kind of cleanup crew for engineered genes deemed harmful to or undesirable in an ecosystem. The initiative, called Safe Genes, comes at a time when so-called "gene drive" systems, which override the standard rules of gene inheritance and natural selection, are raising hopes among some scientists that the technology could alter or suppress populations of disease-carrying insects or other pests in as few as 20 generations.

The Bill and Melinda Gates Foundation sees so much promise in gene drive technology that it plans to double spending on its Target Malaria initiative, which aims to create systems for driving genes in two species of malaria mosquitoes, to $70 million. Yet without careful precautions, a gene drive released into the wild could spread or change in unexpected ways. Kevin Esvelt, head of the Sculpting Evolution lab at MIT Media Lab, which is applying for Safe Genes funding in collaboration with eight other research groups, predicts that eventually, perhaps around 15 years from now, an accident will allow a drive with potential to spread globally to escape laboratory controls. "It's not going to be bioterror," he says, "it's going to be 'bioerror.'"

DARPA itself has been one of the largest public funders of synthetic biology research in the U.S. in recent years, upping its spending on synthetic biology projects to more than $100 million in 2014 from nothing in 2010, according to one analysis. The agency announced its Safe Genes program in September 2016 and plans to award funding to multiple research teams by the first half of 2017. "If we're going to be really bullish about genome engineering," says DARPA program manager Renee Wegrzyn, "we need to be just as aggressive with tools to reverse those changes."

Normally, a parent organism with a given trait passes that genetic code to offspring about half the time. Recent advances combining the gene-editing tool CRISPR–Cas9 (for, clustered, regularly interspaced, short palindromic repeats with a guiding enzyme called Cas9) are now

making it easier for scientists to modify a genome such that nearly all offspring inherit the desired trait.

Wegrzyn's team is now evaluating proposals from researchers outside DARPA to develop "radically different" approaches to remove, replace or inhibit unwanted genetic changes and their effects, whether the culprit involves a gene drive mechanism or a different type of editing tool. "If we get this right [and are] prepared for these accidental situations," Wegrzyn says, "we're going to be 80 percent there to deal with it in a nefarious situation."

The search for ways to eliminate engineered genes from a variety of species and habitats is only one of three focus areas for DARPA's new program. A second area challenges teams who receive funding from Safe Genes to design systems for controlling and reversing gene editing tools like CRISPR–Cas9. This could mean designing an editing system to work only in one type of tissue, for example. Or, as Esvelt's lab suggested in June 2016, drive components could be scattered throughout a genome so the driving mechanism fades from the gene pool as generations pass. Lastly, researchers will be tasked with developing small molecules, antibodies or other means of arming organisms to rebuff genome editors at a molecular level as well as novel ways to deliver the most promising of these inhibitors to cellular or animal hosts—orally, perhaps, or by way of a specially designed virus.

To receive funding from Safe Genes, teams focused on gene-drive technology must work on controls plus at least one of the program's other focus areas—remediation or inhibitors. According to DARPA's detailed proposal guidelines, Safe Genes expects all projects supported by the program to begin with mathematical modeling and testing in contained systems that increase in complexity and scale only after problems are found and fixed in the less risky environment. "I don't think you let a car go out of the garage without brakes or seat belts," Wegrzyn says. "You really need to understand every component of how it works and how you fix the system if anything goes awry."

In addition to DARPA environmentalists, biosafety experts and leading gene drive researchers say a new approach to mitigation and control is needed for the technology to advance safely. According to a recent report by a panel of 15 experts assembled by the National Academies of Sciences, Engineering and Medicine, traditional containment tools will eventually fall short for systems hardwired to spread genetic information.

The idea of "reversal drives," which would overwrite mutated genes with the original sequence, often arises as a promising solution to gene drives gone wild. But the National Academies report warns the technology is an incomplete safeguard that may produce its own unintended effects and fail to undo the ecological impact of the original drive. "A reversal drive," Esvelt says, "will always play catch-up as the unwanted drive spreads through the wild population."

Another option is to create what's called an immunizing reversal drive in a kind of offense-as-defense move that would overwrite the gene drive and also arm the wild population against it. This, Esvelt says, "could solve the problem but would of course spread through the entire wild population itself." Original traits might be restored but at the genetic level the population would still bear components from the fix-it drive.

Suppressing one species may unleash a surge by a competitor that is equally capable of spreading a disease like dengue or malaria. Disrupting a population could also produce ripple effects in other corners of the ecosystem, for example taking a food source from aquatic predators that feed on mosquito larvae. "You couldn't go back in time," says Jason Delborne, a professor of science, policy and society at North Carolina State University who helped produce the National Academies report, and is part of a team that is putting together a proposal for Safe Genes funding. "We shouldn't move

forward being emboldened [by the idea] that we can release a new trait and have things go back to the way it was."

Evolutionary geneticist Austin Burt, who leads Target Malaria's research at Imperial College London and has no affiliation with Safe Genes, concurs. The prospect of remediation, he says, "shouldn't give us a cavalier attitude." Instead, the goal should be to do the incremental work to anticipate and prevent problems. "We have the precedent of biological control," he says, "where if you have an invasive pest that is destroying your crop, you can release a parasitoid wasp," which kills its host. "They do a very careful assessment. They don't have something in their back pocket," to delete errors.

That said, Target Malaria's researchers are already thinking about how they might stop a gene drive in its tracks. In a response to recommendations in the National Academies report, the organization notes two possible strategies for harnessing natural selection to incapacitate a gene drive that is diminishing a population. One route, first suggested by Burt in 2003, is to release a sequence that is resistant—effectively unrecognizable—to the guiding enzyme that finds cuts of DNA in a gene drive. "If that was functional, then that would spread through the population and the population would rebound," Burt explained. An alternative, proposed earlier this year in Nature Biotechnology, involves a suppressor construct, which would essentially program a secondary guiding enzyme to target the guiding component of the original drive.

For now, Wegrzyn wants to keep the door "wide open" to new ideas that can keep pace with advances in genome editing. "There's a lot of speculation going on in the field right now, and you can continue to speculate indefinitely," she says. "But you need to start to collect the data to really see how these systems are going to work."

http://nyti.ms/2fjdmGv

# Who First Farmed Potatoes? Archaeologists in Andes Find New Evidence

***Researchers say the potato may have first been farmed in the Titicaca Basin, which stretches across the boundary of Peru and Bolivia.***

**By STEPH YIN NOV. 18, 2016**

Nobody knows precisely what the Pilgrims' first Thanksgiving feast looked like. According to primary sources, there was fowl (likely including wild turkeys), venison and cornmeal for sure. Possible side dishes were cranberries, pumpkin and stuffing made with onions, nuts and herbs.

Many of these flavors are still Thanksgiving staples. There's one modern favorite, though, that would not have been found at the inaugural Plymouth celebration: mashed potatoes. That's because potatoes are native to South America and had not yet made their way to North America.

Where in South America potatoes first became domesticated, however, is still unknown. Recent genetic studies point to the Andean highlands in southern Peru and northwestern Bolivia as the crop's birthplace, but a lack of direct plant evidence has made it difficult to confirm.

This week, in a study published in the Proceedings of the National Academy of Sciences, archaeologists at the University of California, Merced, report finding such direct evidence — microremains of what seems to be cultivated potatoes on ancient grinding tools from southern Peru. The remains go back as far as 3400 B.C.

"This is the best archaeological evidence indicating that, yes, early on there were indeed potatoes being cultivated in the central Andes," said Tom Dillehay, a professor of anthropology at Vanderbilt University who was not involved in the research.

The authors of the study looked for microscopic starch grains on stone tools recovered from an ancient, high-altitude site called Jiskairumoko,

in the Titicaca Basin of southern Peru. These tools, they suspect, were used to break up the skins of potatoes.

"In the process, tiny starch grains would get embedded inside micropores and cracks" of the stone tools, said Mark Aldenderfer, one of the authors of the study.

He and his co-author, Claudia Rumold, bathed the tools in a sonicator, which dislodged the starch grains from the pores using sonic waves. Then they analyzed the grains under a microscope and compared them to reference samples of other crops and wild plants from the region.

Out of 141 starch samples recovered from 14 tools, 50 "were consistent with cultivated or domesticated potatoes," Dr. Rumold said.

Starch grain analysis, which is a relatively novel method, was key to finding evidence of potatoes because the tubers do not preserve well, Dr. Aldenderfer said. "When a seed burns, you often get something left of a seed husk. When corn cobs burn, you get something left of the cob. When potato burns, it burns up — very seldom do you get actual bits."

The early cultivation of potatoes seems to have been part of a larger shift at Jiskairumoko, from hunting and gathering toward farming and herding, he added. Around the same time, people started to build more complex houses, and the beginnings of a social hierarchy emerged. In 2008, a team led by Dr. Aldenderfer found a gold necklace from Jiskairumoko dating back to 2000 B.C., suggesting that an elite class had formed by then.

As for how the potato spread and changed from thumbnail- to fist-sized over time, many questions remain. "We don't have enough data to know how many times it was domesticated in this particular area, or if it was just once," Dr. Rumold said.

Historians do know that millenniums later, after the Spaniards conquered the Incan Empire, they introduced the potato to Europe. British colonialists then brought the potato to North America, where it flourished and became a staple. Eventually, probably starting in the 1800s, the beloved spud made its way into Thanksgiving traditions. So when you eat your mashed potatoes this holiday, add ancient Andean civilization to your list of things to be thankful for.

***http://bit.ly/2qcxR7d***

## Rice farming in India much older than thought, used as 'summer crop' by Indus civilization

***Domesticated rice farming in South Asia began far earlier than previously believed***

Latest research on archaeological sites of the ancient Indus Civilisation, which stretched across what is now Pakistan and northwest India during the Bronze Age, has revealed that domesticated rice farming in South Asia began far earlier than previously believed, and may have developed in tandem with - rather than as a result of - rice domestication in China.

The research also confirms that Indus populations were the earliest people to use complex multi-cropping strategies across both seasons, growing foods during summer (rice, millets and beans) and winter (wheat, barley and pulses), which required different watering regimes. The findings suggest a network of regional farmers supplied assorted produce to the markets of the civilisation's ancient cities.

Evidence for very early rice use has been known from the site of Lahuradewa in the central Ganges basin, but it has long been thought that domesticated rice agriculture didn't reach South Asia until towards the end of the Indus era, when the wetland rice arrived from China around 2000 BC. Researchers found evidence of domesticated rice in South Asia as much as 430 years earlier.

The new research is published today in the journals Antiquity and Journal of Archaeological Science by researchers from the University of Cambridge's Division of Archaeology, in collaboration with colleagues at Banaras Hindu University and the University of Oxford.

"We found evidence for an entirely separate domestication process in ancient South Asia, likely based around the wild species Oryza nivara. This led to the local development of a mix of 'wetland' and 'dryland' agriculture of local Oryza sativa indica rice agriculture before the truly

'wetland' Chinese rice, Oryza sativa japonica, arrived around 2000 BC," says study co-author Dr Jennifer Bates

"While wetland rice is more productive, and took over to a large extent when introduced from China, our findings appear to show there was already a long-held and sustainable culture of rice production in India as a widespread summer addition to the winter cropping during the Indus civilisation."

Co-author Dr Cameron Petrie says that the location of the Indus in a part of the world that received both summer and winter rains may have encouraged the development of seasonal crop rotation before other major civilisations of the time, such as Ancient Egypt and China's Shang Dynasty.

"Most contemporary civilisations initially utilised either winter crops, such as the Mesopotamian reliance on wheat and barley, or the summer crops of rice and millet in China - producing surplus with the aim of stockpiling," says Petrie.

"However, the area inhabited by the Indus is at a meteorological crossroads, and we found evidence of year-long farming that predates its appearance in the other ancient river valley civilisations."

The archaeologists sifted for traces of ancient grains in the remains of several Indus villages within a few kilometers of the site called Rakhigari: the most recently excavated of the Indus cities that may have maintained a population of some 40,000.

As well as the winter staples of wheat and barley and winter pulses like peas and vetches, they found evidence of summer crops: including domesticated rice, but also millet and the tropical beans urad and horsegram, and used radiocarbon dating to provide the first absolute dates for Indus multi-cropping: 2890-2630 BC for millets and winter pulses, 2580-2460 BC for horsegram, and 2430-2140 BC for rice.

Millets are a group of small grain, now most commonly used in birdseed, which Petrie describes as "often being used as something to eat when there isn't much else". Urad beans, however, are a relative of the mung bean, often used in popular types of Indian dhal today.

In contrast with evidence from elsewhere in the region, the village sites around Rakhigari reveal that summer crops appear to have been much more popular than the wheats of winter.

The researchers say this may have been down to the environmental variation in this part of the former civilisation: on the seasonally flooded Ghaggar-Hakra plains where different rainfall patterns and vegetation would have lent themselves to crop diversification - potentially creating local food cultures within individual areas.

This variety of crops may have been transported to the cities. Urban hubs may have served as melting pots for produce from regional growers, as well as meats and spices, and evidence for spices have been found elsewhere in the region.

While they don't yet know what crops were being consumed at Rakhigarhi, Jennifer Bates points out that: "It is certainly possible that a sustainable food economy across the Indus zone was achieved through growing a diverse range of crops, with choice being influenced by local conditions.

"It is also possible that there was trade and exchange in staple crops between populations living in different regions, though this is an idea that remains to be tested."

"Such a diverse system was probably well suited to mitigating risk from shifts in climate," adds Cameron Petrie. "It may be that some of today's farming monocultures could learn from the local crop diversity of the Indus people 4,000 years ago."

The findings are the latest from the Land, Water and Settlement Project, which has been conducting research on the ancient Indus Civilisation in northwest India since 2008.