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Organ donation in Ontario increased 57 percent since 2006 after new Canadian donation policy

Donation increased 57% since 2006 after introducing a Canadian policy allowing donation of organs after circulatory functions cease

Organ donation in Ontario increased 57% since 2006 when the province introduced a Canadian policy that allows donation of organs after circulatory functions cease, called circulatory determination of death (DCD), according to a new study published in CMAJ (Canadian Medical Association Journal)

Before 2006, deceased organ donation traditionally occurred after neurologic determination of death (NDD), commonly known as brain death, when a person was declared dead after the complete and irreversible loss of all brain functions.

Because of a lack of organ donors and other factors, waiting lists for donations of lungs, kidneys, livers and hearts are long and recipients often die while waiting, depending on the type of organ.

"The most important development in efforts to expand the donor pool has involved donation after [DCD]," writes Dr. Vivek Rao, Multiorgan Transplant Unit, Toronto General Hospital and the University of Toronto, Toronto, Ontario, with coauthors.

Researchers compared data from the pre-DCD period (2002/03 to 2005/06), early DCD period (2006/07 to 2009/10) and recent DCD period (2010/11 to 2013/14) to understand trends in organ donation after introducing the policy.

"Donation after circulatory determination of death has had a positive effect in Ontario in terms of both overall number of donors and transplant activity," state the authors. "Donation after NDD does not appear to have been adversely affected. Although there are disparities among organ groups, we foresee that an active DCD program will continue to have a positive effect for all solid-organ transplant recipients," they conclude.

In a related commentary, Dr. Sam Shemie of Montreal Children's Hospital and McGill University Health Centre & Research Institute, and medical advisor for Deceased Organ Donation, Canadian Blood Services, says that the research paper shows Ontario has seen a rise in numbers of transplants in the province over a 12-year period that is almost entirely attributable to DCD. This important finding is instructive for the rest of the country. Substantial variation in organ donation rates between provinces still exists and can be explained largely by variable degree of DCD implementation.

However, according to Dr. Shemie, the 2015 rate of 18.2 donors per million people falls far below the number of potential donors, estimated at 40-89 donors per million. Canada must continue to focus on increasing organ donation and preventing death and disability for potential transplant candidates.

The research study was conducted by researchers from Toronto General Hospital, University Health Network, St. Michael's Hospital, the University of Toronto, Trillium Gift of Life Network, Toronto, Ontario; and Children's Hospital of Eastern Ontario, Ottawa, Ontario;

http://bit.ly/2yddG4a

MRI contrast agent locates and distinguishes aggressive from slow-growing breast cancer

Case Western Reserve University researchers target tumor protein

CLEVELAND--A new magnetic resonance imaging (MRI) contrast agent being tested by researchers at Case Western Reserve University not only pinpoints breast cancers at early stages but differentiates between aggressive and slow-growing types.

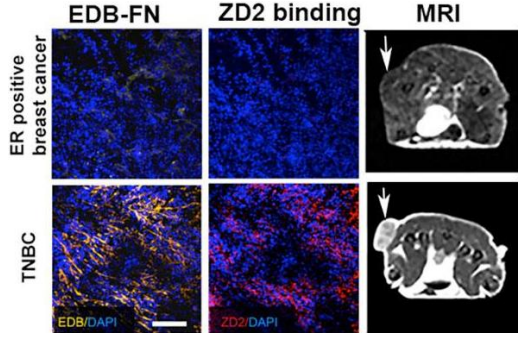
"Doing both will help doctors find the right treatment," said Zheng-Rong Lu, the M. Frank Rudy and Margaret Domiter Rudy Professor of Biomedical Engineering at Case Western Reserve and leader of the research. "There's no such technology available now that we know of."

The gadolinium-based agent is also more efficient and safer than traditional agents, requiring a gadolinium dose 20-times smaller,

easily flushing from the body and leaving no accumulation in tissues, the researchers found in tests with mouse models.

At the low dosage, the agent lights up cancer biomarkers during scans, overcoming the low sensitivity of MRI's for imaging the markers. The research was published today (Sept. 25) in Nature Communications.

To make the agent, Lu and colleagues at Case Western Reserve combined commercially available tri-gadolinium nitride metallofullerene (Gd3N@C80), a highly efficient contrast agent, with a peptide labeled ZD2, which was developed in Lu's lab.



The figure shows the different expression of the biomarker (EDB-FN) and probe binding (ZD2) in slow-growing ER-positive breast cancer (not much yellow and red color representing low expression of the biomarker and low binding), and in triple- negative breast cancer (TNBC, high expression and high binding). As a result, the targeted contrast agent produced weak signal enhancement (brightness) in the former and strong signal (brightness) in the latter as pointed by the arrow. The technology is able to provide accurate detection and risk-stratification of aggressive BC. **Case Western Reserve University**

Compared to the gadolinium used in traditional agents, Gd3N@C80's "structure is different--the gadolinium ions are encaged in a hollow molecule of fullerene that looks like a soccer ball," Lu said. "The cage prevents direct contact between the gadolinium and tissue, and the gadolinium will not be released, which prevents any kind of interaction with tissue." "But the key technology for our targeted contrast agent is the peptide attached," Lu said.

The lab applies ZD2 to the surface of the soccer ball. The peptide specifically targets the cancer protein extradomain-B fibronectin (EDB-FN). EDB-FN, which is associated with tumor invasion, metastasis and drug resistance, is highly expressed in the matrix around cancerous cells in many aggressive forms of human cancers.

In testing on six mouse models, MRI's detected breast cancers in all cases. But the signal created by the accumulation of contrast molecules on three aggressive triple-negative breast cancers (MDA-MB-231, Hs578T and BT549) were significantly brighter. Because slow-moving ER-positive breast cancers (MCF-7, ZR-75-1 and T47D) produce less EDB-FN, fewer molecules attached. While detectible, the signal was muted.

Coauthors of the study are biomedical engineering PhD students Zheng Han and Xiaohui Wu, research assistant Sarah Roelle and undergraduate student Chuheng Chen; and William Schiemann, the Goodman-Blum Professor of Cancer Research at the Case Comprehensive Cancer Center.

Lu's lab is now investigating ways to reduce the cost of producing the agent to make it more attractive for clinical use.

http://bit.ly/2xCdZVy

Antibody protects against Zika and dengue, mouse study shows

Treating pregnant women before infection may protect fetuses from Zika

Brazil and other areas hardest hit by the Zika virus - which can cause babies to be born with abnormally small heads - are also home to dengue virus, which is spread by the same mosquito species.

A new study led by researchers at Washington University School of Medicine in St. Louis shows that an antibody that protects against dengue virus is also effective against Zika in mice.

Antibodies remain in the bloodstream for weeks, so one or a few doses of an antibody-based drug given over the course of a woman's pregnancy potentially could protect her fetus from Zika, with the added benefit of protecting her from both Zika and dengue disease, the researchers said.

Dengue causes high fever, severe headaches, and joint and muscle pain in children and adults but does not directly harm fetuses. "We found that this antibody not only neutralizes the dengue virus but, in

mice, protects both adults and fetuses from Zika disease," said Michael S. Diamond, MD, PhD, the Herbert S. Gasser Professor of Medicine and the study's senior author.

The study is published Sept. 25 in Nature Immunology.

Since dengue and Zika are related viruses, the researchers reasoned that an antibody that prevents dengue disease may do the same for Zika. Diamond and graduate student Estefania Fernandez collaborated with Gavin Screaton, MD, DPhil, of Imperial College London, who had generated a panel of human anti-dengue antibodies years before.

The scientists infected nonpregnant adult mice with Zika virus and then administered one of the anti-dengue antibodies one, three or five days after infection. For comparison, another group of mice was infected with Zika virus and then given a placebo.

Within three weeks of infection, more than 80 percent of the untreated mice had died, whereas all of the mice that received the anti-dengue antibody within three days of infection were still alive, and 40 percent of those that received the antibody five days after infection survived.

To find out whether the antibody also could protect fetuses from infection, the researchers infected female mice on the sixth day of their pregnancies with Zika virus and then administered a dose of antibody or a placebo one or three days later.

On the 13th day of gestation, the amount of Zika's genetic material was 600,000 times lower in the placentas and 4,900 times lower in the fetal heads from the pregnant mice that were treated one day after infection, compared with mice that received the placebo.

However, administering the antibody three days after infection was less effective: It reduced the amount of viral genetic material in the fetal heads nineteenfold and in the placentas twenty-threefold.

These findings suggest that for the antibody to effectively protect fetuses from Zika infection, it must be administered soon after infection. Such a goal may be unrealistic clinically because women rarely know when they get infected. However, giving women the antibody as soon as they know they are pregnant could provide them with a ready-made defense against the virus should they encounter it.

Antibody-based drugs have been used for decades to provide temporary protection against infectious diseases such as rabies when there is no time to vaccinate or, as in the case of Zika, when there is no vaccine available.

The key to using this antibody as a preventive drug would be to make sure that antibody levels in a woman's bloodstream stay high enough to protect her fetus for the duration of her pregnancy. Diamond and colleagues are working on identifying how much antibody a pregnant woman would need to ensure that her fetus is protected from Zika.

They also are exploring ways to extend the antibody's half-life in the blood, to reduce the number of times it would need to be administered.

Having anti-dengue antibodies circulating in the bloodstream for months on end poses a risk, though, because antibodies that protect against one strain of dengue virus sometimes worsen symptoms if a person is infected by another dengue strain.

To avoid the possibility of accidentally aggravating an already very painful disease, the researchers mutated the antibody in four spots, making it impossible for the antibody to exacerbate dengue disease.

"We mutated the antibody so that it could not cause antibody enhancement of dengue infection, and it was still protective," said Diamond, who is also a professor of pathology and immunology, and of molecular microbiology. "So now we have a version of the antibody that would be therapeutic against both viruses and safe for use in a dengue-endemic area, because it is unable to worsen disease."

http://bit.ly/2xLiY5P

People are reluctant to use public defibrillators to treat cardiac arrests

Study suggests members of the public don't know what they are, how to use them or where to find them

A study led the University of Warwick suggests that people are reluctant to use public access defibrillators to treat cardiac arrests.

The analysis of existing international studies, which has been published in the European Heart Journal, suggests that there are a number of factors that prevent members of the public from using them and potentially saving lives.

The researchers' study suggests that many members of the public don't know what an automated external defibrillator (AED) is, where to find one and how to use one. This is despite AEDs being suitable for use by untrained members of the public. Although studies suggest there is variation across the studies they analysed in the number of people willing to use an AED a lack of confidence and fear of harm are common themes.

The research, Barriers and facilitators to public access defibrillation in out-of-hospital cardiac arrest: a systematic review, was conducted by Warwick Medical School, the University of Warwick; the Institute of Digital Healthcare, WMG, the University of Warwick; Heart of England NHS Trust, Birmingham; London Ambulance Service NHS Trust and Imperial College Neurotrauma Centre, St Mary's Hospital, London.

Gavin Perkins, Professor in Critical Care Medicine at Warwick Medical School said: "Public access defibrillation is very effective in certain cases of cardiac arrest outside of hospital. "A study conducted in the US showed that the chance of survival was nearly double in the group that received CPR and were treated with a public access defibrillator compared to the group that received CPR alone. However the number of cases when a public access defibrillator is used is very low - just 0.15-4.3% of cardiac arrests that occur outside of hospitals."

Although only a minority of out of hospital cardiac arrests occur in locations where use of a defibrillator would help save a life AEDs are often poorly accessible or have limited availability; often their location is not known to even emergency services or those running training schemes. They also found that although members of the public saw the value of AED training most hadn't undergone training.

Theo Arvanitis, Professor of e-Health Innovation and Head of Research at the Institute of Digital Healthcare, WMG, at the University of Warwick said: "Investment in more AEDs is great but it's at least as important to maximise use of existing defibrillators.

"Many cardiac arrests that happen in public occur out of 'normal business hours' therefore if an AED is kept in a building there is a good chance the building won't be accessible.

"We would also like to see the message put out that these devices can be used without training. However our study found that those with training were more likely to use an AED so training is important too."

It was found that public-access AEDs were often acquired by donation or fundraising rather than private purchase, and donation was a predictor of AED acquisition among college athletic departments in one study.

The research team also examined the reasons for not obtaining an AED. They were: cost; concerns about liability; not being thought/not being considered necessary; lack of and/or attrition of responsible individuals; there was a good, local emergency service and there was a nearby hospital. One study reported that while 32% cited cost and 37% cited legal concerns as reasons not to obtain an AED, 55% thought affordability and 51% thought legal protection were good reasons to obtain an AED.

They also highlighted that maintenance of AEDs was variable. One study reported that all but one of 206 AEDs were 'operable' and ready for use, but many AEDs were not maintained or had no formal plans in place for maintenance or replacement.

The systematic review conducted by the research team consisted of an analysis of 68 English language articles. Many of these were observational, many collected data retrospectively or were surveys. Due to the nature of the articles surveyed the team recommend further research is needed before making policy proposals.

Barriers and facilitators to public access defibrillation in out-of-hospital cardiac arrest: a systematic review European Heart Journal - Quality of Care and Clinical Outcomes (2017) 0, 1-10 doi:10.1093/ehjqcco/qcx023

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Three or more cups of coffee daily halves mortality risk in patients with both HIV and HCV

Novel five-year study highlights importance of behaviors such as coffee drinking and not smoking on health and survival of HIV-infected patients, report investigators in the Journal of Hepatology

Amsterdam, The Netherlands - Patients infected by both human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are at specific risk of end-stage liver disease and greater risk of cardiovascular diseases and cancer. In addition, HIV infection accelerates the progression of chronic hepatitis C to fibrosis and development of cirrhosis and end-stage liver disease. In these HIV-HCV co-infected patients, drinking at least three cups of coffee each day halved the risk of all-cause mortality according to a new study published in the Journal of Hepatology.

This study is the first to investigate the relationship between coffee consumption and the risk of all-cause mortality in HIV-HCV co-infected patients. "This is a very exciting time for HCV research as a cure that can eradicate the virus is now available for all patients," explained lead investigator Dominique Salmon-Céron, MD, PhD, of the Service des Maladies Infectieuses et Tropicales, Hôpital Cochin, and Université Paris Descartes, Paris, France. "However, even when cured of HCV, patients co-infected with HIV have a higher risk of death with respect to the general population, due to an accelerated aging process that may result from cancer, complications related to diabetes and to liver disease, and from cardiovascular events."

Coffee is known to have anti-inflammatory and liver-protective properties. In the general population, drinking three or more cups of coffee a day has been found to be associated with a 14% reduction in the risk of all-cause mortality. This is probably due to the properties of polyphenols contained in coffee that can protect the liver and also reduce inflammation.

Investigators used data from a five-year follow-up of 1,028 HIV-HCV co-infected patients enrolled in the French national ANRS CO13-HEPAVIH cohort. ANRS CO13-HEPAVIH is an ongoing French nationwide prospective cohort of HIV-HCV co-infected patients that collects both medical and psychosocial/behavioral data over time via annual self-administered questionnaires.

At enrolment, one in four patients reported drinking at least three cups of coffee daily. Over the five years, 77 deaths occurred, almost half attributable to hepatitis C. However, the mortality risk was 80% lower in those who were cured of (i.e. who "cleared") hepatitis C thanks to treatment.

Further analysis showed that drinking at least three cups of coffee daily was associated with a 50% reduction in mortality risk even after taking into account HCV clearance, HIV- and HCV-related factors, and other sociobehavioral factors, such as having a steady partner and not smoking. Healthy behavior change should be promoted by physicians following HCV clearance.

This research highlights the importance of behaviors - coffee consumption and not smoking in particular - on reduced mortality risk. These results can help promote behavioral changes in HIV-HCV patients, which in turn can result in improved survival. With respect to coffee consumption, individuals who do not drink coffee because of caffeine can still benefit from the comparable anti-inflammatory effects of decaffeinated coffee.

First author Maria Patrizia Carrieri, PhD, of the HEPAVIH Study Group, Faculté de Médecine, Aix Marseille University, INSERM, IRD, SESSTIM, Marseilles, France, observed that coffee consumption

provides more protective effects on mortality in the HIV-HCV population than in the general population.

"The results of our study show that while curing HCV is fundamental, it must be complemented by behavioral changes if we are to improve health and survival in HIV-infected patients whether or not they cleared HCV. "I think we need to better monitor coffee consumption, together with other behaviors, such as alcohol use, smoking, physical activity, and to propose interventions to our patients which facilitate healthy behaviors even after HCV clearance. We also suggest that those patients who cannot tolerate a high intake of caffeine should consider drinking a few cups of decaffeinated coffee a day," commented Dr. Salmon-Céron. "Accordingly, I believe that the benefits of coffee extracts and supplementing dietary intake with other anti-inflammatory compounds need to be evaluated in HIV-HCV patients."

http://bit.ly/2fWeHmw

That cup of coffee may not relieve Parkinson's symptoms

Contrary to previous research, caffeine may not relieve movement symptoms for people with Parkinson's disease

Please note the important correction to the press release below. Grams of caffeine has been changed to milligrams.

MINNEAPOLIS - Contrary to previous research, caffeine may not relieve movement symptoms for people with Parkinson's disease, according to a study published in the September 27, 2017, online issue of Neurology®, the medical journal of the American Academy of Neurology.

A previous study, published in Neurology in 2012, suggested that caffeine may help reduce movement symptoms for people with Parkinson's disease. Because the study was small and only six weeks long, the researchers decided to investigate further.

"Caffeine, which is so safe and inexpensive, has been linked to a reduced risk of developing Parkinson's," said study author Ronald B. Postuma, MD, MSc, McGill University in Montreal and member of the American Academy of Neurology. "So it was exciting to think that it could possibly help people who already have the disease."

The study involved 121 people with an average age of 62 who had been diagnosed with Parkinson's disease for an average of four years. Of those, half were given a 200-milligram capsule of caffeine twice daily, once in the morning and once after lunch, the equivalent of three cups of coffee per day, while the other half were given placebo capsules.

To help them adjust to the caffeine, the dose was increased slowly, starting with placebo and reaching 200-milligram at week nine. The study participants were followed for six to 18 months.

Researchers found there was no improvement in movement symptoms for people who had taken the caffeine capsules compared to those who took the placebo capsules. There was also no difference in quality of life. Because of these data showing no benefit to taking caffeine, the study was stopped.

"While our previous study showed possible improvement in symptoms, that study was shorter, so it's possible that caffeine may have a short-term benefit that quickly dissipates," said Postuma. "Regardless, our core finding is that caffeine cannot be recommended as therapy for movement symptoms of Parkinson's disease."

"It is important that promising leads be studied," said Charles B. Hall, PhD, of Albert Einstein College of Medicine in the Bronx, N.Y., who commented on the study for Neurology. "It is also important that the disappointing findings like these be shared so new research can focus on other possible treatments instead."

One limitation of this study was that researchers did not measure caffeine in the blood of people during the study and it's possible some may not have adhered to study requirements, affecting results. Also, the caffeine dose chosen was based upon previous studies and it's possible a higher dose may have different effects.

The study was supported by the Canadian Institute of Health Research, the Webster Foundation and the FRQS (Fonds de Recherche du Québec - Santé).

http://bit.ly/2x1HLne

One-Quarter of Cancer Patients Use Medical Marijuana, Study Finds

One of the most well-known purported uses for medical marijuana is to alleviate symptoms related to cancer treatment, and a new study finds that use of the drug among cancer patients is not uncommon.

By Sara G. Miller, Staff Writer | September 25, 2017 07:06am ET

In the study, which included more than 900 cancer patients in Seattle, nearly one-quarter reported using medical marijuana in the past year. In addition, almost all the participants said they wanted to learn more about medical marijuana, according to the study, published today (Sept. 25) in the journal Cancer.

But existing research on marijuana's effects on cancer-related symptoms is limited, the researchers said. Indeed, the study underscores the need for more research into the risks and benefits of marijuana use among cancer patients, lead study author Dr. Steven Pergam, a researcher at the Fred Hutchinson Cancer Research Center in Seattle, said in a statement.

Cancer patients want information about marijuana use during their treatment, but they aren't getting this information from their doctors, Pergam said. Because of this, patients instead seek information from "alternate, nonscientific sources," he said.

In the study, the researchers surveyed cancer patients at the Seattle Cancer Care Alliance, a cancer treatment center. The survey included questions about marijuana use among cancer patients, as well as questions about the patients' beliefs surrounding the drug.

The researchers found that 24 percent of the patients in the study were "active users," meaning that they had used marijuana in the past year for cancer-related symptoms, and 21 percent reported using the drug in the past month. These rates are more than double those reported in national surveys of any type of marijuana user, the researchers said.

Among the active users, the researchers found that 74 percent reported using marijuana at least once a week, 56 reported using the drug at least once a day and 31 percent reported using the drug multiple times a day. Smoking and consuming edibles were the most common ways of using the drug, the researchers found.

Three-quarters of the active users said they used the drug to help with physical symptoms, including pain and nausea, and two-thirds reported that they used marijuana to help with psychiatric symptoms, including stress and sleep problems.

Active users were more likely than people who never used the drug to cite legalization as a reason for using marijuana, the researchers found. Active users were also younger than those who didn't use the drug or who had used the drug in the past but quit, according to the study.

And though 74 percent of the people in the study said that they would like information on medical marijuana from their cancer teams, less than 15 percent actually received information from their health care providers. Instead, most people sought out information from friends, family members, media sources or other cancer patients, the researchers found.

The researchers noted that the study had limitations. For example, it's possible that the people who completed the survey were more likely to have an interest in medical marijuana, the researchers said. In addition, because the study was carried out at only one cancer-treatment center and in a state where recreational marijuana use is legal, the findings may not apply to people across the country, the researchers said.

http://bit.ly/2x2v9aq

Predatory bacteria found in study of cystic fibrosis patients' lung microbiome

Two 'predators' not detected before in lungs of cystic fibrosis patients

WASHINGTON, DC - Cystic fibrosis patients have a wide variety of bacteria in their lungs, including two 'predators' not detected before, according to a new study of lung microorganisms published this week in mBio®, an online open-access journal of the American Society for Microbiology.

Using a laboratory technique called next-generation sequencing, a group of investigators from Madrid, Spain, studied the bacterial makeup of sputum samples provided by 15 cystic fibrosis patients three to four times over the course of a year. They found a wide range of bacterial species in the samples, including Pseudomonas aeruginosa, Staphylococcus aureus, Burkholderia and Pandorea. Each patient had his or her own bacterial makeup that remained relatively steady over the study period.

What surprised researchers was also finding two types of predator bacteria among the samples. Vampirovibrio, a bacteria that destroys cells by sucking out its contents, was found in 17 samples from 12 patients, while Bdellovibrio, which enters cells and feeds on its proteins, was found in six samples from three patients. The two types were found together in only one patient. Developing a novel computer science model to explain the relationship between these predators and potential prey bacteria, the investigators hypothesized that the predators, in the early stage of disease, may prevent the colonization of bacteria like P. aeruginosa normally associated with cystic fibrosis.

Predator bacteria "are ubiquitous and usually found in environmental aquatic ecosystems," said senior study author Rosa del Campo, of the Microbiology Service at Ramón y Cayal University Hospital. "In humans, a recent study has found them in the intestinal microbiota of healthy individuals and in patients with cystic fibrosis."

The findings indicate that "the lung microbiota in cystic fibrosis patients is more complex than we believed," she said. "Our study suggests that predatory bacteria could be used as a therapeutic strategy to reduce the bacterial load of the lungs of these patients."

Del Campo and colleagues analyzed 56 sputum samples from cystic fibrosis patients at her hospital. Patients were classified by lung function impairment as mild (five patients), moderate (nine patients), or severe (one patient). Among the samples, they found 156 types of bacteria, including Pseudomonas, Haemophilus, Staphylococcus, Pandoraea, Sphingomonas, Saccharibacteria genera incertae sedis, Stenotrophomonas, Leptotrichia, Capnocytophaga, Burkholderia, Oribacterium, Aquabacterium, Lachnoanaerobaculum, Campylobacter and Mycoplasma. P. aeruginosa and S. aureus were found together in the eight patients with the poorest lung function.

The natural evolution of cystic fibrosis is a progressive decline in lung function caused by a vicious circle of inflammation and tissue destruction, which is triggered and maintained by the chronic bacterial colonization of the lower respiratory tract, del Campo said. "It is generally acknowledged that once bacterial colonization is established in the lung, its eradication is almost impossible, despite consistent antibiotic treatment," she said.

The next steps for her team include cultivating the predator bacteria to understand their ability to survive in the lungs and their interaction with prey, and to try using predator bacteria to control the CF lung microbiota, she said.

The study was supported by the Instituto de Salud Carlos III (Institute of Health Carlos III) and by REIPI, the Spanish network for research in infectious diseases, cofinanced by the European Development Regional Fund.

http://wb.md/2k7Xr29

A Supplement That May Block The Toxic Effects of Alcohol

Hello and welcome. I am Dr George Lundberg, and this is At Large at Medscape. September is "be kind to addicts" month (officially National Recovery Month). How can we help?

George D. Lundberg, MD

Of every 100 Americans who drink (140 million), about 12 (16 million) are considered in need of treatment for an alcohol use disorder, and eight will become chemically dependent on alcohol.[1] Of that eight, one will become addicted very early, even after the first drunken episode. The problem is, we do not yet have a way to predict who that one person will be.

Prevention is always the best answer to addiction. Do not drink. If you do drink, do not ignore the warning signs of becoming a problem drinker.

Let me ask you: How is your blood acetaldehyde today; or, more relevant, how was it late last night? You don't know? Why am I not surprised? Most people don't even think about acetaldehyde.

Ethyl alcohol is metabolized to acetaldehyde by alcohol dehydrogenase in the liver. Acetaldehyde is metabolized to acetate by aldehyde dehydrogenase and then to carbon dioxide and water. Depending on the alcohol dose, some of the acetaldehyde may escape hepatic metabolism and enter the general blood circulation.

Acetaldehyde is a close cousin to my old pathology lab friend formaldehyde. We use it to pickle surgical and autopsy tissues for preservation. Both are known carcinogens. Our body's defense mechanism against excess acetaldehyde is the amino acid l-cysteine and glutathione. These molecules, similarly to thiamine, contain a sulfhydryl group that is chemically active against aldehydes.

Unless you are one of those people (typically East Asian) who are genetically deficient in aldehyde dehydrogenase or are taking disulfiram, you can metabolize roughly one stiff drink per hour. If you drink more than that, depending on body weight, gastric contents, and the efficiency of your metabolic alcohol breakdown, acetaldehyde will build up because aldehyde dehydrogenase capability can be overwhelmed.

If you quit drinking at 11:00 PM, then around about 1:00 AM, your acetaldehyde level may be elevated and you may feel symptoms of acetaldehyde toxicity, including skin flushing, tachycardia, palpitations, anxiety, nausea, thirst, chest pain, and vertigo. Of course, you are trying to "sleep it off," so you may not feel toxic until the next morning when that dreaded hangover appears.

Metabolizing Alcohol

My friends in the nutritional supplement community tell me that you can enhance the metabolism of blood alcohol to acetate, carbon dioxide, and water and minimize the acetaldehyde molecular logjam by taking oral supplements. L-cysteine, vitamin C, and vitamin B_1 are purported to help. At supplement doses, they are cheap and harmless at worst. At best: Goodbye, acetaldehyde toxicity; hello, restful sleep. About 200 mg of L-cysteine per ounce of alcohol consumed is sufficient to block a major portion of the toxic effect of acetaldehyde. But because alcohol is absorbed and metabolized rapidly, it may be necessary to take L-cysteine before and concurrently with consumption to maintain protection. Also, an excess of vitamin C (perhaps 600 mg) can help keep the L-cysteine in its reduced state and "on the job" against acetaldehyde. Experts recommend these doses (with or without extra B_1): one round before drinking, one with each additional drink, and one when finished.

Some say that this regimen works very well. Do not ask me for a list of published randomized, double-blind clinical trials. Not yet, at least. Research funding into "harm reduction" from addicting substances has not enjoyed favored status in research priorities.

Unfortunately, this concoction may have little effect on next-day hangovers, the causes of which are complex and resistant to prevention—except, obviously, by not drinking too much, which is, of course, the best answer to alcohol anyway.

With drug users, be redemptive, not punitive.

That is my opinion. I am Dr George Lundberg, and this is At Large at Medscape.

http://nyti.ms/2fyLqxK

How Dinosaurs Swapped Terrifying Teeth for Bird Beaks

Fearsome beasts evolved into birds, replacing their terrifying teeth with beaks

By NICHOLAS ST. FLEUR SEPT. 26, 2017

The world once trembled before the theropods.

This dinosaur group, which included bloodthirsty killing-machines like the Tyrannosaurus rex and velociraptor, was notorious for sharp, serrated teeth that many used to eviscerate prey and strip flesh clean from bones. But over millions of years, the fearsome beasts evolved into today’s flamboyantly feathered birds, replacing their terrifying teeth with beaks.

How the theropod mouth transformed has long been a mystery, but a study published Monday in the Proceedings of the National Academy of Sciences provides insight into a potential evolutionary mechanism behind the transition.

The Limusaurus, a theropod that had teeth in its youth — the skull on the right — but then lost them as it grew into an adult, left, developing a beak instead. **Josef Stiegler**

Amy Balanoff, an evolutionary biologist from Johns Hopkins and an author of the paper, described the findings as further "evidence showing the line of evolution from a Tyrannosaurus rex to a pigeon."

Using fossils and a large comparative analysis of modern animals, Dr. Balanoff and a team of evolutionary biologists, led by Shuo Wang from the Capital Normal University in Beijing, found that the loss of teeth and the emergence of beaks are connected processes in theropods. As the beak grew across the dinosaur's face, it also inhibited the growth of teeth, the team suggested. On an evolutionary scale this transition happened until theropods developed mouths that resembled the bird beaks seen today.

In earlier research, Dr. Wang's team discovered an emu-like theropod called Limusaurus that began life as a baby with teeth, but lost them as it grew older and morphed into an adult with a beak.

A fossil jaw from the early Cretaceous bird Sapeornis showing vestigial tooth holes. **Hailong Zang**

For their most recent paper, he and his colleagues examined more dinosaur jaw fossils and found two other theropods that underwent transitions similar to Limusaurus: an early Cretaceous bird called Sapeornis, which resembled modern birds, and a small caenagnathid oviraptorosaur, which resembled a velociraptor but with a beak.

"This demonstrates an evolutionary process of the beak for the first time," said Dr. Wang. All three theropods had beaks but with vestigial, or functionless, tooth sockets.

"Based on these three dinosaurs, we now have evidence for three distinctly different lineages that lose their teeth during postnatal development to have a beak," said Josef Stiegler, a doctoral candidate at the George Washington University in D.C. He added, that the findings suggest there may be more examples in the fossil record.

A rendering of the Limusaurus. **Levi bernardo, via Wikimedia Commons**

After collecting the fossil evidence, the team sought further support for their hypothesis that the processes of teeth loss and beak development were connected. So they performed a comparative and statistical analysis of thousands of modern vertebrates to understand the shared characteristics of animals that develop beaks.

They found that beaked animals tended to be born from eggs laid on land and from embryos that had a structure on the tip of their snouts known as a caruncle. The facial structure was made of keratin, the substance found in fingernails, and was used to break through the egg before falling off shortly after. Beaked groups like birds and turtles have caruncles, but snakes and nearly all lizards do not.

Mr. Stiegler linked their analysis to what they found in the fossil record. He said the transition they saw in the jaws of the Limusaurus — where hatchlings and juveniles lose their teeth as they became adults — may have been how the change from toothy dinosaur to beaked bird began.

"But as evolution progressed, we hypothesized that that transition happened earlier and earlier in development until it was happening only in the embryo," said Mr. Stiegler. Their comparative and statistical analysis supported the hypothesis, he said.

The team also suggested that a protein called bone morphogenetic protein 4, or BMP4, may simultaneously stop teeth from growing in embryos and stimulate the development of a beak. In the developing embryo, the beak originates near the caruncle and then gradually expands backward. But Mr. Stiegler cautions that BMP4 is likely not the only factor behind the mechanism, and that additional research is needed to determine the root cause.

Stephen Brusatte, a paleontologist from the University of Edinburgh who reviewed the paper, said that the study was a great example of how fossils and genetics can be used together to understand how the birds we know today evolved from ferocious dinosaurs.

“Beaks actually cause teeth to disappear,” he said. “This simple fact helped shape one of the major transitions in the history of evolution.”

http://bbc.in/2xMwWEq

'Instant' blood test for heart attacks

A blood test that could rule out a heart attack in under 20 minutes should be used routinely, say UK researchers.

A team from King's College London have tested it on patients and say the cMyC test could be rolled out on the NHS within five years. They claim it would save the health service millions of pounds each year by freeing up beds and sending well patients home.

About two-thirds of patients with chest pain will not have had a heart attack. A heart trace, called an ECG, can quickly show up major heart attacks, but it is not very good at excluding more common, smaller ones that can still be life-threatening.

Currently, patients with suspect chest pain and a clear ECG can have a different heart-attack blood test, called troponin, when they arrive at A&E. But it needs to be repeated three hours later to pick up signs of heart muscle damage.

Alison Fullingham, 49 and from Bolton, did not realise she was having a heart attack when she experienced pain in her upper chest, neck and jaw. Despite a small change in her ECG, doctors initially suspected she was having a simple panic attack. It was only hours later when her troponin tests came back that the correct diagnosis was reached.

Rapid diagnosis

Levels of cMyC (cardiac myosin-binding protein C) in the blood rise more rapidly and to a higher extent after a heart attack than troponin proteins, studies suggest. That means doctors can use the new test to rule out a heart attack in a higher proportion of patients straightaway, according to the researchers who report their trial findings in the journal Circulation.

They carried out troponin and cMyC blood tests on nearly 2,000 people admitted to hospitals in Switzerland, Italy and Spain with acute chest pain. The new test was better at giving patients the all-clear within the first three hours of presenting with chest pain.

Dr Tom Kaier, one of the lead researchers, funded by the British Heart Foundation (BHF) at St Thomas' Hospital, London, said: "Our research shows that the new test has the potential to reassure many thousands more patients with a single test, improving their experience and freeing up valuable hospital beds in A&E departments and wards across the country." He says if the test were to be used routinely, it could provide doctors with reliable results within 15 to 30 minutes. It is only being used for research at the moment, however.

Dr Kaier's hospital carries out around 7,800 troponin blood tests each year. By his calculations, switching to cMyC would save his hospital £800,000 through reduced admissions. Extrapolate that to other NHS hospitals and the savings could be millions of pounds, he says.

Prof Simon Ray, from the British Cardiovascular Society, said more research was needed before the new test could replace the troponin test. "Unlike currently available blood tests which need to be repeated at least three hours after pain it looks as though a single test is enough to make a confident decision on whether a patient has or has not suffered a heart attack. Not only can it be done earlier after the onset of symptoms but it also seems to be better at discriminating between heart attacks and other causes of chest pains. This is very important."

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Life on Earth may date back 3.95 bn years: study

Rudimentary life may have existed on Earth 3.95 billion years ago, a time when our infant planet was being bombarded by comets and had hardly any oxygen, researchers said Wednesday.

A team presented what they say is the oldest-known fossil evidence for life on the Blue Planet—grains of graphite, a form of carbon, wedged into ancient sedimentary rocks in Labrador, Canada.

The previous most ancient life traces were reported in March, from a site in Quebec estimated at between 3.8 billion and 4.3 billion years old, though an author of the new study called that dating process "highly controversial." "This is the oldest evidence," Tsuyoshi Komiya of The University of Tokyo insisted in an email exchange with AFP. "Our samples are also the oldest supracrustal rocks preserved on Earth"—a type similar to the formation which contained the Quebec samples.

Fossil evidence for early organisms is scarce, and rocks that remain from that period are often poorly preserved. A key difficulty for scientists on a quest to find the oldest life on Earth is proving that organic remains were produced by living organisms rather than geological processes.

This field of study is aimed not only at pinpointing the start of life on our planet, but also to shed light on the possibility of life having existed—or still existing—on other planets such as Mars.

For the new study, Komiya and a team studied graphite, a form of carbon used in pencil lead, in rocks at Saglek Block in Labrador, Canada. They measured its isotope composition, the signature of chemical elements, and concluded the graphite was "biogenic"—meaning it was produced by living organisms. The identity of the organisms, or what they looked like, remains a mystery.

"We will analyse other isotopes such as nitrogen, sulphur and iron of the organic matter and accompanied minerals to identify the kinds of organisms," said Komiya of the next step. "In addition, we can estimate the environment" in which the organisms lived by analysing the chemical composition of the rock itself.

If the findings are accurate, it means life took hold on Earth just a geological second after its formation some 4.5 billion years ago. Before the Quebec fossils, which were also described in Nature, the oldest traces of life were found in Greenland's ice cap and dated to 3.7 billion years ago.

More information: Takayuki Tashiro et al. Early trace of life from 3.95 Ga sedimentary rocks in Labrador, Canada, Nature (2017). DOI: 10.1038/nature24019

http://bit.ly/2x52txw

Research sheds new light on how Earth and Mars were created

Analysing a mixture of earth samples and meteorites, scientists from the University of Bristol have shed new light on the sequence of events that led to the creation of the planets Earth and Mars.

Planets grow by a process of accretion - a gradual accumulation of additional material - in which they collisionally combine with their neighbours. This is often a chaotic process and material gets lost as well as gained. Massive planetary bodies impacting at several kilometres per second generate substantial heat which, in turn, produces magma oceans and temporary atmospheres of vaporised rock. Before planets get to approximately the size of Mars, gravitational attraction is too weak to hold onto this inclement silicate atmosphere. Repeated loss of this vapour envelope during continued collisional growth causes the planet's composition to change substantially.

Dr Remco Hin from the University of Bristol's School of Earth Sciences, led the research which is published today in Nature.

He said: "We have provided evidence that such a sequence of events occurred in the formation of the Earth and Mars, using high precision measurements of their magnesium isotope compositions.

"Magnesium isotope ratios change as a result of silicate vapour loss, which preferentially contains the lighter isotopes. In this way, we estimated that more than 40 per cent of the Earth's mass was lost

during its construction. "This cowboy building job, as one of my co-authors described it, was also responsible for creating the Earth's unique composition."

The research was carried out in an effort to resolve a decades long debate in Earth and planetary sciences about the origin of distinctive, volatile poor compositions of planets.

Did this result from processes that acted in the mixture of gas and dust in the nebula of the earliest solar system or is it consequence of their violent growth?

Researchers analysed samples of the Earth together with meteorites from Mars and the asteroid Vesta, using a new technique to get higher quality (more accurate and more precise) measurements of magnesium isotope ratios than previously obtained.

The main findings are three-fold:

Earth, Mars and asteroid Vesta have distinct magnesium isotope ratios from any plausible nebula starting materials

The isotopically heavy magnesium isotope compositions of planets identify substantial (~40 per cent) mass loss following repeated episodes of vaporisation during their accretion

This slipshod construction process results in other chemical changes during growth that generate the unique chemical characteristics of Earth.

Dr Hin added: "Our work changes our views on how planets attain their physical and chemical characteristics. "While it was previously known that building planets is a violent process and that the compositions of planets such as Earth are distinct, it was not clear that these features were linked. "We now show that vapour loss during the high energy collisions of planetary accretion has a profound effect on a planet's composition.

"This process seems common to planet building in general, not just for Earth and Mars, but for all planets in our Solar System and probably beyond, but differences in the collision histories of planets will create a diversity in their compositions."

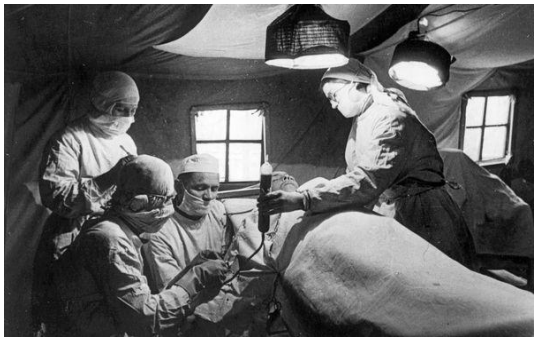
'Magnesium isotope evidence that accretional vapour loss shapes planetary compositions' by R. Hin, C. Coath, P. Carter, F. Nimmo et al in Nature.

http://go.nature.com/2kbkqta

Transfusion: Too much of a good thing

The ability to give donated blood to patients has saved countless lives. But the routine nature of such transfusions is being rethought.

- **Bianca Nogrady**



A blood transfusion is conducted in a field hospital on the Russian Western Front during the Second World War. **akg-images**

For a medical treatment to be approved by regulatory bodies, it must go through a rigorous sequence of laboratory testing, studies in animals and clinical trials to establish its safety and efficacy.

Yet there is a centuries-old treatment used every day in intensive-care units and emergency departments worldwide that, until two decades ago, had never been put through the large-scale studies that evidence-based medicine demands.

The procedure in question is blood transfusion. Since the early 1800s, when the first recorded human-to-human transfusion was conducted, saving a woman who was bleeding heavily after giving birth, transfusions have become a mainstay of critical-care medicine.

But the long-held consensus on transfusion may not, in fact, be best practice. To begin with, people with certain conditions who receive blood might do just as well without it. There is also a suggestion that transfused blood itself — aside from the associated risks of infection or rejection — may have immunological and physiological effects on the body that are not necessarily benign. “People have been practicing transfusion for a long time but we didn't always have the good-quality evidence base to help us to know how to do it,” says Erica Wood, a specialist in transfusion medicine at Monash University in Melbourne, Australia.

More than 30 clinical trials, covering a range of patient groups and medical scenarios, have examined the effects of providing transfusions under only the most urgent of circumstances, as measured by the level of oxygen-carrying protein haemoglobin in the patient's blood. These trials overwhelmingly have found no difference in death rate — or in other outcomes such as stroke, sepsis, kidney failure, pneumonia or wound infection — between transfusing blood to the patient when the haemoglobin level drops below a 'liberal' threshold of 9–10 grams of haemoglobin per decilitre or a more 'restrictive' threshold of 7–8 grams per decilitre[1].

Changing the default

A rethink of the transfusion threshold began in 1999 with a trial that looked at transfusions in critically ill people[2], set against a backdrop of increasing concern about blood-borne diseases and the cost of transfusions. This pivotal study, involving 838 intensive-care patients in Canada, found that transfusing blood only when a patient's haemoglobin level dropped to 7 grams per decilitre — as opposed to below 10 grams per decilitre, which had been the standard since the 1940s — would not increase the risk of poor outcomes.

The death rate from all causes within 30 days of patients' admission to intensive care was similar regardless of whether the decision to transfuse blood was implemented at the higher or lower haemoglobin level. In fact, patients who were given a transfusion under the more-restrictive threshold were less likely to die during their hospital stay, and had slightly lower levels of organ dysfunction.

“If you don't transfuse, you can't get side effects from blood”

The Canadian trial marked a turning point for transfusion medicine, says Jeffrey Carson, an internist at the Robert Wood Johnson Medical School at Rutgers University in New Jersey. “If you don't transfuse, you can't get side effects from blood,” he says. “If it doesn't improve outcomes, there's no good reason to use more blood.”

Wood says clinicians are now focusing on why someone might need blood - for example, being referred to the emergency department with severe anaemia - and addressing that reason directly.

“Many people are safely treated with intravenous iron, rather than transfusion,” she says. “If we give them somebody else's red blood cells, it might increase their haemoglobin today, but those red blood cells will not last a long time - and you haven't fixed their problem, which is a lack of iron.”

The re-evaluation of transfusions is also changing surgical practice. James Isbister, a haematologist at the Sydney Medical School, says that, at present, most transfusions are given on a prophylactic basis. “The doctor is either expecting a problem or wants to cover themselves for something that may or may not happen,” he notes.

Instead of relying on a post-surgery blood transfusion to prevent anaemia, clinicians are working to identify and address anaemia in patients long before they go under the knife, as well as taking steps to minimize blood loss during operations.

“When you look through the alternatives to transfusion, most of them are, in fact, good clinical medicine,” Isbister says. “The message is transfusion should not be a default decision until you've really worked out what the problem is and the best way to treat it.”

There are also people for whom a blood transfusion is truly life-saving: those who have lost huge amounts of blood owing to trauma or to bleeding during childbirth; those with conditions affecting the red blood cells, such as sickle-cell anaemia or thalassaemia; and those whose bone marrow has been depleted by chemotherapy. “There are a lot of times when blood is really needed for life-saving,” says Majed Refaai, a pathologist at the University of Rochester Medical Center in New York. But he objects to transfusions being given simply to raise a patient's haemoglobin level.

The threshold question

Such thinking is becoming the norm. Indeed, guidelines for when to perform transfusions have become more restrictive worldwide,

including those used in the United States, Australia, the United Kingdom and much of Europe. But a restrictive threshold and a lower level of haemoglobin may not be suitable for all patients.

One such group comprises people who have experienced a heart attack or who are undergoing heart surgery, says Carson. He points to a trial in people receiving heart surgery that suggested the more restrictive transfusion threshold was actually associated with a slightly higher rate of mortality[3]. Given that a heart attack is the result of a blockage in the arteries supplying blood — and therefore oxygen — to the muscles of the heart, it stands to reason that boosting the blood supply could help to limit the damage, Carson says.

“The nature of oxygen metabolism in the heart is that it extracts a large percentage of the oxygen that a red blood cell delivers — much higher than other parts of the body,” he says.

Carson and colleagues conducted a pilot study[4] in 110 people being treated for a heart attack, which hinted at better outcomes when a liberal transfusion threshold of 10 or more grams of haemoglobin per decilitre was used, and they are now embarking on a follow-up study in 3,500 people. Similar concerns exist for people who have experienced injury to the brain — another organ that is acutely sensitive to reduced blood flow and oxygen levels.

A group of diseases that might also benefit from a more liberal threshold for transfusion are the blood cancers: leukaemia, myeloma and lymphoma. Zoe McQuilten, a haematologist at Monash University, says that people with conditions that require regular transfusions are very different from the acutely ill patients who are most often the subject of trials on transfusion.

For one thing, they are not in hospital and are living close to normal lives — regular transfusions notwithstanding — yet they are assessed using the same haemoglobin thresholds as people in intensive care, McQuilten says. An upcoming feasibility study hopes to address this by taking a different approach to the question. Instead of exploring whether a restrictive threshold is as safe as a liberal threshold in the critically ill, “we're asking would a higher haemoglobin level result in a higher quality of life in patients who are chronically transfused,” she says.

Do no harm

There is also the long-standing question of whether transfusions are entirely benign. Aside from potential issues of contamination and severe immune reactions, there is the possibility that the transfused blood itself could be causing harm.

Refaai argues that because blood is essentially a 'liquid' organ, a transfusion is equivalent to an organ transplant, with its attendant risks. He points to growing evidence that, under the same circumstances, patients who undergo the same procedure with the same risk factors actually do better if they don't have a transfusion compared to if they do.

For example, transfusions have been associated with an increased risk of infection in recipients. McQuilten says this could be explained by the iron hypothesis, which states that older red blood cells are more likely to be broken down than fresh ones in the first few hours following transfusion. This is thought to lead to the release of haemoglobin and iron from the damaged cells into the extracellular space that, in turn, can promote the growth of bacteria.

Another concern is that storage could have adverse effects on blood. Blood products comprising red blood cells typically have a shelf life of up to 42 days. But Jamie Cooper, a critical-care physician and director of the Australian and New Zealand Intensive Care Research Centre at Monash University, says that red blood cells may undergo structural and biochemical changes during storage that could have harmful consequences for recipients. For example, instead of retaining a round, smooth and flexible disc-like shape, older red blood cells become more rigid and pointed or spiky, which is also known as spiculation.

“We're worried that spiculated older cells might not travel so well through the microcirculation,” Cooper says. “This might be a problem

with critically ill patients who have shock, as they have lots of changes in microcirculation."

To make matters even more complicated, there's the possibility that extremely fresh blood may also make patients more vulnerable to acquiring outside infections compared to blood of an intermediate age. Cooper says that there might be a 'sweet spot' for the age of stored blood: a storage duration that minimizes the possible risks of both fresh and older red blood cells. "It could be that a red cell in a bag is like a good Chianti; it has to sit there for a while and develop a bit of age."

Several large studies have assigned patients randomly to receive transfusions of either fresh or older blood, with mixed results. Cooper says the challenge is to conduct a study large enough to detect what could be small differences in outcomes relating to the age of blood.

"It is very important, because it's so critical that blood transfusion is safe," Cooper says. Given the frequency of blood transfusions, and the vulnerability of those receiving them, there is little room for uncertainty. "If a blood transfusion was bad for you, even a tiny bit," says Cooper, "it would be better if we were more judicious."

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http://bit.ly/2x4IQFO

Red blood cells for transfusion like a good red -- a little older, a little better

Transfusion of older stored red blood cells is safe and associated with fewer side effects

A landmark Australian research trial has found the transfusion of older stored red blood cells is safe and surprisingly, associated with fewer side effects.

In the TRANSFUSE trial, researchers from the Australian and New Zealand Intensive Care Research Centre at Monash University in Melbourne led teams in 5 countries to investigate the effect of the age of transfused red blood cells on critically ill patient's outcomes.

In a study published in the New England Journal of Medicine on September 27th, the team demonstrated that fresher blood was no better than older blood.

Unexpectedly they also found fewer transfusion reactions, including fever, with the older blood; and in the most severely ill patients, the transfusion of older blood was associated with fewer deaths.

Lead researcher Professor Jamie Cooper said "older blood appears to be like a good red wine- better with some age.

The findings of our trial confirm that the current duration of storage of red blood cells for transfusion is both safe and optimal".

In Australia, red blood cells are stored for up to 42 days before transfusion.

Routine practice in most hospitals is to allocate the oldest available compatible blood.

Concerns regarding changes in the red blood cells for transfusion during storage, have led some countries to reduce this to 35 days, and some doctors to request fresher blood for specific patients under the belief the "fresh must be best".

"Such practices can significantly reduce the availability of blood for transfusion" said Professor Cooper.

"Our study shows these practices are not required and are potentially counterproductive".

The TRANSFUSE trial was of 5000 Intensive Care patients in Australia, New Zealand, Finland, Ireland and Saudi Arabia. This ground-breaking research was performed in collaboration with the Australian and New Zealand Intensive Care Society Clinical Trials Group, and the Irish Critical Care-Clinical Trials Group. It was made possible by grants from the National Health and Medical Research Council, the Health Research Council of NZ, and the Health Research Board of Ireland. TRANSFUSE was supported by the Australian Red Cross Blood Service, the Australian National Blood Authority and the national blood transfusion services of New Zealand, Ireland, and Finland.

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New test rapidly diagnoses Zika

Paper-based diagnostic avoids false positives from Dengue fever and other related viruses

CAMBRIDGE, MA -- MIT researchers have developed a paper-based test that can diagnose Zika infection within 20 minutes. Unlike existing tests, the new diagnostic does not cross-react with Dengue virus, a close relative of the Zika virus that can produce false positives on many Zika tests.

This test could offer an easy-to-use, cheap, and portable diagnostic in countries where Zika and Dengue are both prevalent and the gold-standard test that measures viral RNA in the bloodstream is not available.

"It's important to have a single test that can differentiate between the four serotypes of Dengue and Zika, because they co-circulate. They're spread by the same mosquito," says Kimberly Hamad-Schifferli, an associate professor of engineering at the University of Massachusetts at Boston, a visiting scientist in MIT's Department of Mechanical Engineering, and a co-senior author of the paper.

The researchers worked with scientists around the world to test the new device on patient samples and confirmed that it can accurately distinguish Zika virus from related viruses.

Lee Gehrke, the Hermann L.F. von Helmholtz Professor in MIT's Institute for Medical Engineering and Science (IMES), is also a senior author of the study, which appears in the Sept. 27 issue of Science Translational Medicine. The paper's first authors are IMES research scientist Irene Bosch and Department of Mechanical Engineering postdoc Helena de Puig.

No more false positives

One of the biggest challenges in diagnosing Zika is that many of the tests are based on antibodies that interact with a viral protein called NS1, which is found in the bloodstream of infected patients. Unfortunately, many other viruses from the same family, known as flaviviruses, have similar versions of NS1 and can produce a false positive.

Flaviviruses include West Nile virus and the virus that causes yellow fever, as well as Dengue virus.

In an effort to create a more precise diagnostic, the MIT team set out to find antibodies that would interact exclusively with NS1 protein produced by the Zika virus, as well as antibodies specific to NS1 from each of the four different strains of the Dengue virus.

To achieve this, the researchers exposed mice to Zika and Dengue viruses and then screened the resulting antibodies, in pairs, against every flavivirus' version of the NS1 protein. This allowed them to identify pairs of antibodies that react only with one version of NS1 and not any of the others.

"We knew by informatics analysis that if we looked enough, and we teased out the repertoire of the B cells of these animals, we would eventually find those antibodies," Bosch says. "We were able to tease out the very few antibodies within the repertoire that would give you uniqueness in the detection."

The researchers used these pairs to create five separate tests, one for each virus.

They coated strips of paper with one antibody from each pair, while the second antibody was attached to gold nanoparticles. After adding the patient's blood sample to a solution of these nanoparticles, the paper strip is dipped into the solution.

If the target NS1 protein is present, it attaches to the antibodies on the paper strip as well as the nanoparticle-bound antibodies, and a colored spot appears on the strip within 20 minutes.

This approach requires five test strips per sample to test for each virus, but the researchers are now working on a version that would test for all five with one strip.

Most countries where Zika and Dengue are prevalent do not allow patient samples to be shipped out of the country, so the researchers

traveled to several countries, including Mexico, Colombia, India, and Brazil, to test their devices with patient samples.

They found that their results were comparable to those obtained by polymerase chain reaction (PCR) tests, which detect viral RNA in the bloodstream.

PCR tests are not widely used in areas where Zika virus is found because they require trained personnel and lab equipment that are not available everywhere.

Emerging viruses

Dengue infects hundreds of millions of people annually, mostly in tropical regions. It is usually not fatal, but in areas where there is more than one serotype circulating, it is more likely to produce a severe, potentially life-threatening illness.

A diagnostic that can distinguish between all four serotypes of Dengue fever could give doctors a way to discover early on when a new serotype has entered their region.

"When we have traveled to the places where these viruses are problems, the people there unanimously say that they need more surveillance. They need to know which viruses are circulating in their environments," Gehrke says.

The researchers believe that their approach should also enable them to quickly develop diagnostic tests for other related viruses that might emerge in the future.

"By already screening this group of antibodies that we have against all these antigens we have, like West Nile, we already know how well they react. So that's information we could use in the future to develop additional tests that can be used to detect other emerging viruses," Gehrke says.

They are now working on a diagnostic for the emerging Powassan virus, which is carried by the same tick that spreads Lyme disease. Powassan, found mainly in the northeastern United States and the Great Lakes region, causes a severe form of encephalitis.

The research was funded by the U.S. Public Health Service and the Science, Technology and Innovation Fund of Colombia.

http://bbc.in/2xNCONE

UK 'eliminates measles' for first time

The elimination of measles has been achieved in the UK for the first time, the World Health Organization says.

The global health body classes a country as having eliminated the disease when it has stopped it freely circulating for at least three years.

While there are still small clusters, many of these are brought in from abroad and they are not spreading.

But health experts said there should be no complacency, warning there were several large outbreaks across Europe.

The news comes just a week after it was announced England had achieved the target of getting 95% of children to have had the first dose of the measles, mumps and rubella vaccine by their fifth birthday. Wales, Scotland and Northern Ireland were already achieving it.

That figure is considered important because it ensures herd immunity, meaning the disease cannot spread because of the high level of vaccination rates. MMR vaccination rates dipped after a panic caused by discredited former doctor Andrew Wakefield, who falsely claimed in the late 1990s that the jab caused autism.

Before that the UK was on track to achieve measles elimination.

'Huge achievement'

The announcement does not, however, mean that measles has been wiped out. Last year there were over 500 cases in England, many linked to clusters of cases among young people going to festivals. But what was important was that the disease was not able to spread more widely.

During the first six months of this year there have been fewer than 100 cases in England along with small clusters in Wales and Northern Ireland, which were linked to Romania where there is a major outbreak. It marks a major shift from previous years. In 1967 - the year before the vaccine was introduced - there were over 460,000 cases and 99 deaths. By the 1980s that had been brought down to around 10,000 cases a year and even five years ago there were over

2,000 cases a year. Deaths are now rare. Since 2006 there have only been two children who have died from the disease.

Dr Mary Ramsay, head of immunisation at Public Health England, said: "This is a huge achievement and a testament to all the hard work by our health professionals in the NHS to ensure that all children and adults are fully protected with two doses of the MMR vaccine.

"We need to ensure that this is sustained going forward by maintaining and improving coverage of the MMR vaccine in children and by catching up older children and young adults who missed out."

Across Europe 42 out of 53 countries have now achieved elimination status.

http://bit.ly/2yA9jfK

Bones of Stone Age boy challenge single-origin theory of modern humans

DNA analysis points to no one cradle of humanity but a whole African nursery. Tim Wallace reports.

The 2,000-year-old bones of a boy found on a beach in South Africa have provided more grounds to challenge the prevailing theory that modern humans had a single origin in north-eastern Africa.

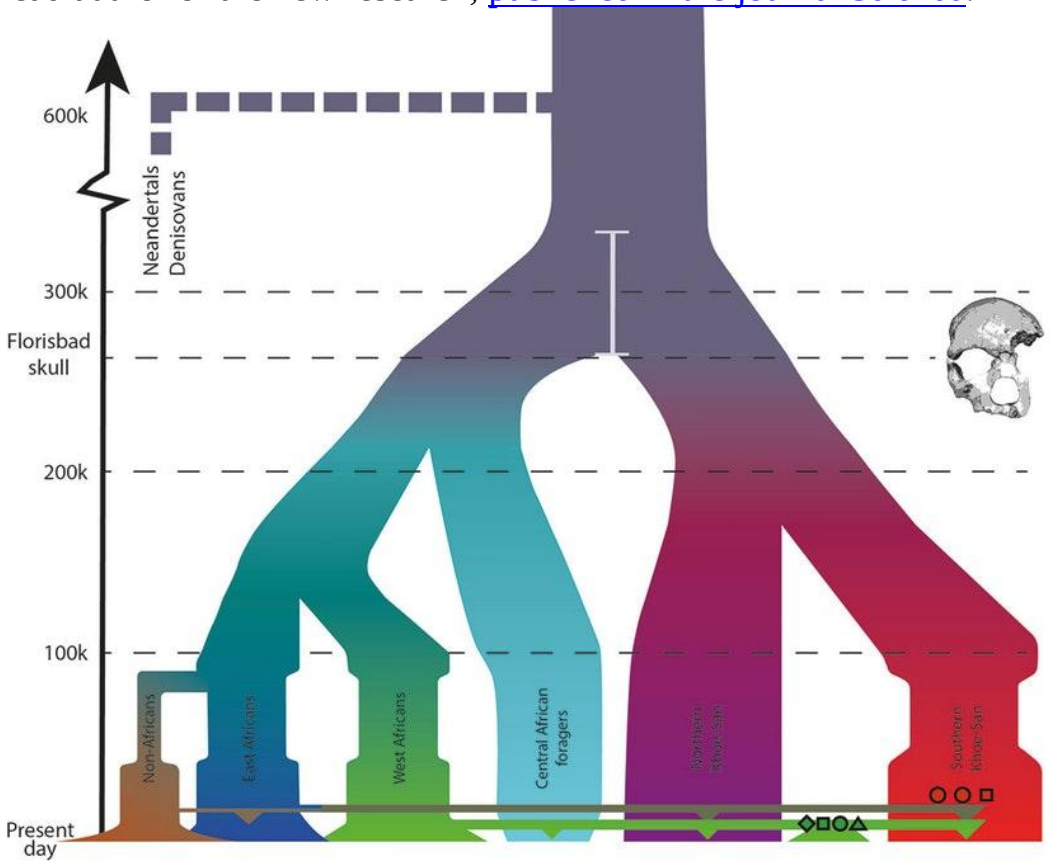
That fraying theory, based on fossils found at Omo Kibish and elsewhere in Ethiopia, dates the emergence of modern humans to about 180,000 years ago.

However, by using DNA analysis as a 'molecular clock' to calculate the length of time since the boy's ancestors diverged genetically from other groups of modern humans, scientists in South Africa and Sweden estimate that modern humans must have existed between 260,000 and 350,000 years ago.

This pushing back of the estimated date of the emergence of modern humans by at least 100,000 years is roughly in line with research published in June that dated human remains and other artefacts found at the Jebel Irhoud archaeological site in Morocco as about 300,000 years old.

The finding lends weight to the hypothesis there was not just a single cradle of modern humankind in north-eastern Africa but, rather, an entire continental nursery.

"It seems that both genetics and archaeology are converging on this point that there might be multiple places in Africa that archaic humans transitioned from Homo erectus to H. heidelbergensis to modern humans," says Carina Schlebusch of Uppsala University in Sweden, lead author of the new research, published in the journal *Science*.



Demographic model of African history and estimated divergences. Vertical coloured lines represent migration. Down-pointing triangles represent admixture into another group. Southern African hunter-gatherers are shown by red symbols, Iron Age farmers by green symbols. **C. Schlebusch et al. Science (2017)**

Scientists have been hesitant about alternatives to the single-origin idea because of the demise of a previous 'multiregional' theory that once competed with the 'Out of Africa' hypothesis, Schlebusch says. That theory, suggesting separate groups of modern humans evolved from ancient hominin groups around the world, was disproven by DNA analysis showing Homo sapiens fossils throughout the rest of world were much closer genetically to each otherthan those from Africa, and therefore could not have evolved independently.

"The multiregional theory was wrong in terms of how the globe was populated," Schlebusch agrees, "but it is not necessarily wrong about how humans evolved in Africa."

It seemed unlikely that such potentially history-changing evidence would come from the bones of the stone-age boy known as Ballito Bay A – named after the place the bones were found on a beach in the KwaZulu-Natal region of South Africa.

Exposed to sand, salt, water and other weathering elements in a subtropical climate that is hot and humid, the bones were poor candidates for DNA analysis.

"We had more hope for our other samples, which were from caves," says Schlebusch. "Caves generally are much better because the climate is very stable and cool, so the DNA doesn't degrade. But these samples for some reason worked very well."

Given the lack of supporting archaeological artefacts, the only thing known with certainty about the boy is what his genes tell us: he was a member of the San branch of the Khoe-San peoples of southern Africa. He likely lived a hunter-gatherer lifestyle and spoke with the clicks that linguistically unify the San with the Khoe, who practised a nomadic form of pastoral farming.

The Khoe-San are not only genetically distinct from Europeans and Asians but also from other Africans. Research suggests that they are a branch of modern humans that diverged early from our oldest common H. sapiens ancestors.

What makes Ballito Bay A special, from a contemporary scientific perspective, is his relative genetic "purity', meaning his ancestry involved fewer procreative liaisons with members of other human groups than the other specimens.

This made it easier for Schlebusch and her colleagues to use his DNA as a 'molecular clock', comparing it to the DNA of other specimens and estimating how long it would have taken for various mutations to have evolved from a common ancestor.

DNA dating isn't infallible. It requires making assumptions about a rate of genetic mutation from one generation to the next, and also about the length of each generation.

"Molecular clocks are very tricky to use, especially when rates are calculated using modern, or near-modern, genetic data only," notes Alan Cooper at the University of Adelaide in South Australia, who is a world-recognised leader in the field of ancient DNA.

"Better estimates of the mutation rate and generation time could bring these dates down by quite a large amount."

On that basis, though being "somewhat sceptical about the very large dates," Cooper says the research by Schlebusch and her colleagues is certainly interesting.

"Even if we consider the dating as rather 'aspirational', they have demonstrated deep genetic splits in human genetic diversity, considerably larger than before, and demonstrated that southern Africa should be considered as playing a more central role in the evolutionary story."

Schlebusch acknowledges that mutation-rate and generation estimates can be debated, but says the results of DNA dating are still valuable on a relative scale, and in league with other lines of inquiry.

"I really think ancient DNA studies in Africa will make a big contribution. We're at the stage now where we are going to meet up with palaeontological and archaeological estimates to see how archaic humans transitioned to modern humans."

http://bit.ly/2xSTraX

Medication that treats parasite infection also has anti-cancer effect

Ivermectin exerts an anti-tumor effect on epithelial ovarian cancer cells

Osaka, Japan - Osaka Researchers, in partnership with other Japanese and U.S. scientists, report a new gene target, KPNB1, for treatment against epithelial ovarian cancer (EOC). EOC is the fifth leading cause of cancer-related deaths in women and has a particularly grim outlook upon diagnosis. They also find that ivermectin exerts an anti-tumor effect on EOC cells by interacting with the KPNB1 gene. Because ivermectin is already approved to treat parasitic infections in patients, experiments for its effectiveness in an anti-cancer regimen is expected to significantly lower costs compared to untested drug compounds. The study can be read in Proceedings of the National Academy of Sciences.

"EOC is a challenging disease to treat because of its heterogeneity. The mortality rate has stayed steady for decades. We need new drugs and also new drug targets," says Osaka University Gynecologist Michiko Kodama, who first-authored the study.

To search for new drug target genes for EOC, Kodama did two in vivo screenings, one shRNA based and the other CRISPR/Cas9 based. Several were found including ERBB2, but because there are already drugs that target ERBB2 in clinical use, she settled her attention on the gene with the second highest rank in the screening, KPNB1.

Kodama confirmed that KPNB1 has features consistent of an oncogene, finding that its overexpression significantly accelerated EOC cell proliferation and survival, while its inhibition induced apoptosis. "We found KPNB1 activation and inhibition had a direct effect on the expression of apoptosis factors," she says.

Adding to the likelihood that this gene has a role in EOC, she found that the prognosis for EOC patients diminished with higher KPNB1 expression. "This does not show KPNB1 is a cause of EOC, but it does show it could be a target", she added.

It has been estimated that drug repositioning takes one third the time and cost for an experimental drug to receive federal approval compared with drug discovery. Therefore, to find drug candidates that can suppress the oncogenetic properties of KPNB1, Kodama sought only clinically-approved drugs, settling on ivermectin.

"Ivermectin inhibits importin /-mediated nuclear transport. KPNB1 is a member of the importin family," she explains, adding that this family imports proteins into the cell nucleus.

She found that ivermectin had pro-apoptotic effects in EOC cells, but not if the KPNB1 activity was already artificially suppressed. Moreover, ivermectin had a synergistic effect when combined with paclitaxel, the currently preferred drug for EOC treatment.

Because EOC cancer is heterogeneous, the best therapeutic regimens will likely involve a combination of drugs. Through comprehensive screenings for mutants and clinically-approved drugs, Kodama is hopeful that drug repositioning will bring such regimens to patients faster. "We do not understand the molecular mechanisms for the synergistic effect. Ivermectin and paclitaxel have been in clinical use for several decades, which should facilitate clinical trials," she said.

http://bit.ly/2x5Rk4y

Coastal Critters Make Epic Voyages After 2011 Tsunami

Marine species survived rafting thousands of kilometers on debris swept into the water by the giant wave, scientists say.

By Ashley Yeager | September 28, 2017

Pieces of plastic and other ocean debris gave coastal critters a ride to other continents following the enormous earthquake-generated tsunami that hit the coast of Tohoku in Japan in 2011. Researchers studied the marine life attached to plastic fragments, fishing vessels, and large docks carried into the Pacific Ocean after the temblor and found that hundreds of species had rafted thousands of kilometers in the longest hitchhike of coastal species ever recorded.

"We have known for many years that oceanic rafting is happening and has happened throughout the history of our Earth," Martin Thiel, a marine biologist at Catholic University of the North in Chile, tells *The Scientist* by email. "What is surprising is the magnitude of this event and that we can document this as it happens."

Coauthor John Chapman of Oregon State University inspects a Japanese vessel that washed ashore on Long Beach, Washington. **Russ Lewis**

Thiel, who was not involved in the new study, explains that in the past, scientists have relied on genetic markers to identify previous rafting events. In the new work, published today (September 28) in *Science*, Williams College marine scientist James Carlton and colleagues recorded the diversity of animal communities on 634 pieces of Japanese tsunami marine debris, including vessels, docks, buoys, crates, wood, and other objects that turned up on US shorelines.

A Japanese buoy carrying Japanese oysters, **Crassostrea gigas*****, found floating offshore at Alsea Bay, Oregon, in 2012.*** **James T. Carlton**

Having traversed roughly 7,000 kilometers across the Pacific, the material carried with it living animals from 289 Japanese coastal marine species, representing 16 phyla. Five invertebrate groups—mollusks, annelids, cnidarians, bryozoans, and crustaceans—made up 85 percent of the species diversity.

Carlton tells *The Scientist* the count of smaller critters, those less than a millimeter, is probably an underestimate. "It's really hard to collect the tiny stuff," he says. What has been detected so far has mostly been incidental; it was sent along with samples of much larger organisms. "It's hard to believe some of these creatures rafted all the way from Japan to Hawaii, Washington, Oregon, and other regions of North America," Carlton says. "Nothing in the previous records told us that these organisms could travel this far."

This study shows how a sudden pulse of debris from a catastrophic event can provide a mechanism for species to cross oceans, Jon Waters, a marine biologist and geneticist at the University of Otago in Dunedin, New Zealand, tells *The Scientist* by email. "For species that can settle on or cling to these debris, there's real potential for a long ride to a new place."

Waters notes that some of the rafting species found traversing the Pacific Ocean are unsurprising to find, including obligate rafters such as the goose barnacle *Lepas* and the rafting marine gastropod mollusk *Fiona*. Others are truly coastal species that, in this case, have come an unusually long way, notably, starfish, sea anemones, chitons, and some sponges, Carlton says. They've never rafted before, they have never been picked up in ships' ballast tanks or transported by other means, and therefore had not been seen in North America before the tsunami.

Rafting on plastic marine debris, in comparison to natural debris, allows for essentially unlimited transport because the plastic will remain intact for years, decades, or even longer, Kara Lavender Law, a physical oceanographer at the Sea Education Association, tells *The Scientist* by email. As a result, she says, humans have provided a previously nonexistent mechanism for species dispersal—only time will tell what the long-term impacts will be.

The Japanese sea star **Asterias amurensis** ***on a fisheries dock from Misawa, Japan, found washed ashore near Newport, Oregon, in June 2012*** **John W. Chapman**

Ocean rafting could intensify species invasions, Carlton notes. No introductions of new species to North American coasts have been detected since the tsunami. But there are lag times in the growth of non-native species populations, so they may go unspotted for years or

decades, he says, and his team is keeping an eye out for any that take up residence outside their native habitats.

J. Carlton et al., "Tsunami-driven rafting: Transoceanic species dispersal and implications for marine biogeography," Science, doi:10.1126/science.aao1498, 2017.

http://bit.ly/2x7Da2K

UTA study says zinc can halt the growth of cancer cells

Study may provide a road map for treatment and prevention

Zinc supplements can significantly inhibit the proliferation of esophageal cancer cells, according to a new study co-authored by a University of Texas at Arlington researcher.

Previous studies had shown that zinc is essential for maintaining human health and protects the esophagus from cancer. However, it has never been fully understood why zinc has the ability to prevent cancer in the esophagus. In this study, a team led by Zui Pan, an associate professor of nursing at UTA's College of Nursing and Health Innovation and a noted esophageal cancer researcher, discovered that zinc selectively halts the growth of cancer cells but not normal esophageal epithelial cells. The finding was published this month in The FASEB Journal, the official journal of the Federation of American Societies for Experimental Biology.

Esophageal cancer is the sixth leading cause of human cancer deaths around the world, according to the National Cancer Institute. The institute estimates that there were almost 16,000 esophageal cancer deaths in the United States in 2016. The average five-year survival rate is less than 20 percent. Pan said this study could provide a pathway for better esophageal cancer prevention and treatment.

"Zinc deficiency has been found in many cancer patients," said Pan, whose study was funded in part by a research grant from the National Institutes of Health - National Cancer Insitute. "Both clinical data and animal studies have shown that this mineral is very important for overall body health and for cancer prevention."

Zinc is an important element in many proteins and many enzymes and the absence of zinc makes it impossible for cells to function, she added. "But previously we didn't know why the same physiological concentrations of zinc inhibit cancer cell growth but not normal cells. Our study, for the first time to our knowledge, reveals that zinc impedes overactive calcium signals in cancer cells, which is absent in normal cells, and thus zinc selectively inhibits cancer cell growth." said Pan. "It now appears that zinc and calcium can have a cross talk, meaning that they can be linked."

An insufficient amount of zinc can lead to the development of cancers and other diseases, Pan said. "That's why it is important to have a good diet," she said. Zinc enriched foods include spinach, flax seeds, beef, pumpkin seeds and seafood like shrimp and oysters.

Pan said that in the future they will study these two signals link, how they impact each other and how researchers can take advantage of what they know. Such a step will guide them in developing a better prevention and treatment strategy, she said.

Anne Bavier, dean of UTA's College of Nursing and Health Innovation, called Pan's study a classic example of UTA's commitment to high impact research. "It re-affirms UTA's position as a major player in the global battle against cancer," said Bavier. "Zui's work on esophageal cancer gets straight to the heart our goal at the College of Nursing and Health Innovation to help solve health problems to build a healthier world."

UTA's Strategic Plan 2020 Bold Solutions | Global Impact includes a major focus on Health and the Human Condition.

http://bit.ly/2q0Yso7

Parkinson's disease involves degeneration of the olfactory system

Scientists discover anatomical link for the loss of smell in Parkinson's disease

The first symptom of Parkinson's disease is often an impaired sense of smell. This neurodegenerative disease primarily causes irreparable damage to nerve cells in a brain area involved in movement control. How it affects the olfactory system has been unclear. Researchers at

the Max Planck Research Unit for Neurogenetics in Frankfurt and the University of Auckland in New Zealand have now carried out a study comparing the olfactory bulbs of individuals with and without Parkinson's disease. The researchers found that the total volume occupied by the functional units in the olfactory bulb - the so-called glomeruli - is in Parkinson's cases only half that in normal individuals. Moreover, the distribution of the glomeruli within the olfactory bulb is altered in Parkinson's cases.

Nine out of ten patients with Parkinson's disease suffer from defects of the sense of smell in the early stages of the disease - often years before the appearance of the motor symptoms that are characteristic of the disease. The motor symptoms are caused by a loss of nerve cells in the region of the substantia nigra in the brain that is responsible for controlling movement. What causes this cell death has not yet been fully clarified, but a key role appears to be played by Lewy bodies. These are inclusions, inside the cells, that contain a misfolded, defective version of the alpha-synuclein protein. Lewy bodies are found in the olfactory bulb before they appear in the substantia nigra.

The so-called olfactory vector hypothesis for Parkinson's disease proposes that environmental factors, such as viruses, heavy metals or pesticides, are risk factors or even causes of the condition. No other sensory system than the olfactory system is in such close contact with the external environment - the inhaled air. The hypothesis posits that the disease-causing agent is introduced from the nasal cavity into the olfactory bulb, where Parkinson's disease is triggered and gradually spreads through other parts of the brain.

Intact tissue samples required

The human olfactory bulb remains poorly studied. Research on this brain structure depends critically on the availability of pristine samples, which are typically procured post mortem, from brain donors. The Neurological Foundation of New Zealand Douglas Human Brain Bank in Auckland, New Zealand works closely with families of patients suffering from neurodegenerative diseases to ensure ethical and effective collection of post mortem brain samples from diseased and non-diseased cases. The precarious location of the olfactory bulb below the bulk of the brain and the many axons that connect it to the olfactory mucosa mean that special efforts must be made to protect the morphology of the olfactory bulb when collecting the samples.

The New Zealand-based researchers were able to collect olfactory bulbs fit for an in-depth quantitative study. In a globe-spanning project, the researchers processed the post mortem olfactory bulbs chemically, cut ten-micrometer thin sections throughout its entire length, and stained the sections with fluorescently labeled antibodies. The labeled sections were then scanned in Frankfurt, and the images reconstructed in 3D allowing for quantitative whole-olfactory bulb analyses.

New quantitive parameter

As glomeruli of the human olfactory bulb are difficult to count unambiguously, the researchers came up with a new, quantitative parameter: the global glomerular voxel volume. This quantity is the sum of the volume of all glomeruli. These are formed by the coalescence of axons of olfactory sensory neurons making synapses with olfactory bulb neurons. Having defined this new parameter, the researchers compared the values between olfactory bulbs from normal and Parkinson's disease cases, and found that it was reduced by more than half. Whether the decrease is the result of Parkinson's disease cases having fewer or smaller glomeruli, or is due to a combination of these two effects, remains to be seen.

In addition, the distribution of the glomeruli was altered. The olfactory bulbs of normal cases had 70 percent of their glomerular component in the bottom half of the olfactory bulb, but the olfactory bulbs of Parkinson's disease cases contained only 44 percent in the bottom half. "The preferential deficit of the glomerular component in the bottom half of the olfactory bulb, close to the olfactory mucosa, is consistent with the olfactory vector hypothesis of Parkinson's disease", states Peter Mombaerts, M.D., Ph.D., director of the Max Planck Research

Unit for Neurogenetics. The scientists also discovered that the greater the number of Lewy bodies with aggregated alpha synuclein, the smaller the glomerular component of the olfactory bulb. "This relationship could be an indication that the Lewy bodies are the cause of the reduction in glomerular volume," explains Dr. Bolek Zapiec, first author of the paper. The question now is which type of neurons in the olfactory bulb is affected first or foremost in Parkinson's disease. Next the researchers would like to identify the neurons in the olfactory bulb that are the most vulnerable.

Original publication

Bolek Zapiec, Birger V. Dieriks, Sheryl Tan, Richard L. M. Faull, Peter Mombaerts, Maurice A. Curtis A ventral glomerular deficit in Parkinson's disease revealed by whole olfactory bulb reconstruction. Brain; 3 September, 2017

http://bit.ly/2fId9Qi

Frequent sauna bathing keeps blood pressure in check

Frequent sauna bathing reduces the risk of elevated blood pressure, according to an extensive follow-up population-based study carried out at the University of Eastern Finland.

The risk of developing elevated blood pressure was nearly 50% lower among men who had a sauna 4-7 times a week compared to men who had a sauna only once a week. These findings were published recently in the American Journal of Hypertension.

The same researchers have previously shown that frequent sauna bathing reduces the risk of sudden cardiac death, and cardiovascular and all-cause mortality. Elevated blood pressure is documented to be one of the most important risk factors of cardiovascular diseases. According to the research group, underlying protective mechanisms may include the beneficial effects of regular sauna bathing on blood pressure.

The Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD) involved 1,621 middle-aged men living in the eastern part of Finland. Study participants without elevated blood pressure of over 140/90 mmHg or with diagnosed hypertension at the study baseline were included in this long-term follow-up study. Based on their sauna bathing habits, men were divided into three sauna frequency groups: those taking a sauna once a week, 2-3 times a week, or 4-7 times a week. During an average follow-up of 22 years, 15.5% of the men developed clinically defined hypertension. The risk of hypertension was 24% decreased among men with a sauna frequency of 2-3 times a week, and 46% lowered among men who had a sauna 4-7 times a week.

Sauna bathing may decrease systemic blood pressure through different biological mechanisms. During sauna bathing, the body temperature may rise up to 2 °C degrees, causing vessels vasodilation. Regular sauna bathing improves endothelial function, i.e. the function of the inside layer of blood vessels, which has beneficial effects on systemic blood pressure. Sweating, in turn, removes fluid from the body, which is a contributing factor to decreased blood pressure levels. Additionally, sauna bathing may also lower systemic blood pressure due to overall relaxation of the body and mind.

A recent analysis of the same study also revealed that those taking a sauna frequently have a lower risk of pulmonary diseases.

Research articles: Zaccardi F, Laukkanen T, Willeit P, Kunutsor SK, Kauhanen J, Laukkanen JA. Sauna Bathing and Incident Hypertension: A Prospective Cohort Study. Am J Hypertens. 2017 Jun 13. doi: 10.1093/ajh/hpx102.

Kunutsor SK, Laukkanen T, Laukkanen J. Sauna bathing reduces the risk of respiratory diseases: a long-term prospective cohort study. Letter to the Editor. Eur J Epidemiol 2017 Sep 13. doi: 10.1007/s10654-017-0311-6

http://bit.ly/2yBfMY2

The science behind why some people love animals and others couldn't care less

Some people are into pets, however, while others simply aren't interested. Why is this the case?

September 29, 2017 by John Bradshaw, The Conversation

The recent popularity of "designer" dogs, cats, micro-pigs and other pets may seem to suggest that pet keeping is no more than a fad. Indeed, it is often assumed that pets are a Western affectation, a weird relic of the working animals kept by communities of the past.

About half of the households in Britain alone include some kind of pet; roughly 10m of those are dogs while cats make up another 10m. Pets cost time and money, and nowadays bring little in the way of material benefits. But during the 2008 financial crisis, spending on pets remained almost unaffected, which suggests that for most owners pets are not a luxury but an integral and deeply loved part of the family.

Some people are into pets, however, while others simply aren't interested. Why is this the case? It is highly probable that our desire for the company of animals actually goes back tens of thousands of years and has played an important part in our evolution. If so, then genetics might help explain why a love of animals is something some people just don't get.

The health question

In recent times, much attention has been devoted to the notion that keeping a dog (or possibly a cat) can benefit the owner's health in multiple ways – reducing the risk of heart disease, combating loneliness, and alleviating depression and the symptoms of depression and dementia.

As I explore in my new book, there are two problems with these claims. First, there are a similar number of studies that suggest that pets have no or even a slight negative impact on health. Second, pet owners don't live any longer than those who have never entertained the idea of having an animal about the house, which they should if the claims were true. And even if they were real, these supposed health benefits only apply to today's stressed urbanites, not their hunter-gatherer ancestors, so they cannot be considered as the reason that we began keeping pets in the first place.

The urge to bring animals into our homes is so widespread that it's tempting to think of it as a universal feature of human nature, but not all societies have a tradition of pet-keeping. Even in the West there are plenty of people who feel no particular affinity for animals, whether pets or no.

The pet-keeping habit often runs in families: this was once ascribed to children coming to imitate their parents' lifestyles when they leave home, but recent research has suggested that it also has a genetic basis. Some people, whatever their upbringing, seem predisposed to seek out the company of animals, others less so.

So the genes that promote pet-keeping may be unique to humans, but they are not universal, suggesting that in the past some societies or individuals – but not all – thrived due to an instinctive rapport with animals.

The DNA of today's domesticated animals reveals that each species separated from its wild counterpart between 15,000 and 5,000 years ago, in the late Palaeolithic and Neolithic periods. Yes, this was also when we started breeding livestock. But it is not easy to see how this could have been achieved if those first dogs, cats, cattle and pigs were treated as mere commodities.

If this were so, the technologies available would have been inadequate to prevent unwanted interbreeding of domestic and wild stock, which in the early stages would have had ready access to one another, endlessly diluting the genes for "tameness" and thus slowing further domestication to a crawl – or even reversing it. Also, periods of famine would also have encouraged the slaughter of the breeding stock, locally wiping out the "tame" genes entirely.

But if at least some of these early domestic animals had been treated as pets, physical containment within human habitations would have prevented wild males from having their way with domesticated females; special social status, as afforded to some extant hunter-gatherer pets, would have inhibited their consumption as food. Kept isolated in these ways, the new semi-domesticated animals would have been able to evolve away from their ancestors' wild ways, and become the pliable beasts we know today.

The very same genes which today predispose some people to take on their first cat or dog would have spread among those early farmers. Groups which included people with empathy for animals and an

understanding of animal husbandry would have flourished at the expense of those without, who would have had to continue to rely on hunting to obtain meat. Why doesn't everyone feel the same way? Probably because at some point in history the alternative strategies of stealing domestic animals or enslaving their human carers became viable.

There's a final twist to this story: recent studies have shown that affection for pets goes hand-in-hand with concern for the natural world. It seems that people can be roughly divided into those that feel little affinity for animals or the environment, and those who are predisposed to delight in both, adopting pet-keeping as one of the few available outlets in today's urbanised society.

As such, pets may help us to reconnect with the world of nature from which we evolved.

http://bit.ly/2hFe1Wv

Who Built Ancient Egypt's Great Pyramid? Hidden Text Holds Clues to Thousand-Year-Old Mystery

Archaeologists believe they have found the key to unlocking a mystery almost as old as the Great Pyramid itself

By Callum Paton On 9/25/17 at 7:00 AM

Archaeologists believe they have found the key to unlocking a mystery almost as old as the Great Pyramid itself: Who built the structure and how were they able to transport two-ton blocks of stone to the ancient wonder more than 4,500 years ago?

Over the years, researchers posited a number of competing theories as to how the pharaohs engineered the monumental structure, which remained the tallest on earth well into the middle ages.

Experts had long established that the stones from the pyramid's chambers were transported from as far away as Luxor, more than 500 miles to the south of Giza, the location of the Great Pyramid, but had never agreed how they got there.

However, the diary of an overseer, uncovered in the seaport of Wadi al-Jafr, appears to answer the age-old question, showing the ancient Egyptians harnessed the power of the Nile to transport the giant blocks of stone.

According to a new British documentary Egypt's Great Pyramid: The New Evidence, which aired on the U.K.'s Channel 4 on Sunday, the Great Pyramid, also known as the Pyramid of Khufu, was built using an intricate system of waterways which allowed thousands of workers to pull the massive stones, floated on boats, into place with ropes.

Along with the papyrus diary of the overseer, known as Merer, the archaeologists uncovered a ceremonial boat and a system of waterworks. The ancient text described how Merer's team dug huge canals to channel the water of the Nile to the pyramid.

Archaeologist Mark Lehner, who has devoted his career to uncovering who built the pyramids, explained how his team had uncovered a waterway hidden beneath the Giza plateau. It is believed that the stones which went into the pyramid were delivered to this area.

The experts also made new discoveries about boat building in the bronze age civilization. By restoring the wooden planks from the ceremonial boat and then scanning them with a 3D laser, they archeologists could discern how they were first assembled.

A separate team of archaeologists is currently working to make an internal map of the Great Pyramid at Giza using laser technology. The group, from the ScanPyramids project, has announced the discovery of a series of voids in the pyramid which they believe may be hidden rooms.

http://bit.ly/2xWmniF

'Revolutionary' new gesture control tech turns any object into a TV remote

New gesture control technology that can turn everyday objects into remote controls could revolutionise how we interact with televisions, and other screens

Imagine changing the channel of your TV simply by moving your cup of tea, adjusting the volume on a music player by rolling a toy car, or rotating a spatula to pause a cookery video on your tablet.

New gesture control technology that can turn everyday objects into remote controls could revolutionise how we interact with televisions, and other screens - ending frustrating searches for remotes that have slipped down the side of sofa cushions.

This image shows targets in the corner of a TV screen. Each target rotates around its corresponding function. The user matches the rotational movement with any object, or part of their body, to create a coupling and active the control. Lancaster University

In a paper - 'Matchpoint: Spontaneous spatial coupling of body movement for touchless pointing' - which will be presented at the UIST2017 conference in Quebec City this October, researchers from Lancaster University show a novel technique that allows body movement, or movement of objects, to be used to interact with screens. The 'Matchpoint' technology, which only requires a simple webcam, works by displaying moving targets that orbit a small circular widget in the corner of the screen. These targets correspond to different functions - such as volume, changing channel or viewing a menu. The user synchronises the direction of movement of the target, with their hand, head or an object, to achieve what researchers call 'spontaneous spatial coupling', which activates the desired function.

Unlike existing gesture control technology, the software does not look for a specific body part it has been trained to identify - such as a hand. Lancaster's technology looks for rotating movement so it doesn't require calibration, or the software to have prior knowledge of objects. This provides much more flexibility and ease for the user as it works even while hands are full, and while stood or slouching on the sofa.

Users also do not need to learn specific commands to activate different functions, as is the case with some gesture controlled televisions on the market, and the user is able to decouple at will.

When selecting volume adjustment or channel selection, sliders appear. The user moves their hand, head, or object, in the required direction indicated by the slider to change the volume or to find the desired channel.

As well as televisions, the technology can also be used with other screens. For example, YouTube tutorials, such as mending bikes or baking cakes, could be easily paused and rewound on tablet computers without users having to put down tools or mixing bowls.

Lancaster University researcher Christopher Clarke selects a channel to watch by using his mug as a remote control. He moves his drink left or right until finding the station he wants to watch. **Lancaster University**

Multiple pointers can be created to allow more than one user to point at drawings or pictures on interactive whiteboards simultaneously. Matchpoint also allows users to manipulate images on whiteboards by using two hands to zoom in and out, and rotate images.

In addition to short-term couplings, users can also link stationary objects to controls, which even when left for prolonged periods will retain their control function. For example, a mug sat on a table could change a track on a music player when moved left or right, and a rolling toy car could be used to adjust volume. Objects can lose their coupling with controls simply by removing them from the camera's field of view.

Christopher Clarke, PhD student at Lancaster University's School of Computing and Communications, and developer of the technology, said: "Spontaneous spatial coupling is a new approach to gesture control that works by matching movement instead of asking the computer to recognise a specific object.

"Our method allows for a much more user-friendly experience where you can change channels without having to put down your drink, or

change your position, whether that is relaxing on the sofa or standing in the kitchen following a recipe.

"Everyday objects in the house can now easily become remote controls so there are no more frantic searches for remote controls when your favourite programme is about to start on another channel, and now everyone in the room has the 'remote'. You could even change the channel with your pet cat."

Researchers believe Matchpoint is also suitable to be used as an accessibility tool for people who are unable to use traditional pointers, such as remote controls and a mouse and keyboard.

The researchers on the paper are Christopher Clarke and Professor Hans Gellersen, both of Lancaster University's School of Computing and Communications.

http://bit.ly/2fJPE9x

Doctors define 'safe and effective' margins for 'one and done' skin removal around suspicious moles

By carefully tracing a line of at least 2 millimeters outside of and around the edges of a mole that is suspected of being a cancer, doctors can remove all of its cells and avert the need for a second surgery.

The recommendation for such a tightly defined surgical margin is the result of a study led by researchers at Perlmutter Cancer Center at NYU Langone Health and published online Oct. 2 in the Journal of the American Academy of Dermatology.

According to researchers, such margin guidelines are needed because as many as two-thirds of the hundreds of thousands of suspicious skin moles removed each year in the United States require re-excision (further cutting out of mole cells missed on the first attempt). Physicians warn that second procedures introduce more risk of infection, bleeding, and scarring, as well as inconvenience and unnecessary costs.

"Although the vast majority of suspicious-looking skin moles do not turn out to be cancerous melanomas, once a decision has been made to remove a mole, there should be a clearer standard margin," says senior study investigator and dermatologist David Polsky, MD, PhD. Currently, he says, most physicians cut out either just the darkest portion of a suspicious mole, or when removing the entire mole, opt for a very small, imprecise 1 millimeter margin around the mole's edge.

"Our study shows that a 'one and done' approach with a clearly defined, slightly larger margin is safer and more effective in completely removing suspicious moles with a single procedure than the current non-standardized approach," adds Polsky, the Alfred W. Kopf, MD, Professor of Dermatologic Oncology at NYU Langone and director of its pigmented lesion section in the Ronald O. Perelman Department of Dermatology.

For the study, researchers removed 151 suspicious skin moles in 138 men and women, all patients at NYU Langone, which provided all supplies and funding for the study. Most biopsies came from the arms, legs, and backs.

All patients underwent the biopsy procedure, involving complete mole removal with a 2 millimeter margin, between January and August 2015. Researchers then monitored the patients for close to a year and a half after their procedures and found that none had any further suspicious growths at their biopsy sites.

Lab testing showed that more than 90 percent of biopsied moles were completely removed by using the single procedure, with 11 (7 percent) diagnosed as melanoma, one of the most aggressive forms of skin cancer.

"While our study did not directly compare use of the wider margin to a narrower margin, the common practice of removing moles with narrow margins and performing a second 'clean-up' procedure suggests a need to move toward wider margins during the initial procedure," says Polsky.

According to Polsky, the decision to remove a suspicious skin mole, or so-called atypical or dysplastic nevus, is complex and somewhat subjective. Physicians, he says, look at a variety of factors including

the shape and internal colors of the mole, as well as how dark and uneven it is.

Keeping track of skin moles on the body is important, experts say, because people with 50 or more flat or slightly raised, circular segments of pigmented skin cells are at higher risk of melanoma than those who have fewer moles. Physicians usually remove several moles for every melanoma diagnosed, so that no cancers are missed.

Polsky says if further data support the current findings, he hopes that other cancer centers will also adopt his "one and done" approach, and, if so, he will recommend changes to the next edition of practice guidelines issued by the American Academy of Dermatology.

Besides Polsky, other NYU Langone researchers involved in the study were lead study investigator Vitaly Terushkin, MD; Elise Ng, MD; Jennifer Stein, MD, PhD; Susan Katz, MD; David Cohen, MD; and Shane Meehan, MD.

http://bit.ly/2fJqD5c

By decoding how HPV causes cancer, researchers find a new potential treatment strategy

Discovering a new strategy that might provide targeted treatment for human papillomaviruses

WASHINGTON -- A study that teases apart the biological mechanisms by which human papillomaviruses (HPV) cause cancer has found what researchers at Georgetown University Medical Center say is a new strategy that might provide targeted treatment for these cancers.

HPV is responsible for the majority of cervical cancer and a substantial portion of head and neck and anal cancers, but therapy available to date is surgery and non-specific chemotherapy.

The new study, published Oct. 2 in the journal Oncotarget, found that E6, an oncoprotein produced by the virus, interacts with several other molecules in host cells in a manner that ensures infected cells cannot die. If they are immortal and continue to multiply, cancer develops.

"There is no targeted treatment now for these cancers since German virologist Harald zur Hausen, PhD, discovered in 1983 that HPV can cause cervical cancer. Recently, the numbers of HPV-linked head and neck cancers have increased in the U.S. Now we have a chance to develop and test a very specific, potentially less toxic way to stop these cancers," says the study's lead author, Xuefeng Liu, MD, associate professor of pathology at Georgetown University Medical Center. Liu is director of Telomeres and Cell Immortalization for the medical center's Center for Cell Reprogramming.

Liu and his team have previously found that the HPV E6 oncoprotein interferes with the well-known p53 tumor suppressor to increase telomerase activity that extends the life span of infected cells. A telomerase is a protein that allows a cell to divide indefinitely when it would have stopped after a certain number of divisions.

In this study, researchers found that E6 also interacts with myc, a protein produced by the Myc gene, which controls gene expression in all healthy cells. They concluded that telomerase activity is dependent on E6-myc proteins hooking on to each other.

This means, says Liu, that designing a small molecule that stops E6 from joining up with myc should shut down persistent activation of telomerase. A small molecule could bind to E6 in the same spot that myc would, or bind on to myc in the same spot that E6 would, thus preventing an E6-myc complex.

"This small molecule would not be toxic to all normal cells or, importantly, to master stem cells, because myc would not be affected," says Liu. "It could be a unique treatment, targeted specifically to HPV cancers."

Georgetown researchers are now working on a prototype chemical to interfere with E6/Myc binding.

Study co-authors include pathologist Richard Schlegel, MD, PhD, a co-inventor of Georgetown-owned technology leading to the HPV vaccines; first author Yiyu Zhang, MD; Aleksandra Dakic, PhD; Renxiang Chen, PhD; and research specialist Yuhai Dai, all of the Center for Cell Reprogramming.

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