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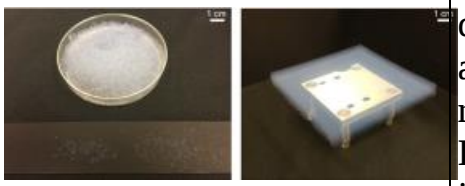
Silica aerogel could heat the surface of Mars enough to sustain life

Insulating material could replicate the effects of Earth's atmosphere on the red planet, warming it by 50°C

By Anthony King

Spreading a thin layer of silica aerogel over the surface of Mars could increase the temperature enough for crops to be grown, scientists have shown using models of the Martian climate.

They say this intervention could transform the planet's surface within decades, rather than the centuries thought necessary for large-scale planetary modification.



Silica aerogel, shown as particles (left) and a tile (right) has one of the lowest thermal conductivities of all known materials **Source: © R Wordsworth, L Kerber and C Cockell/Springer Nature Limited 2019**

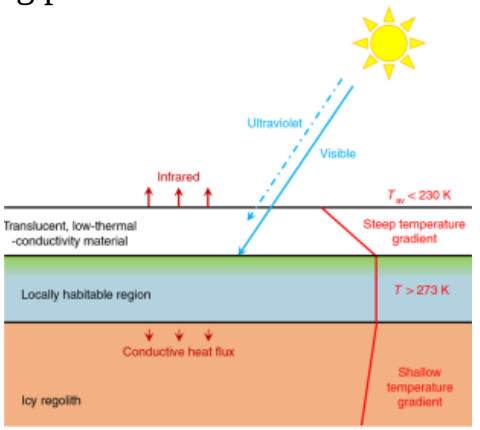
'Silica aerogel is remarkably translucent, yet its thermal conductivity is one of the lowest of all known materials,' says Robin Wordsworth, a planetary climate scientist at Harvard University. These gels consist of nanoscale networks of interconnecting silica clusters and are more than 97% air.

A coating just two to three centimetres thick could replicate the effects of Earth's atmosphere on the surface of the red planet, allowing enough visible light for photosynthesis to pass through, while increasing the temperature of the underlying surface by 50°C. The models, which focussed on an ice-rich, mid-latitude location, suggested this would be enough to keep water liquid to a depth of several metres throughout the Martian year. The silica aerogel would also shield terrestrial lifeforms from ultraviolet wavelengths.

'Our initial inspiration for this was a natural process on the Martian surface, the solid-state greenhouse effect,' says Wordsworth. Light travels through carbon dioxide ice deposits, creating warmth beneath the surface which is trapped by the insulating snowpack. Heating leads to the explosive release of CO_2, which generates dark spots observable from planetary orbiters.

However, over the majority of the surface the Martian atmosphere is so thin that it cannot muster a greenhouse effect sufficient to boost temperatures above the melting point of water.

Previous 'terraforming Mars' theories proposed releasing carbon dioxide and water into the atmosphere from Martian reservoirs such as polar ice. However, research has revealed inadequate amounts of water and carbon dioxide on Mars to increase the temperature above the melting point of water.



The 'habitability concept' for Mars Wordsworth and colleagues developed **© R Wordsworth, L Kerber and C Cockell/Springer Nature Limited 2019**

Wordsworth envisions a mat of silica aerogel covering the surface in order to raise the temperature enough to grow basic forms of life, such as algae. Large pressurised domes could eventually be used for cultivating crops or sustaining habitable environments for humans.

'The larger the area, the greater the volume, the more resistant it would be to diurnal and seasonal temperature changes,' Wordsworth says. Silica aerogels are themselves fairly fragile, so would need to be reinforced or combined with other materials.

'We don't know how easily silica aerogel manufacturing techniques employed on Earth can be adapted to Martian conditions. Therefore, there's a lot of work to be done to test this on Mars,' comments Germán Martínez, planetary scientist and Mars habitability expert at the Lunar and Planetary Institute in Houston, Texas. However, he

adds that ‘a big advantage is that this approach can be further tested in extreme environments on Earth today’.

Wordsworth says the team now plans to run field tests in regions such as the Atacama Desert in Chile and Antarctic dry valleys, as these are ‘the closest approximations that we have for the Martian surface’. He also suggests that synthetic biology might play a part in improving the habitability of Mars, taking advantage of organisms such as diatoms which utilise silica as a building material on Earth.

References ***R Wordsworth, L Kerber and C Cockell,*** **Nature Astronomy,** ***2019,*** ***DOI: 10.1038/s41550-019-0813-0***

http://bit.ly/2JGFzGs

Study highlights importance of female roles in matrilineal families

Females—not males—may provide the backbone on which complex society is built

by University of New Mexico

What do termites, elephants, whales, hyenas, and some human societies have in common? The core of their societies is female. According to a new study led by researchers at The University of New Mexico researchers, females—not males—may provide the backbone on which complex society is built.

Published in *Philosophical Transactions of the Royal Society*, Series B, the study reviews evidence from human and animal studies to question assumptions underlying claims that men are always central to the functioning of human families.

"Anthropologists have argued for a long time that men are central to building successful human families," said Siobhán Mattison, assistant professor of evolutionary anthropology and director of the Human Family and Evolutionary Demography Lab at UNM and the study's lead author. This male-centered view emphasizes male provisioning of their wives and children, monogamy, and nuclear families.

"But human families are much more complex than that," Mattison said, "and, while it is undoubtedly the case that men provide important contributions to their families under many circumstances, they are also frequently the least reliable providers."

The study focuses on a large minority of human societies—17 percent—that are called "matrilineal." In humans, this means that women inherit family property, children belong to their mothers' lineages, or newly-married couples live in close proximity to the wife's kin.

Even in these matrilineal societies, anthropologists have claimed that men are more important than women. Moreover, instead of provisioning their own children, men in these societies supposedly give what they have to their sisters' sons.

But Mattison and her colleagues scoured the literature to find hard evidence of these avuncular transfers and came up empty-handed.

"As evolutionary biologists and anthropologists, we looked not only at human cases, but also at animals and in no case could we find credible evidence of males choosing their nieces and nephews over their own children," Mattison said.

This led Mattison and her colleagues to speculate that men in many matrilineal societies take on more peripheral roles than anthropologists have often argued, and that men might even enjoy a relative lack of responsibility.

Rob Quinlan, co-author and professor of Anthropology at Washington State University said, "I think the important message is that patriarchy is not a human universal. Power can be concentrated in women as the core of at least some communities and family systems. So, even in cultures where men are supposed to be providers and leaders, on the ground, under the right circumstances, wealth and influence can be about personal qualities rather than

gender norms. Our study emphasizes that these female-centered ecologies may not be as rare as people thought."

"We were really surprised to see how differently people studying humans and people studying animals view female-centered societies," said Darragh Hare, a co-author on the study who is a postdoctoral fellow in evolutionary anthropology at UNM.

"Some of the most exciting aspects of social organization, for example achieving large-scale cooperation, accumulating vast stores of ecological knowledge, and multiple generations helping to rear offspring, occur in species with female-centered societies," Hare said.

Mattison hopes that this study will encourage others to consider the female perspective more carefully.

"This has implications for the quality of our science—where we want to understand the full range of how people contribute to families across societies. We may have previously overemphasized the significance of men in the full range of human societies. Future work will clarify that. In the meantime, our review suggests that matriliny with a strong female core is perfectly sustainable given the reliability of female kinship networks."

"Glass ceilings can invoke scientific findings to justify constraining women to roles related to mothering, but women do just about everything in some societies—planting, harvesting, childcare, politicizing—you name it. If nothing else, our study shows the vast flexibility in a human family and economic system, undermining any claims about universal differences in men's and women's capabilities and roles."

The study is published alongside others addressing the significance of female-biased kinship in humans and animals in a special theme issue edited by Mattison and colleagues published today in *Phil Trans*.

More information: *Siobhán M. Mattison et al. The expendable male hypothesis, Philosophical Transactions of the Royal Society B: Biological Sciences (2019). DOI: 10.1098/rstb.2018.0080* *Siobhán M. Mattison et al. The expendable male hypothesis, Philosophical Transactions of the Royal Society B: Biological Sciences (2019). DOI: 10.1098/rstb.2018.0080*

http://bit.ly/2O4BAYy

Treating stroke patients just 15 minutes earlier can save lives

UCLA-led study also finds that busier hospitals provide better stroke care

Initiating stroke treatment just 15 minutes faster can save lives and prevent disability, according to a new UCLA-led study, published today in *JAMA*. The research also determined that busier hospitals -- those that treat more than 450 people for stroke each year -- have better outcomes than those that treat fewer than 400 stroke patients per year.

Researchers at the David Geffen School of Medicine at UCLA and five other institutions in the U.S. and Canada, examined data for 6,756 people who experienced ischemic strokes. The patients' median age was 71, and 51.2% were women.

The researchers looked at stroke patients' treatment results in light of their "door-to-puncture" time -- that is, the interval from their arrival at the hospital to the time their treatment began.

The data showed that for every 1,000 people whose door-to-puncture time was 15 minutes sooner, 15 fewer died or were discharged to hospice care, 17 more were able to walk out of the hospital without assistance and 22 more could care for themselves after being discharged from the hospital. Researchers found that patients' median time from arriving at the hospital to the beginning of treatment was one hour, 27 minutes, and the median time from the onset of symptoms to treatment was three hours, 50 minutes.

All of the patients in the study were treated with endovascular reperfusion therapy, which is used to treat strokes caused by a blockage in one of the major arteries of the brain.

The study is one of the largest to quantify the number of patients per thousand that could be saved by earlier stroke treatment, and to do so using real-world data as opposed to a clinical trial, according to Dr. Reza Jahan, the study's co-lead author and a professor of interventional neuroradiology at the Geffen School of Medicine.

About 795,000 people in the U.S. have strokes each year, and about 140,000 die as a result. Ischemic strokes, which occur when a vessel supplying blood to the brain is obstructed, account for 87% of all strokes. (Other types of strokes include hemorrhagic strokes and transient ischemic attacks, which are sometimes referred to as mini strokes.)

Based on the study's results, shaving 15 minutes off of treatment time could potentially improve results for thousands of people each year.

The study found that hospitals that perform endovascular reperfusion therapy on more than 50 patients per year generally begin treatment faster than hospitals that perform fewer than 30; and that initial treatment tends to be delayed at hospitals that are not certified as comprehensive stroke centers or are located in the Northeast, as well as for people who have a stroke during hospital "off hours" -- weekends, holidays, and before 7 a.m. and after 6 p.m. on weekdays.

"We're trying to improve treatment with better staffing on off hours and getting doctors to the hospital quicker when they're on call," Jahan said. "Patients who arrive at the hospital at 2 a.m. should be treated no differently than people who arrive at 2 p.m."

Treatment delays also are more likely for people who live alone or fail to recognize their own stroke symptoms.

Based on the study results, the American Heart Association has already published new goals regarding how fast patients should be treated at comprehensive stroke centers, Jahan said.

The paper's other UCLA authors are Dr. Jeffrey Saver, a professor of neurology and director of the Comprehensive Stroke and Vascular Neurology Program at the David Geffen School of Medicine at UCLA, co-lead author of the study, and Dr. Gregg Fonarow, the Eliot Corday Chair in Cardiovascular Medicine and Science and director of the Ahmanson-UCLA Cardiomyopathy Center at the David Geffen School of Medicine at UCLA.

The data reviewed in the study is from the from the American Heart Association's Get With The Guidelines-Stroke database, and the research team analyzed results for people who were treated for stroke at 231 U.S. hospitals between January 2015 and December 2016.

https://wb.md/2JDdvUi

Cut Just 300 Calories a Day to Benefit Heart, Even in the Healthy

Reducing daily food intake by 300 calories over 2 years leads to improvements in body composition and cardiometabolic risk factors that could result in reduced risk of CVD

Liam Davenport

Reducing daily food intake by the equivalent of just a couple of cookies, or around 300 calories, over 2 years leads not only to improvements in body composition but a range of cardiometabolic risk factors that could result in reductions in the incidence of cardiovascular disease, the results of an innovative study suggest.

The Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) trial is a phase 2 study involving more than 200 normal to slightly overweight but otherwise healthy individuals up to aged50 years.

They were assigned to a personalized calorie restriction diet combined with individual and group counseling sessions aimed at reducing energy intake by 25%, or an ad libitum control group, who continued with their normal diet.

William E. Kraus, MD, Duke University School of Medicine, Durham, North Carolina, and colleagues report that individuals in the intervention group actually achieved an average reduction in energy intake of almost 12% over 2 years, with an average weight loss of 7.5 kg (approximately 16.5 lbs).

This was associated with significant improvements in lipid levels over baseline, as well as better insulin sensitivity, metabolic syndrome scores, and C-reactive protein levels. The research, published online July 11 in *Lancet Diabetes & Endocrinology*, showed that, in comparison, there were no significant changes in individuals assigned to their normal diet.

So the significant cardiometabolic improvements seen in the study were achieved despite the majority of patients in the intervention group not even hitting their targets for energy intake and weight reduction.

"This shows that even a modification that is not as severe as what we used in this study could reduce the burden of diabetes and cardiovascular disease that we have in this country," Kraus observed in a press release by Duke.

"People can do this fairly easily by simply watching their little indiscretions here and there, or maybe reducing the amount of them, like not snacking after dinner."

The changes seen are "of substantial public health importance, even when started in people who are healthy, young, and middle-aged, and not obese," Kraus and colleagues stress.

In an accompanying editorial, Frank B. Hu, MD, PhD, Departments of Nutrition and Epidemiology, Harvard TH Chan School of Public Health, Boston, Massachusetts, describes the study as "groundbreaking."

He singled out as strengths the large sample size, careful measurement of energy intake and expenditure, relatively high retention and compliance rates, and detailed data on biomarkers of aging and cardiometabolic risk.

Fat Loss Accounted for 70% of Weight Loss in Intervention Group

Kraus and colleagues explain that severe calorie restriction has a "powerful protective effect" against atherosclerotic risk factors such as carotid artery intimal-media thickening (IMT), reduced left ventricular diastolic function, and poor heart rate variability, they note.

However, the impact of longer term calorie restriction on cardiometabolic risk factors in younger, healthy adults is less clear.

The researchers therefore conducted CALERIE, a randomized controlled trial involving individuals from three US clinical centers who were normal weight or slightly overweight, defined as a body mass index (BMI) of 22.0-27.9 kg/m^2.

Men aged 21-50 years and premenopausal women aged 21-47 years were included. Participants were randomized in a 2:1 ratio to a calorie restriction intervention aimed at reducing calorie intake by 25% or to ad libitum control group.

Overall, 218 participants were randomized to the intervention (n = 143) or control group (n = 75). The average age of participants was 38 years, and approximately 70% were women. Over 75% were white, and 11% to 15% were African American.

Participants in the calorie restriction group were prescribed a 25% restriction in calorie intake based on energy requirements estimated from doubly labeled water measurements over a 4-week period at baseline. A prescribed diet was chosen from six eating plans, modified to suit cultural preference.

Individuals were then fed three meals per day, every day, at their clinical center for 1 month, during which they were instructed on the basis of calorie restriction. In addition, an in-house meal was

provided alongside intensive group and individual behavioral counseling once a week for the first 24 weeks of the study.

Those assigned to the control group continued their regular diet and received no specific dietary intervention or counseling. They were followed every 3 months.

The degree of weight loss achieved by each participant was assessed and compared against a trajectory at the end of year 1, followed by weight loss maintenance for the remaining 12 months.

Energy intake in the calorie restriction group was reduced by a mean of 19.5% over the first 6 months, then crept back up to a mean reduction of 9.1% after 6 months, to average 11.9% over the 2 years of the study.

There was no change in average daily energy intake in the control group. Compared with baseline, individuals in the intervention group experienced a reduction in weight of 8.4 kg at 1 year and 7.5 kg at 2 years ($P < .001$).

Although participants in the control group achieved a small degree of weight loss at 1 year, there was no significant change at 2 years.

Similar results were seen for BMI, percentage body fat, fat mass, and fat-free mass, with individuals in the calorie restriction group having significant reductions over baseline at years 1 and 2 ($P < .001$ for all), but no significant changes recorded in the control group (ad libitum diet).

The team calculated that, overall, fat loss at 2 years accounted for 71% of the weight loss seen in the calorie restriction group.

Improvements in Lipids, CRP, and Insulin Sensitivity

The results also showed that, compared with baseline, the calorie restriction intervention was associated with significant reductions in low-density lipoprotein cholesterol (LDL-C) levels, triglycerides, and total cholesterol to high-density lipoprotein cholesterol (HDL-C) ratio at 1 and 2 years ($P < .001$).

Individuals in the intervention group also had significant increases in HDL-C levels from baseline at both year 1 and 2 ($P < .001$).

Again, there were no significant differences in lipoprotein levels versus baseline in participants assigned to the ad libitum group.

For between-group comparisons, the intervention was associated with significant improvements versus controls in LDL-C levels, triglycerides, and total cholesterol to HDL-C ratio at 1 and 2 years, and HDL-C levels at 2 years.

Finally, the researchers looked at a range of other cardiometabolic risk factors and found that calorie restriction led to a series of improvements over the control group across the study period.

Specifically, the intervention was associated with greater insulin sensitivity over the ad libitum diet at 2 years ($P < .0001$), as well as significant reductions in high-sensitivity C-reactive protein (CRP) levels ($P = .012$), and a significantly lower metabolic syndrome score ($P < .0001$).

Researchers say the exact mechanism by which calorie restriction benefits health is not clear, but Kraus notes, "We have collected blood, muscle, and other samples from these participants and will continue to explore what this metabolic signal or 'magic molecule' might be."

Nevertheless, "These data...indicate that inexpensive and safe dietary interventions, such as moderate calorie restriction, can be implemented early in life to optimize cardiometabolic health and reduce the lifetime risk of developing some of the most common, disabling, and expensive chronic diseases."

Long-Term Calorie Restriction Is Hard in Obesogenic Environment

Hu writes in his editorial that previous studies have shown even modest weight gain of around 5 kg during young and middle adulthood is associated with a significantly increased risk of type 2

diabetes, cardiovascular disease, obesity-related cancer, and premature death.

The new study results, although encouraging, nevertheless underline the "challenges" of achieving "long-term calorie restriction in free-living populations."

He adds that there are other approaches to weight loss, such as intermittent energy restriction or fasting, carbohydrate restriction, and the Mediterranean diet, to name a few.

"Improving the food environment by making healthy food choices more accessible, affordable, and the norm while reducing the accessibility of ultra-processed and highly palatable foods is essential to supporting healthy food choices and behavior," Hu writes. "To this end, policy solutions including sugar taxes, financial incentives for producing and purchasing healthy foods, food labeling, and better regulation of food marketing are needed to improve the global food environment."

The study was supported by the National Institute on Aging (NIA) and National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Health (NIH), NIA/NIH Cooperative Agreement, NIH General Clinical Research Center, Diabetes Research Training Center, and NIH Clinical Nutrition Research Unit. Hu has reported receiving grants from the NIH, research support from the California Walnut Commission, honoraria for lectures from Metagenics and Standard Process, and honoraria from Diet Quality Photo Navigation.

Lancet Diabetes Endocrinol. Published online July 11, 2019. Abstract, Editorial

http://bit.ly/2JU9E4p

Australian plants extracting high-value metals from mining wastes

Increasingly scarce metals are being recovered from mining waste by University of Queensland researchers, who are making the most of native plants' metal-absorbing nature.

by University of Queensland

Phytomining involves harvesting metals from the living tissue of a group of plants known as hyperaccumulators, which retain metals in high concentrations after absorbing them through their roots.

UQ's Sustainable Minerals Institute (SMI) researcher Dr. Philip Nkrumah has been developing the phytomining technology at the Centre for Mined Land Rehabilitation.

"Australia is one of the world's leading mineral resources nations with a number of mines around the country generating large quantities of processed mining wastes," he said.

"These wastes, often stored in tailings facilities, contain valuable metals including cobalt, and represent some of the largest untapped resources globally."

Tapping into this waste through phytomining not only creates additional revenue streams, it offers a sustainable solution to supply-side issues the industry is going to face.

"Cobalt consumption is projected to rise by between eight and ten percent annually but supplies are likely to be limited by 2050, so the industry needs to identify additional sources," Dr. Nkrumah said.

"Phytomining is an innovative solution because it complements the global supply chain for critical minerals like cobalt while promoting the circular economy by utilising mining waste.

"Some species of plants can contain up to one percent of cobalt or four percent of nickel in their shoots, translating to more than 25 percent metal in their ash which is dubbed 'bio-ore.'"

"The high purity of bio-sourced metals makes them especially suited for applications in the electrochemical industry, like producing rechargeable batteries."

Intensive screening efforts in global herbaria had led to the discovery of more than 100 hyperaccumulator plants new to science.

Fieldwork at the Queensland's MMG Dugald River Mine discovered zinc hyperaccumulation in the native legume *Crotalaria novae-hollandiae*, which opens up the possibility of zinc phytomining.

http://bit.ly/2SqWdfP

Measles is killing more people in the DRC than Ebola—and faster

"Frankly, I am embarrassed to talk only about Ebola," WHO director-general says.

Beth Mole - 7/16/2019, 8:25 AM

As the world anxiously monitors the outbreak of Ebola in Democratic Republic of the Congo, health officials note that a measles outbreak declared last month in the country has killed more people—mostly children—and faster.

Since January 2019, officials have recorded over 100,000 measles cases in the DRC, mostly in children, and nearly 2,000 have died. The figures surpass those of the latest Ebola outbreak in the country, which has tallied not quite 2,500 cases and 1,665 deaths since August 2018.

The totals were noted by World Health Organization Director-General, Tedros Adhanom Ghebreyesus, in a speech today, July 15, at the United Nations Office in Geneva, Switzerland.

"Frankly, I am embarrassed to talk only about Ebola," Dr. Tedros said (he goes by his first name). He gave the speech in response to two new developments in the Ebola outbreak.

That is that two Ebola responders were murdered in their home in the DRC city of Beni and that officials on Sunday had identified the first case of Ebola in Goma, a DRC city of over one million at the border with Rwanda.

"Both of these events encapsulate the challenges we continue to face on a daily basis in DRC," he said. Tedros was referring to the scattering of disease—including Ebola and measles—as violence hampers outbreak responses and access to medical care.

Since January, officials have counted 198 attacks on health responders, which left seven dead and 58 healthcare workers and patients injured.

Ebola control

The current Ebola outbreak is the second largest on record (surpassed only by the 2014 West African outbreak that sickened more than 28,000, killing 11,000). WHO experts have expressed "deep concern" about it, noting the risks that it could spread to neighboring countries in the region.

Still, they determined on three separate occasions so far that the outbreak does not meet the criteria of a public health emergency of international concern, or PHEIC.

In the latest development, health officials jumped into action when a 46-year-old pastor tested positive for Ebola in the DRC city of Goma.

The pastor was on an evangelical mission and had recently traveled from Butembo, which has grappled with the viral disease since last December.

While there, the pastor had delivered sermons in seven churches and laid his hands on worshippers, some of whom were ill.

Though he began experiencing symptoms while in Butembo, he traveled by bus to Goma on July 12 with 18 other people.

The bus passed through three health checkpoints on its way, but the pastor showed no symptoms and gave different names at each checkpoint. This is possibly because he was trying to conceal his identity and health status, officials said.

By the afternoon of the 14th, healthcare workers in Goma confirmed he had Ebola and transferred him to an Ebola treatment center. Officials have since tracked down the other 18 bus passengers. Today, the DRC health ministry decided to send the pastor back to Butembo for further treatment, according to Doctors without Borders.

"Because of the speed with which the patient was identified and isolated, and the identification of all the other bus passengers

coming from Butembo, the risk of it spreading in the rest of the city of Goma is small," the ministry said in a statement.

Viral spread

So far, the Ebola outbreak has largely stayed in DRC's North Kivu and Ituri provinces, which sit on the eastern side of the country and border South Sudan, Uganda, and Rwanda.

The measles outbreak, on the other hand, has spanned at least 23 of the country's 26 provinces. The health ministry declared an outbreak on June 10 and noted a 700% spike in the case count over the count in the first half of last year.

"And yet it gets little international attention," Dr. Tedro noted, adding that malaria also kills more than 50,000 people each year in the DRC.

Just like with the Ebola outbreak, violence, population movements, and community fear have kept the measles outbreak simmering.

"We often talk about the need to bridge the humanitarian-development nexus," Dr. Tedro said.

"This is the moment to practice what we preach. WHO is committed not just to ending this [Ebola] outbreak, but to strengthening DRC's health system... To build trust, we must demonstrate that we are not simply parachuting in to deal with Ebola and then leaving once it's finished."

While health officials face unique challenges to curbing disease in the DRC, the republic is far from the only country to face a boom in measles cases. In 2018, WHO and UNICEF tallied nearly 350,000 measles cases worldwide, a figure more than twice that of 2017. Many countries reported outbreaks, with some of the largest being in Ukraine, the Philippines, and Brazil.

So far in 2019, the US is experiencing the largest measles outbreak since 1992. Access to vaccines plays a large role in the rise, as does vaccine refusal. The WHO listed vaccine hesitancy as one of the top ten threats to global health in 2019.

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Lifestyle can wind back dementia risk, study suggests

Having an active mind might help as well.

Paul Biegler reports.

Your fate, at least when it comes to dementia, is not inextricably bound to your genes, it seems.

According to a new study published in the journal *JAMA*, adopting a healthy lifestyle can wind back the risk of dementia conferred by a bad deal from the genetic lottery.

“This research delivers a really important message that undermines a fatalistic view of dementia,” says lead researcher David Llewellyn, an epidemiologist at the University of Exeter, UK.

“Some people believe it's inevitable they'll develop dementia because of their genetics. However, it appears that you may be able to substantially reduce your dementia risk by living a healthy lifestyle.”

The researchers took a deep dive into the UK Biobank, an open-access treasure trove for health researchers that contains genetic and health-related data for half a million Brits, collected between 2006 and 2010.

They homed in on people aged 60 and over, and of European descent, who had no signs of dementia at enrolment and for whom genetic info was available. That whittled the numbers down to just under 200,000.

Those people were classed as having low, intermediate or high genetic risk for dementia based on the findings of an earlier Alzheimer’s study (which only included people of European background, hence the limited remit of the current study).

The researchers also calculated a “healthy lifestyle score” for participants based on whether they smoked, did exercise, had a good diet and had only moderate alcohol consumption.

The group was followed for a median period of eight years to log whether a diagnosis of dementia was made.

The bad news is that, yes, your genes have a loud say in whether you get dementia. Just 0.63% of those with low genetic risk did, but that figure nearly doubled – to 1.23%– for people with high genetic risk.

It is also a bit grim if your habits veer from the health conscious. Having an "unfavourable" lifestyle upped the risk of dementia by 35% compared to people with a healthy lifestyle.

But for people able to nail a healthier lifestyle, things look decidedly rosier. When the researchers looked at people in the high genetic risk category for dementia, having a healthier lifestyle lowered their dementia risk by a not inconsiderable 32% against those with less healthy habits.

"This is the first study to analyse the extent to which you may offset your genetic risk of dementia by living a healthy lifestyle," says co-author Elżbieta Kuźma, also from the University of Exeter's Medical School.

"Our findings are exciting as they show that we can take action to try to offset our genetic risk for dementia. Sticking to a healthy lifestyle was associated with a reduced risk of dementia, regardless of the genetic risk," she said.

When it comes to dementia, however, physical health is but one part of the equation.

A separate study published in the journal *JAMA Neurology* asks whether having an active mind across the lifespan might also keep dementia at bay.

The theory of "cognitive reserve" holds that stimulating the noggin in early and middle age puts brainpower in the bank for later life, breeding resilience to age- and disease-related brain changes.

However, according to the researchers, who were led by Xiuying Qi and Weili Xu from Tianjin Medical University in Tianjin, China, hard evidence for a protective effect of cognitive reserve on dementia is limited.

Their study aimed to fill that knowledge gap. They analysed data from just over 1600 adults, with no cognitive impairment, who were enrolled in The Rush Memory and Aging Project. It's an ongoing study trying to pin down the risk factors for neurodegenerative diseases such as dementia.

Participants – 75% women and with a mean age of just under 80 – were given a "cognitive reserve score" based on brownie points they'd notched up over the years.

That meant tallying how long they stayed at school and the extent to which they did mind-challenging activities such as reading books, writing letters and visiting libraries.

But cognitive reserve also hinges on social factors. The researchers allocated points for going to restaurants and sporting events, visiting friends, making trips and going to church. And they totted up the size of each person's network of family and friends.

Participants were followed for a mean period of six years to see if they got dementia.

The benefits of an active mind, it would seem, rival those of healthy habits.

People with the highest levels of cognitive reserve had a nearly 40% reduction in dementia risk compared to those with the least cognitive reserve.

But perhaps one of the most surprising findings came from a slightly macabre quirk in the study. Many participants – more than 600 in fact – volunteered their brains for autopsy.

The researchers measured the presence of typical brain changes of dementia, including blood vessel changes as well as the amyloid plaques seen in Alzheimer's disease. Even when those changes were present, the team found, having a high cognitive reserve could still ward off dementia.

The result is a valuable lesson for people keen to stay sharp in their later years.

“Our findings suggest that accumulative educational and mentally stimulating activities enhancing cognitive reserve throughout life might be a feasible strategy to prevent dementia, even in people with high Alzheimer disease or vascular pathologies,” the authors conclude.

https://wb.md/2JGOoQH

New Alzheimer's Drug Candidate a Head Scratcher

A trial of a new Alzheimer's drug candidate is proving to be a bit of a head scratcher for researchers.

Sue Hughes

Phase 2 results of edonerpic maleate (Fujifilm Toyama Chemical Co) reduced cerebrospinal fluid (CSF) tau levels but had no clinical benefit at 1 year.

"This drug has an interesting preclinical profile and a strong rationale for clinical testing in Alzheimer's. It is disappointing not to have shown any benefit on symptoms in a well-powered clinical study," study investigator Howard Feldman, MD, University of California San Diego School of Medicine, told *Medscape Medical News*. The study was published online July 9 in *JAMA Neurology*.

Preclinical Promise

Edonerpic maleate has shown promise in preclinical studies, with findings suggesting it may guard against amyloid-induced neurotoxicity and memory deficits. It has also been shown that it preserves hippocampal synapses and spatial memory in tau transgenic mice.

In an earlier phase 2 trial in Alzheimer's disease (AD), a dose of 224 mg/day of edonerpic maleate for 1 year did not demonstrate efficacy on primary and secondary outcomes, but there was post hoc evidence for a positive cognitive effect in patients with moderate impairment who had Mini-Mental State Examination (MMSE) scores of less than 20.

For the current study, 484 patients with mild to moderate AD and MMSE scores of 12 to 22, and who were taking stable doses of donepezil or rivastigmine, with or without memantine, were randomly assigned 1:1:1 to placebo, 224 mg of edonerpic maleate, or 448 mg of edonerpic maleate, once daily.

After 1 year, no effect was seen on the two co-primary outcomes: scores on the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog) and Alzheimer's Disease Cooperative Study–Clinical Impression of Change (ADCS-CGIC).

Discontinuation of treatment because of adverse events occurred in 4% of placebo patients vs 13.9% of the edonerpic maleate 224 mg group and 14.6% of the 448 mg group. The most frequent adverse events were diarrhea and vomiting.

CSF biomarker outcomes showed no difference in amyloid beta levels between the various groups, but did show a significant reduction in tau vs placebo in the high-dose edonerpic maleate group.

"We don't want to overstate it, but we saw an intriguing effect on CSF tau and phospho-tau — both were significantly reduced in the treatment group compared with the placebo group," said Feldman.

"But this was only in a small subgroup of about 60 people who agreed to undergo lumber punctures. This was not the primary hypothesis of the study and must be interpreted with caution. I would say this is an interesting finding that merits further study, but we can't say much more about this at present," he added.

The authors note that although there may be a suggestion that the 448 mg edonerpic maleate dose was associated with decreased p-tau and total tau, baseline values were not balanced and the effect sizes were implausibly large. Any inference that edonerpic maleate

showed neuroprotection in this study would be speculative and would lack supporting clinical evidence, they note.

However, they add there is a possibility that the drug "eventually may be shown to have neuroprotective effects in other conditions, other tauopathy, earlier-stage Alzheimer disease, and potentially in cerebrovascular injury models."

	Placebo baseline	Placebo change from baseline	Edonerpic maleate 448 mg baseline	Edonerpic maleate 448 mg change from baseline	Difference versus placebo	*P* value
Tau (pg/mL)	1147	28.2	1085	-101	-129	.01
Phospho-Tau (pg/mL)	102.8	0.29	95.0	-7.3	-7.59	.03

Table. CSF Tau and Phospho-Tau Results

"Tau has been identified as a potential biomarker of Alzheimer's, and it has been the view that lowering tau should be beneficial, but at present we don't have any validation that altering any biomarker in this disease makes any difference to clinical symptoms," Feldman added.

The investigators also found an increase in ventricular volume in the 448-mg edonerpic maleate group compared with placebo (29.16 procedure-defined units vs 23.17 procedure-defined units). This was unexpected, said Feldman, and again the meaning is uncertain.

The investigators also note that although increased ventricular volumes have generally suggested brain volume loss, where such findings have been described with amyloid-lowering treatment, the effect has been explained as related to amyloid removal, fluid shifts, or neuroinflammatory effects with fluid shifts.

Another analysis showed reduced hippocampal volume loss with the lower edonerpic maleate dose compared with placebo, which the researchers note is also of unclear significance in the absence of clinical effect.

Still Hopeful

Feldman said he does not know if any further studies of edonerpic maleate in AD are planned.

"The future of the development of this drug is not our decision. It is up to the company. But these results do not provide any clinical evidence that it is effective."

He explained that the drug modifies microglial function.

"This is an interesting target. It is thought that the pathology of Alzheimer's seems to trigger the activation of microglia and the release of inflammatory cytokines. There has long been interest in pursuing anti-inflammatory approaches in Alzheimer's. This is one of those approaches by targeting microglial function."

However, said Feldman, the lack of clinical benefit in the study does not necessarily mean this approach is ineffective.

"We may need to focus earlier in the disease process. We are starting to get better at identifying Alzheimer's pathology in waiting. We have PET ligands for amyloid and tau, and 25% of the population over age 55 test positive for amyloid on PET scan. Some may argue that we should be intervening at this stage even though these individuals do not have any dementia symptoms," he said.

Feldman also emphasized that AD researchers need to diversify their approach.

"We are working on identifying additional biomarkers," he noted. "We need to explore many other new targets until we find one that correlates with symptomatic benefit."

The study was funded by Fujifilm Toyama Chemical Co Ltd. Feldman reports receiving grants and travel expenses from Toyama Chemical Co Ltd during the conduct of the study.

JAMA Neurol. Published online July 8, 2019. Full text

http://bit.ly/2JSjDa5

People Are Overdosing on Wasp Spray in West Virginia

Several people in a county in West Virginia recently overdosed from wasp spray, which they used as an alternative to methamphetamine, according to news reports.

By Rachael Rettner, Senior Writer

Police in Boone County say they've seen a rise in residents abusing wasp spray to achieve a meth-like high, according to local news outlet WCHS. The practice is believed to have played a role in three overdoses in the county last week, WCHS reported.

"People are making a synthetic type [of] methamphetamine out of wasp spray," Sgt. Charles Sutphin, of the West Virginia State Police, told WCHS.

The practice is known as "wasping," and it has emerged as a concerning drug trend in recent years, according to a 2018 report from ABC News. Users either combine the wasp spray with meth, or use the spray by itself as a meth substitute.

People can crystallize the spray liquid on hot metal sheets, which allows the substance to be inhaled or injected, ABC News reported.

Bug sprays contain active ingredients called pyrethroids, which stun and kill insects; but in humans, the chemicals can interfere with nerve signaling, which can lead to abnormal sensations, and in some cases, seizures or paralysis, ABC News reported.

The chemicals can also lead to increased heart rate, difficulty breathing, headache, nausea, problems with coordination, and swelling and burning sensations.

Police in Boone County are working with medical centers to determine the best treatment for those who abuse the spray, WCHS reported.

http://bit.ly/2JMSjds

310 million-year-old tree fossils to reveal new ancient animals

Able to venture deep into the lycopsid forests, away from the water's edge, thanks to the innovation of the amniotic egg

Author Hillary Maddin*

Over 150 years ago, geologist Sir William Dawson made an astounding discovery in the Joggins Cliffs, along the shores of Nova Scotia's Bay of Fundy. Within the lithified remains of a giant tree-like fern were the bones of a tiny, 310 million-year-old animal.

This animal was unlike any other seen thus far. It was able to venture where no vertebrate (back-boned) animal had ventured before, deep into the lycopsid forests, away from the water's edge. This was all thanks to an evolutionary innovation: the amniotic egg.

Although animals had previously ventured onto land in the earlier Devonian Period, animals with an amniotic egg — such as modern reptiles, birds and yes, even mammals — do not need to return to the water to reproduce, as modern amphibians still do. The amniotic egg is a self-contained pond, where the embryo and all its food and waste are stored surrounded by a protective, desiccation-resistant shell.

In this illustration from 'Air-Breathers of the Coal Period' by John William Dawson, 'Hylonomus Lyelli' is represented leaping in pursuit of an insect.

Dawson Brothers.

This new kind of animal, that Dawson would name *Hylonomus lyelli*, remains the earliest amniote in the fossil record. Since then, many other animals, some strange and some familiar, have been added to the list of discoveries at Joggins Cliffs at the Bay of Fundy. These include microsaurs, temnospondyls and *Dendrerpeton*

acadianum. In 2008, the Joggins Fossil Cliffs were designated a UNESCO World Heritage Site. And the cliffs haven't ceased sharing their secrets — each colossal tidal cycle erodes and exposes more of the ancient ecosystem that once thrived in its formerly equatorial location.

Ancient fern records

The initial discovery of the paleontological significance of Joggins took place in 1842, when British geologist Sir Charles Lyell travelled to Nova Scotia. Ten years later, Lyell and local geologist Sir William Dawson together studied the strata of the 310 million-year-old cliffs. Within the cliffs stood the bodies of giant trees, frozen in time. However, these trees are unlike those in forests today. Rather they were ancient, giant ferns that would have towered 20 to 30 metres above the forest floor.

These ferns are what make Joggins in particular critical to our understanding of early tetrapod evolution. That's because when they died, their soft inner cores rotted away, leaving behind their firm outer bark and a hollow interior.

It's within these hollowed-out stumps that animal remains were trapped and protected for over 300 million years, and where we find them today.

A collaborative effort between researchers and institutions is collecting material for future study. **Hillary Maddin, Author provided**

New discoveries

I'm not going to lie: significant fossil finds at Joggins are few and far between. But it's the unparalleled potential of the next big discovery that keeps me coming back to the site year after year. And we may now have the best chance of that next big discovery.

After a back-breaking, 15-year collaborative effort between the Nova Scotia Museum, Saint Mary's University, Nova Scotian geologist John Calder, the Joggins Fossil Institute and Joggins native Brian Hebert, a new collection of giant fossiliferous trees — representing the largest collection amassed since the site was discovered — is ready for fresh eyes.

Over the next number of years, meticulous manual preparation will reveal tiny new bones, one by one. What makes the newly discovered material so special is that they were collected from strata lower in the Joggins section than any previous material. The fossils within will become new earliest records of animals that we recognize as members of groups of animals that are still alive today — amphibians, reptiles and mammals — and many that are now extinct. We will see for the first time what these trailblazers looked like, and how many different kinds were present in this early phase of tetrapod evolution.

Tetrapod evolution

These animals will teach us many new things about one of the most important phases in tetrapod evolution: the establishment of the first terrestrial, vertebrate communities. We will analyze their anatomy and, through comparisons with living animals, learn about what these animals may have been doing when they were alive.

For example, we can examine the condition of their teeth to learn about what they might have been eating. With the explosion of terrestrial plants at the time, we can see how long it took before animals became herbivorous, and how their strategies might be similar or alternatively, completely different, from those of modern-day herbivores.

We can also examine their bones to learn about what kinds of activities they were doing in these new environments. We're seeing evidence at slightly younger Carboniferous localities that animals had already begun diversifying ecologically. We see the first

burrowing animals and some possibly arboreal animals (animals who spend most of their lives living in trees).

Were the animals at Joggins already doing these things? If so, we would learn it took relatively little time for animals to exploit the many aspects of their new environment. If not, well then, it will appear as though it took some time for these trailblazers to get their footing in the terrestrial realm.

Fossiliferous beach at Joggins Fossil Cliffs, Nova Scotia, Canada.
Shutterstock

Together these discoveries and new analyses will revise our understanding of the Carboniferous Period. No longer will we think of it as a boring, stagnant swamp filled with unspecialized creatures. A new picture is now emerging, one of a dynamic environment that quickly filled up with animals with many new adaptations and abilities.

Vertebrate Paleontologist, Assistant Professor, Carleton University

Disclosure statement

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https://wb.md/2LwAeDV

Safety Lapses Spurred Septic Knee Arthritis Outbreak

41 patients with injection-associated bacterial arthritis among 250 visits to the clinic

Diana Swift

On March 6, 2017, the New Jersey Department of Health received reports from a hospital that three patients who had been admitted for treatment of septic arthritis had all received intra-articular injections for osteoarthritic knee pain at the same private outpatient clinic in suburban New Jersey.

The next day, the facility, identified in media reports as the Osteo Relief Institute Jersey Shore in Wall Township, voluntarily closed after receiving numerous complaints from patients of severe postinjection pain and swelling. In a letter to patients, the management of the clinic attributed these reactions to intrinsic contamination of the manufactured injectable agents — anesthetics and contrast agents — and advised patients to seek medical attention if they developed symptoms.

Responding to the complaints, on March 13, state and local health authorities made an unannounced visit to the clinic, write Kathleen M. Ross, MPH, of the New Jersey Department of Health in Trenton, and colleagues in a report published online today in *Infection Control and Hospital Epidemiology.*

They conducted an environmental inspection of the premises, interviewed the staff, and observed the staff performing mock injection procedures. The team also evaluated the clinic's prevention practices and medical waste handling procedures and reviewed medical records and office documents. What they saw led them to issue an immediate request to local healthcare providers to identify patients who had received injections at this facility and who subsequently sought care for septic arthritis.

The investigation identified 41 patients with injection-associated bacterial arthritis among 250 visits to the clinic during the period March 1 to March 6. Of these, 28 were men; the median age of the patients at time they received injections was 70 years (range, 52 – 86 years).

Cultures of synovial fluid or tissue from 15 of these cases revealed bacteria consistent with oral flora, the most common being *Streptococcus mitis-oralis* (n = 10).

"Unfortunately, breaches in infection control — some more serious than others — are very common," study coauthor Edward I. Lifschitz, MD, also of the New Jersey Department of Health, told

Medscape Medical News. "Most of the time, even 'bad practice' does not lead to infection, but it opens the door, so that with a little bad luck — for example, someone coughing in the wrong place at the wrong time — can lead to an infection."

And bad luck can be costly. Of the 41 patients, 33 (81%) required surgical debridement of the infected joints, 25 patients required referral to an inpatient rehabilitation facility or skilled nursing facility, and 11 (37%) required home-care services.

Costs for treating Medicare beneficiaries in the group (n = 31) came to more than $912,000; the average claim payout was $29,422 per patient in total services associated with initial injections and subsequent medical services. Total claims to Medicare exceeded $5.3 million.

High volume at the center may have played a role in the safety lapses. "We were especially surprised at the number of procedures the clinic did in a day's time," coauthor David. A. Henry, MPH, health officer for the Monmouth County Regional Health Commission, told *Medscape Medical News.* Scheduling records suggested that as many as 85 patients a day were receiving injections. "As we were leaving after one inspection, people were lined up outside asking when the clinic was going to open again. They were in pain," Henry said.

Infection Control Lapses Common

The assessment team found multiple gaps in infection control and injection safety practices, including the lack of hand-washing stations or alcohol-based rubs in the examination rooms, long-exposed syringes, improperly cleaned vials, and the nonuse of masks by practitioners. Other breaches involved nonsterile gloves, syringes with injectable substances drawn up to 4 days in advance, inappropriate handling of materials, and reuse of single-use and multidose vials. Furthermore, the center had no suitable work area to transfer injectables from 500-mL bulk containers to single-dose vials.

Single-use medications, including pharmacy bulk packaged products, typically lack antimicrobial preservatives and can be contaminated with microorganisms when handled outside of pharmacy conditions, Ross's group pointed out in a previous study.

In addition, the inspection found that the tables on which patients received injections were cleaned "at most" once a day, despite recommendations that surfaces be cleaned before each procedure unless a clean barrier is put in place.

The osteoarthritis clinic reopened after health authorities confirmed it had implemented recommendations from the Centers for Disease Control and Prevention's *2016 Guide to Infection Prevention for Outpatient Settings: Minimum Expectations for Safe Care* with assistance from an infection prevention consultant. Testimony to the effectiveness of these precautions is that no new cases of knee infection have been reported for the clinic.

Henry said the outbreak spurred a lot of media attention at the time and outrage on the part of patients and their families. By early May, 18 patients had filed lawsuits against the clinic and its parent company.

"The real heroes in all this were the infection control nurses at the area hospitals," said Henry. "They started to piece this together and tipped us off to the problem." One other local clinic had problems, he said, but these were swiftly dealt with.

So should health authorities make more preemptive visits to private clinics? "In an ideal world, my answer would be yes," said Lifshitz. "However, with over 25,000 physicians in New Jersey alone and with very limited public health resources, this is not a practical solution." He noted that the state recently passed licensing legislation for such "one-room" surgical centers.

"We respond when there is an outbreak or suspected outbreak or when we receive a report of a potentially significant breach of infection control," he continued, "so we are not in a position to comment on what most such clinics do."

The outbreak at this clinic would appear to be atypical. Most facilities observe adequate precautions. The risk for iatrogenic septic arthritis after intra-articular injection is low, with an estimated prevalence of 10 to 40 cases per 100,000 injections. Approximately 20,000 cases occur annually in the United States (7.8 cases per 100,000 person-years), according to the authors.

However, the outbreak underscores the need to adhere to infection prevention recommendations. "Outbreaks related to unsafe injection practices indicate that certain healthcare personnel are either unaware, do not understand, or do not adhere to basic principles of infection prevention and aseptic techniques, confirming a need for education and thorough implementation of infection prevention recommendations," they write.

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

Infect Control Hosp Epidemiol. Published online July 17, 2019. Abstract

http://bit.ly/2Oa3VfZ

DEA tracked every opioid pill sold in the US. The data is out—and it's horrific

Just three drug makers and six distributors were behind the flood.

Beth Mole - 7/18/2019, 5:12 AM

Between 2006 and 2012, opioid drug makers and distributors flooded the country with 76 billion pills of oxycodone and hydrocodone—highly addictive opioid pain medications that sparked the epidemic of abuse and overdoses that killed nearly 100,000 people in that time period.

As the epidemic surged over the seven-year period, so did the supply. The companies increased distribution from 8.4 billion in 2006 to 12.6 billion in 2012, a jump of roughly 50%. In all, the deluge of pills was enough to supply every adult and child in the country with around 36 opioid pills per year. Just a 10-day supply can hook 1 in 5 people into being long-term users, researchers have determined.

Members of the International Brotherhood of Teamsters hold signs while protesting during the McKesson Corp. annual meeting at the Irving-Las Colinas Chamber of Commerce in Irving, Texas, US, on Wednesday, July 26, 2017.

The stunning supply figures were first reported by the Washington Post and come from part of a database compiled by the Drug Enforcement Administration that tracked the fate of every opioid pill sold in America, from manufacturers to individual pharmacies. A federal court in Ohio released the data this week as part of a massive consolidated court case against nearly two-dozen opioid makers and distributors, brought by nearly 2,000 cities, towns, and counties. The local governments allege that the opioid companies conspired to saturate the country with the potent painkillers to soak up billions in profits. The companies deny the allegations, arguing generally that they were serving the needs of patients.

According to an analysis of the data by the Post, just three companies made 88% of the opioid pills: SpecGx, Actavis Pharma, and Par Pharmaceutical, a subsidiary of Endo Pharmaceuticals. Purdue Pharma ranked fourth, making 3% of the pills. Just six companies distributed 75% of the pills: McKesson Corp., Walgreens, Cardinal Health, AmerisourceBergen, CVS, and Walmart.

The Post also noted that the distribution was concentrated in certain places, finding that West Virginia, Kentucky, South Carolina, Tennessee, and Nevada had the top pill-per-person-per-year rates of

all states, ranging from 66.5 to 54.7. West Virginia, which had the highest distribution rate, also had the highest opioid death rate during this period. But certain rural areas were also hard hit, with Norton, Virginia, receiving 306 pills per person per year and Mingo County, West Virginia, receiving 203.

While the local governments suing the companies have had access to this data during the litigation, it was only released to the public after the Washington Post and HD Media, publisher of the Charleston Gazette-Mail of West Virginia, sued and waged a year-long legal battle. The drug companies had fought to keep the data hidden from the public, arguing that it revealed "transactional data" that could be used by competitors. The Department of Justice also argued against the release, saying it could compromise investigations.

A three-judge panel sided with the media organizations last month. This past Monday, US District Judge Dan Polster removed a protective order allowing the release of part of the DEA's database, called Automation of Reports and Consolidated Order System, or ARCOS. Data from years beyond 2012 are still being withheld to protect the companies and DOJ investigations. From 1999 to 2017, nearly 400,000 people in the US died from an opioid overdose, according to the Centers for Disease Control and Prevention.

http://bit.ly/2Oa4qXp

Many of the deadliest cancers receive the least amount of research funding

'Embarrassing' or stigmatized cancers like lung and liver are underfunded

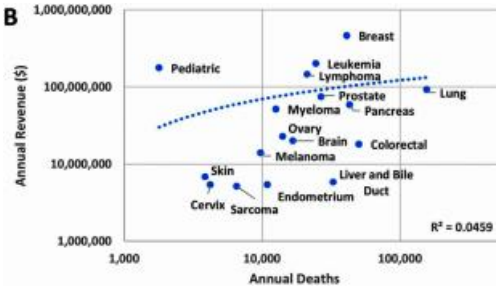
Poorly funded cancers: colon, endometrial, liver and bile duct, cervical, ovarian, pancreatic and lung

Well-funded cancers: breast, pediatric, leukemia and lymphoma

All cancers with stigmatized behavior (i.e. lung cancer and smoking) are poorly funded

Underfunding of these common cancers could negatively impact research, drug development

CHICAGO --- Many of the deadliest or most common cancers get the least amount of nonprofit research funding, according to a new Northwestern Medicine study that examined the distribution of nonprofit research funding in 2015 across cancer types.



Scatter plots using logarithmic scales for both the x and y axes of annual revenue versus mortality. **Northwestern University**

Colon, endometrial, liver and bile duct, cervical, ovarian, pancreatic and lung cancers were all poorly funded compared to how common they are and how many deaths they cause, the study found. In contrast, breast cancer, leukemia, lymphoma and pediatric cancers were all well-funded, respective to their impact on society.

The study is the first to compare nonprofit funding distribution in the United States across cancer types. It will be published July 18 in the Journal of the National Comprehensive Cancer Network.

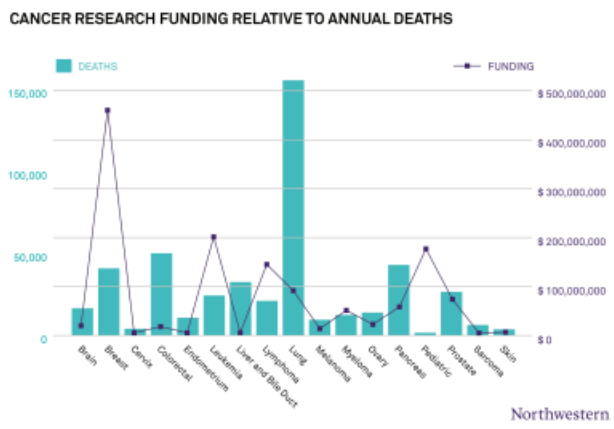
"The goal of this study is not to divert funds away from cancers that are well-supported, but rather expand funding for other cancers that aren't getting enough support currently," said corresponding author Dr. Suneel Kamath, who was the chief fellow in the department of hematology and oncology at Northwestern University Feinberg School of Medicine when he conducted the study. "These are all deadly and life-altering diseases that deserve our attention and support."

Cancer-related nonprofit organizations play an important role in funding medical research, supporting the education of patients and their families and influencing health policy. Underfunding of these common cancers could negatively impact research, drug

development and the number of FDA drug approvals for poorly funded cancers.

"Well-funded patient advocacy organizations should be applauded for their successes," said co-author Dr. Sheetal Kircher, assistant professor of hematology and oncology at Feinberg and a Northwestern Medicine oncologist. "We hope to bring awareness to the organizations with less relative funding so we can collaborate to improve funding and outcomes for all patients with cancer."

The study also explored factors that may influence which cancers receive more public support over others. Cancers that are associated with a stigmatized behavior, such as lung cancer with smoking or liver cancer with drinking, were all poorly funded.



A look at the how much nonprofit research funding each type of cancer receives relative to the number of annual deaths caused by that cancer.
Northwestern University

"Shame and discomfort with talking about our bowels and 'private parts' may be reducing funding for diseases like colon or endometrial cancer," Kamath said.

The nationwide study, conducted between October 2017 and February 2018, used IRS tax records to identify all nonprofit organizations that support any type of cancer and made at least $5 million in annual revenue in 2015. The scientists examined 119 organizations with a total of $5.98 billion in annual revenue. Most of this ($4.59 billion) went to general cancer charities with no focus on one disease (e.g. American Cancer Society).

The authors compared the amount of revenue for each cancer type with the number of new cases, number of deaths and number of years of life lost to see if the amount of funding for each cancer is proportional to how common and/or deadly it is.

Dr. Al Benson, professor of hematology and oncology at Feinberg and a Northwestern Medicine oncologist, also is a study author. Benson and Kircher also are members of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

The study was not funded or supported by any government, nonprofit or industry entities.

http://bit.ly/2Z3RMu6

Red wine's resveratrol could help Mars explorers stay strong, says Harvard study

Nutraceuticals that preserve muscle in reduced gravity will support long-term space missions

Mars is about 9 months from Earth with today's tech, NASA reckons. As the new space race hurtles forward, Harvard researchers are asking: how do we make sure the winners can still stand when they reach the finish line?

Published in *Frontiers in Physiology*, their study shows that resveratrol substantially preserves muscle mass and strength in rats exposed to the wasting effects of simulated Mars gravity.

Space supplements

Out in space, unchallenged by gravity, muscles and bones weaken. Weight-bearing muscles are hit first and worst, like the soleus muscle in the calf.

"After just 3 weeks in space, the human soleus muscle shrinks by a third," says Dr. Marie Mortreux, lead author of the NASA-funded study at the laboratory of Dr. Seward Rutkove, Beth Israel Deaconess Medical Center, Harvard Medical School. "This is accompanied by a loss of slow-twitch muscle fibers, which are needed for endurance."

To allow astronauts to operate safely on long missions to Mars - whose gravitational pull is just 40% of Earth's - mitigating strategies will be needed to prevent muscle deconditioning.

"Dietary strategies could be key," says Dr. Mortreux, "especially since astronauts travelling to Mars won't have access to the type of exercise machines deployed on the ISS."

A strong candidate is resveratrol: a compound commonly found in grape skin and blueberries that has been widely investigated for its anti-inflammatory, anti-oxidative, and anti-diabetic effects.

"Resveratrol has been shown to preserve bone and muscle mass in rats during complete unloading, analogous to microgravity during spaceflight. So, we hypothesized that a moderate daily dose would help mitigate muscle deconditioning in a Mars gravity analogue, too."

Mars rats

To mimic Mars gravity, the researchers used an approach first developed in mice by Mary Bouxsein, PhD, also at Beth Israel Deaconess, in which rats were fitted with a full-body harness and suspended by a chain from their cage ceiling.

Thus, 24 male rats were exposed to normal loading (Earth) or 40% loading (Mars) for 14 days. In each group, half received resveratrol (150 mg/kg/day) in water; the others got just the water. Otherwise, they fed freely from the same chow.

Calf circumference and front and rear paw grip force were measured weekly, and at 14 days the calf muscles were analyzed.

Resveratrol to the rescue

The results were impressive.

As expected, the 'Mars' condition weakened the rats' grip and shrank their calf circumference, muscle weight and slow-twitch fiber content. But incredibly, resveratrol supplementation almost entirely rescued front and rear paw grip in the Mars rats, to the level of the non-supplemented Earth rats.

What's more, resveratrol completely protected muscle mass (soleus and gastrocnemius) in the Mars rats, and in particular reduced the loss of slow-twitch muscle fibers. The protection was not complete, though: the supplement did not entirely rescue average soleus and gastrocnemius fibers cross-sectional area, or calf circumference.

As reported previously, resveratrol did not affect food intake or total body weight.

Perfecting the dose

Previous resveratrol research can explain these findings, says Dr. Mortreux. "A likely factor here is insulin sensitivity.

"Resveratrol treatment promotes muscle growth in diabetic or unloaded animals, by increasing insulin sensitivity and glucose uptake in the muscle fibers. This is relevant for astronauts, who are known to develop reduced insulin sensitivity during spaceflight."

The anti-inflammatory effects of resveratrol could also help to conserve muscle and bone, and other anti-oxidant sources such as dried plums are being used to test this, adds Dr. Mortreux.

"Further studies are needed to explore the mechanisms involved, as well as the effects of different doses of resveratrol (up to 700 mg/kg/day) in both males and females. In addition, it will be important to confirm the lack of any potentially harmful interactions of resveratrol with other drugs administered to astronauts during space missions."

https://www.frontiersin.org/articles/10.3389/fphys.2019.00899/full

http://bit.ly/2SrFB7X

Conjoined Twins Fused at the Head Now Separated After More Than 50 Hours of Surgery

Medical endeavor required a team of 100 medical professionals

By Rachael Rettner, Senior Writer

Twin girls who were born joined at the head have been successfully separated after a months-long medical endeavor that required more than 50 hours of major surgery and a team of 100 medical professionals, doctors announced this week.

The 2-year-old twins, Safa and Marwa Ullah, were born with an extremely rare condition called craniopagus, which means they shared a portion of their skull and brain tissue, according to Great Ormond Street Hospital (GOSH) in London, the facility where the separation surgery was performed.

Conjoined twins are very rare to begin with, occurring at a rate of about 1 in 2.5 million births worldwide, and of these, only about 5% are craniopagus, the hospital said in a statement.

Twins Safa and Marwa Ullah were born with an extremely rare condition called craniopagus, which means they were connected at the head and shared a portion of their skull and brain tissue. Above, an image of the twins after their separation surgery. **Great Ormond Street Hospital**

The twins were brought from their home in Pakistan to GOSH when they were 19 months old. They required three major operations that took place from October 2018 to February 2019, the statement said. The girls' recovery took time, and they were finally well enough to leave the hospital on July 1, according to The New York Times.

Surgeries to separate craniopagus twins are complex and challenging, and they need to be broken down into a series of smaller steps, the hospital said.

For the first several procedures, doctors focus on separating the twins' brains and blood vessels, and then doctors insert a piece of plastic to separate the two brains. Next, during another procedure, the skulls must be separated and the tops of their heads reconstructed with the twins' own bone and skin.

To aid in planning the surgeries, doctors created a replica of the twins' anatomy with virtual-reality technology, and they also used 3D-printed plastic models of the twins' brains, skulls and blood vessels to practice the surgery.

"We are delighted we have been able to help Safa and Marwa and their family. It has been a long and complex journey for them, and for the clinical team looking after them," Dr. Noor ul Owase Jeelani, former head of neurosurgery at GOSH, and Dr. David Dunaway, head of the Craniofacial Unit at GOSH, who together led the girls' surgery, said in a statement. The hospital separated two other sets of craniopagus twins, in 2006 and 2011.

https://wb.md/2M6JvSr

Blood Biomarker Identifies Multiple Neurologic Disorders

Blood levels of neurofilament light (NfL) can distinguish patients with several different neurodegenerative conditions from healthy people, new research indicates.

Megan Brooks

LOS ANGELES —NfL is not specific for any one condition, but it could be "valuable as a relatively inexpensive and fast test for accumulating neurodegeneration in the brain" when used in the clinic and in clinical trials, said study investigator Abdul Hye, PhD, of the Institute of Psychiatry, Psychology and Neuroscience, King's College London, United Kingdom.

Hye presented the study at a press briefing here at the Alzheimer's Association International Conference (AAIC) 2019.

Multiple Conditions

NfL is a structural protein that forms the internal skeleton of neurons. When neurons are damaged, NfL is released into cerebrospinal fluid and blood. It is currently being studied as a potential biomarker for many different neurologic diseases.

NfL is an "excellent axonal injury biomarker," Hye told the briefing. Differences in NfL levels in blood between healthy people and patients with neurodegenerative diseases are widely accepted, but

less is known about how plasma concentrations of NfL differ across neurodegenerative disorders, he explained.

To investigate whether NfL is a "cross neurodegenerative" blood-based biomarker, the researchers compared plasma NfL concentrations across multiple neurodegenerative and neurologic conditions in more than 2300 individuals from two cohorts.

Conditions included mild cognitive impairment (MCI), Alzheimer disease (AD), frontotemporal dementia (FTD), dementia with Lewy bodies (DLB), Parkinson disease (PD), and primary tauopathies. Several other conditions, such as vascular dementia, Down syndrome (DS), amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and clinical depression, were also included. Healthy control persons were also included.

Both cohorts showed similar increases in NfL across multiple neurodegenerative conditions, said Hye.

The lowest average NfL concentrations were found in control persons and clinically depressed individuals (30 and 11 pg/mL, respectively). The highest plasma NfL concentrations were found in patients with ALS (143.9 pg/mL), DS-D (80 pg/mL), and DLB (79.6 pg/mL). Compared with control persons, statistically significant differences in plasma NfL concentrations were observed for patients with FTD, corticobasal syndrome (CBS), DS-D, DLB, and ALS.

Using a plasma NfL concentration cutoff of 44.7 pg/mL, abnormal levels predicted more than 80% of cases of ALS, 100% of cases DS-D, 60% of cases of CBS, and more than 50% of FTD cases. NfL levels were abnormal in only 2% of healthy control persons, a finding that strengthened the choice of cutoff point, the researchers say.

However, in both cohorts, NfL concentrations were abnormal in only 20% to 30% of those with AD, "which is not the best," Hye told the briefing. The researchers replicated this finding using data from the Alzheimer's Disease Neuroimaging Initiative (ADNI).

Global Race

Reached for comment, Howard Fillit, MD, founding executive director and chief science officer of the Alzheimer's Drug Discovery Foundation, told *Medscape Medical News*, "What we are seeing with NfL in the blood is that it kind of predicts who is having active neurodegeneration but isn't clinically really sick yet.

"NfL in the blood is a sign of axonal damage in the brain, but it's not specific to any one neurodegenerative disease, like Alzheimer's disease. But it still could have a role in the diagnostic algorithm," said Fillit.

He noted that there are "reliable and sensitive assays for NfL, and you can detect elevated levels of NfL in the blood, but right now, the NfL tests are research-use only."

Bruce Lamb, PhD, vice chair of the Alzheimer's Association Medical and Scientific Advisory Group, who moderated the press briefing at AAIC 2019, where the results were presented, said that currently, there is a "global race to uncover and develop blood-based biomarkers of Alzheimer's disease and other dementias."

Blood-based biomarkers will be "essential and would be welcome by clinicians, researchers, and the public because in general, they are cheaper, easier to administer, less invasive, and more accessible than all other technologies currently available. The hope is that we can develop these as early detection tools and use them to track the impact of therapeutic interventions," said Lamb.

He said the Alzheimer's Association is actively funding research into blood-based biomarkers. "While these tests are not quite ready for prime time, we are actually much closer than I think we even thought we would be just a few years ago," said Lamb.

Funding for the study was provided by the National Institute for Health Research, the European Research Council, the Swedish Research Council, the Knut and Alice Wallenberg Foundation, the Marianne and Marcus Wallenberg Foundation, the Swedish

Alzheimer Foundation, the Swedish Brain Foundation, the Parkinson Foundation of Sweden, the Skaåne University Hospital Foundation, and the Swedish federal government. Hye, Lamb, and Fillit have disclosed no relevant financial relationships.
Alzheimer's Association International Conference (AAIC) 2019: Abstract P2-618. Presented July 15, 2019.

http://bit.ly/2GlRZBI

Northern Marshall Islands More Radioactive than Chernobyl and Fukushima, New Research Finds

New research in PNAS shows radiation levels are still far higher than in areas affected by the Chernobyl and Fukushima accidents

Enrico de Lazaro

From 1946 to 1958, the U.S. tested 67 nuclear weapons in the **Marshall Islands**, a remote constellation of atolls in the Pacific Ocean that was then a U.S. trust territory.

Two atolls, Bikini and Enewetak, were used as ground zero for the tests, which caused unprecedented environmental contamination.

According to new research, presented in three papers in the ***Proceedings of the National Academy of Sciences***, radiation levels in some regions of the islands are still far higher than in areas affected by the **Chernobyl** and **Fukushima** nuclear accidents.

The U.S. performed nuclear testing on Bikini and Enewetak Atolls in the northern Marshall Islands between 1946 and 1958.

On March 1, 1954, the U.S. military detonated its largest thermonuclear weapon on an island located in the northwestern rim of Bikini Atoll. The weapon, code-named Castle Bravo, released an energy equivalent to 15 million tons of TNT (15 megatons).

The Marshall Islands have experienced rapid growth since the 1960s. Most of the nation's residents live on two crowded islands and are unable to return to their home islands because of nuclear contamination.

"Our three studies showed that the concentration of nuclear isotopes on some of the islands was well above the legal exposure limit established in agreements between the U.S. and Republic of the Marshall Islands," said lead authors Emlyn Hughes and Malvin Ruderman and their colleagues from Columbia University.

In the first study, the researchers assessed current radiological conditions on four affected atolls (Enewetak, Bikini, Rongelap, and Utirik) in the northern Marshall Islands.

They measured external gamma radiation on nine islands and concentrations of americium-241, cesium-137, plutonium-238, and plutonium-239/240 in the soil samples from 11 islands.

In the second study, the scientists measured concentrations of plutonium-239/240, plutonium-238, americium-241, bismuth-207, and cesium-137 in cores from the Bravo bomb crater site.

"We found radiation levels orders of magnitude above background for plutonium-239/240, americium-241, and bismuth-207 in the top 25 cm of sediment across the entire Bravo crater, the location of the largest aboveground U.S. nuclear weapons test," they said.

In the third study, the team determined the levels of cesium-137 contamination for over 200 fruits, primarily coconuts and pandanus, from 11 islands on four atolls.

They found that contamination remains above limits set by international safety standards in some measured fruits.

"Based upon our results, we conclude that to ensure safe relocation to Bikini and Rongelap Atolls, further environmental remediation appears to be necessary to avoid potentially harmful exposure to radiation," the researchers said.

Maveric K.I.L. Abella et al. *Background gamma radiation and soil activity measurements in the northern Marshall Islands.* PNAS, *published online July 15, 2019; doi: 10.1073/pnas.1903421116*

Emlyn W. Hughes et al. *Radiation maps of ocean sediment from the Castle Bravo crater.* PNAS, *published online July 15, 2019; doi: 10.1073/pnas.1903478116*

Carlisle E.W. Topping et al. In situ *measurement of cesium-137 contamination in fruits from the northern Marshall Islands.* PNAS, *published online July 15, 2019; doi: 10.1073/pnas.1903481116*

http://bit.ly/32CIlUC

Chest X-rays contain information that can be harvested with AI

Study finds chest X-rays contain 'hidden' information that can be harvested with artificial intelligence to predict long-term mortality

BOSTON - The most frequently performed imaging exam in medicine "the chest X-ray" holds 'hidden' prognostic information that can be harvested with artificial intelligence (AI), according to a study by scientists at Massachusetts General Hospital (MGH). The findings of this study, to be published in the July 19, 2019 issue of JAMA Network Open, could help to identify patients most likely to benefit from screening and preventive medicine for heart disease, lung cancer and other conditions.

AI technology automates many aspects of our daily lives, such as your smartphone's speech-recognition function, photo tagging on social media, and self-driving cars. AI is also responsible for major advances in medicine; for example, several groups have applied AI to automate diagnosis of chest X-rays for detection of pneumonia and tuberculosis.

If this technology can make diagnoses, asked radiologist Michael Lu, MD, MPH, could it also identify people at high risk for future heart attack, lung cancer, or death? Lu, who is director of research for the MGH Division of Cardiovascular Imaging and assistant professor of Radiology at Harvard Medical School, and his colleagues developed a convolutional neural network, a state-of-the-art AI tool for analyzing visual information, called CXR-risk. CXR-risk was trained by having the network analyze more than 85,000 chest X-rays from 42,000 subjects who took part in an earlier clinical trial. Each image was paired with a key piece of data: Did the person die over a 12-year period? The goal was for CXR-risk to learn the features or combinations of features on a chest X-ray image that best predict health and mortality.

Next, Lu and colleagues tested CXR-risk using chest X-rays for 16,000 patients from two earlier clinical trials. They found that 53% of people the neural network identified as "very high risk" died over 12 years, compared to fewer than 4% of those that CXR-risk labeled as "very low risk." The study found that CXR-risk provided information that predicts long-term mortality, independent of radiologists' readings of the x-rays and other factors, such as age and smoking status.

Lu believes this new tool will be even more accurate when combined with other risk factors, such as genetics and smoking status. Early identification of at-risk patients could get more into preventive and treatment programs. "This is a new way to extract prognostic information from everyday diagnostic tests," says Lu. "It's information that's already there that we're not using, that could improve people's health."

Co-authors of the JAMA Network Open paper are Michael T. Lu, MD, MPH, director of research for the MGH Division of Cardiovascular Imaging and assistant professor of Radiology at Harvard Medical School; Alexander Ivanov, BS, clinical research coordinator of MGH's Cardiac MR PET CT Program; Thomas Mayrhofer, PhD, a lecturer at HMS and a professor of Economics at Stralsund University of Applied Sciences in Germany; Ahmed Hosny, MS, of the department of Radiation Oncology, Dana-Farber Cancer Institute; Hugo J.W. L. Aerts, PhD, director, Computational Imaging and Bioinformatics Laboratory (CIBL) and associate professor at Harvard University; Udo Hoffmann, MD, MPH, director of the Cardiac MR PET CT Program, MGH and a professor of Radiology at HMS.

http://bit.ly/2XUvb6S

Take a bath 90 minutes before bedtime to get better sleep

Researchers in the Cockrell School of Engineering found that bathing 1-2 hours before bedtime in water of about 104-109 degrees Fahrenheit can significantly improve your sleep

Biomedical engineers at The University of Texas at Austin may have found a way for people to get better shuteye. Systematic review protocols -- a method used to search for and analyze

relevant data -- allowed researchers to analyze thousands of studies linking water-based passive body heating, or bathing and showering with warm/hot water, with improved sleep quality. Researchers in the Cockrell School of Engineering found that bathing 1-2 hours before bedtime in water of about 104-109 degrees Fahrenheit can significantly improve your sleep.

"When we looked through all known studies, we noticed significant disparities in terms of the approaches and findings," said Shahab Haghayegh, a Ph.D. candidate in the Department of Biomedical Engineering and lead author on the paper. "The only way to make an accurate determination of whether sleep can in fact be improved was to combine all the past data and look at it through a new lens."

The paper explaining their method was recently published in the journal Sleep Medicine Reviews.

In collaboration with the UT Health Science Center at Houston and the University of Southern California, the UT researchers reviewed 5,322 studies. They extracted pertinent information from publications meeting predefined inclusion and exclusion criteria to explore the effects of water-based passive body heating on a number of sleep-related conditions: sleep onset latency -- the length of time it takes to accomplish the transition from full wakefulness to sleep; total sleep time; sleep efficiency -- the amount of time spent asleep relative to the total amount of time spent in bed intended for sleep; and subjective sleep quality.

Meta-analytical tools were then used to assess the consistency between relevant studies and showed that an optimum temperature of between 104 and 109 degrees Fahrenheit improved overall sleep quality. When scheduled 1-2 hours before bedtime, it can also hasten the speed of falling asleep by an average of 10 minutes.

Much of the science to support links between water-based body heating and improved sleep is already well-established. For example, it is understood that both sleep and our body's core temperature are regulated by a circadian clock located within the brain's hypothalamus that drives the 24-hour patterns of many biological processes, including sleep and wakefulness.

Body temperature, which is involved in the regulation of the sleep/wake cycle, exhibits a circadian cycle, being 2-3 degrees Fahrenheit higher in the late afternoon/early evening than during sleep, when it is the lowest. The average person's circadian cycle is characterized by a reduction in core body temperature of about 0.5 to 1 F around an hour before usual sleep time, dropping to its lowest level between the middle and later span of nighttime sleep. It then begins to rise, acting as a kind of a biological alarm clock wake-up signal. The temperature cycle leads the sleep cycle and is an essential factor in achieving rapid sleep onset and high efficiency sleep.

The researchers found the optimal timing of bathing for cooling down of core body temperature in order to improve sleep quality is about 90 minutes before going to bed. Warm baths and showers stimulate the body's thermoregulatory system, causing a marked increase in the circulation of blood from the internal core of the body to the peripheral sites of the hands and feet, resulting in efficient removal of body heat and decline in body temperature. Therefore, if baths are taken at the right biological time -- 1-2 hours before bedtime -- they will aid the natural circadian process and increase one's chances of not only falling asleep quickly but also of experiencing better quality sleep.

The research team is now working with UT's Office of Technology Commercialization in the hopes of designing a commercially viable bed system with UT-patented Selective Thermal Stimulation technology. It allows thermoregulatory function to be manipulated on demand and dual temperature zone temperature control that can be tailored to maintain an individual's optimum temperatures throughout the night.

https://wb.md/2XW39Yw

Could Cheap Drug Metformin Prevent Dementia in Black Patients?

African American patients with type 2 diabetes taking metformin showed a substantial reduction in risk for dementia compared with similar patients started on a sulfonylurea; this effect was particularly evident among those in the 50 to mid-60s age bracket.

Becky McCall

And the effect was far less marked in white patients, according to a new, large retrospective study of Veterans Health Administration data.

Middle-aged African American patients (50-64 years) taking metformin showed a 40% risk reduction, while those aged 65-74 years showed a 29% lower risk of dementia compared with similar patients taking a sulfonylurea. White patients, meanwhile, only showed around a 4% risk reduction on metformin compared with sulfonylureas.

"Based on our evidence, this reduced risk is not a result of glycemic control but could be due to metformin's potential to reduce risk of vascular events as well as vascular dementia," lead author Jeffrey Scherrer, PhD, from Saint Louis University School of Medicine, Missouri, told *Medscape Medical News*.

Scherrer, who is also with the Harry S. Truman Veterans Administration Medical Center, Columbia, Missouri, speculates that metformin might reduce systemic inflammation; the latter is a consequence of diabetes that occurs more commonly in African American patients, he said.

He noted the large treatment effect observed in black patients, which he said is "unusual" given the large sample size. Calling the findings "remarkable," he said they may point to a novel approach with a cheap drug for reducing the risk of dementia in African Americans with type 2 diabetes.

"If there's a concern about dementia, metformin is a safe drug that could potentially be started earlier, however, replication of these results is needed," he stressed to *Medscape Medical News*. The study was published in the July/August issue of *Annals of Family Medicine*.

African Americans Have Higher Rates of Type 2 Diabetes and Dementia

Prior evidence from observational studies has suggested metformin, compared with sulfonylureas, is associated with an 8% to 10% decrease in dementia risk, say the researchers.

Scherrer, who is an epidemiologist, said he and his colleagues wanted to evaluate race differences associated with the effect of metformin on dementia, because of the higher prevalence of dementia in African Americans and the consequences of type 2 diabetes on dementia risk, which are greater in blacks than whites.

They studied 73,761 African American and white patients aged 50 years or older from the Veterans Health Administration database. At study start, patients were free of dementia and were naive to diabetes medications, other than starting on metformin or a sulfonylurea monotherapy.

Incidence of dementia was determined by diagnostic code; mild cognitive impairment was not included.

Metformin's Protective Effect Appears Independent of Glycemic Control

Over a mean follow-up of around 6.5 years, regardless of age, the African American participants showed a greater than 25% lower risk of dementia if they took metformin compared with a sulfonylurea (hazard ratio [HR], 0.73; 95% CI, 0.6 - 0.89).

In contrast, white patients had just a 4% to 8% lower risk (HR, 0.96; 95% CI, 0.9 - 1.03), he noted in an interview with *Medscape Medical News*.

"Importantly, in addition to the baseline balancing of variables, we controlled for the duration of time spent in a hypoglycemic state after medication start. We still arrived at the same result, so the findings are independent of glycemic control."

The team also adjusted for a wide range of confounding variables, including ischemic heart disease, stroke, hypertension, diabetes complications, and HbA_{1c}, as well as psychiatric disorders, alcohol dependence, illicit drug abuse, and nicotine dependence/smoking.

When stratified further by age group, in African Americans aged 50-64 years, dementia risk was reduced (HR, 0.60; 95% CI, 0.45 - 0.81). This effect was not seen among white patients in the same age group (HR, 0.94; 95% CI, 0.81 - 1.09).

In the 65-74 years age bracket of white patients, there appeared to be a 10% lower risk of dementia on metformin compared with a sulfonylurea (HR, 0.90; 95% CI, 0.82 - 0.99), a result that confirmed findings of a prior study, said Scherrer.

In African Americans of the same age, dementia risk was reduced by around 29% (HR, 0.71; 95% CI, 0.53 - 0.94).

Notable Protective Effects of Metformin in African Americans

"What I think is remarkable...is the over 40% reduced risk in African Americans [50-64 years of age] on metformin, and around a 29% lower risk in the 65-74 years age group," emphasized Scherrer.

"It's not a surprise that the oldest patients [75 years plus] have reduced benefit because there are so many other risk factors for dementia at this age and less opportunity for metformin's protective relationship with dementia to take effect."

"What is strange is why is metformin causing a protective effect in African Americans? Given we know they have worse glycemic control and more diabetes-related adverse events, what else does metformin do that might be relevant here?"

Reflecting on the potential mechanisms, Scherrer said that the drug could be working by reducing systemic inflammation.

"This finding is a large effect, which is unusual to find in such a large sample. This is atypical," he observed.

He and his colleagues concluded: "There are no existing medications to prevent dementia." The current findings "suggest that someday this inexpensive, widely available treatment could be broadly prescribed to substantially reduce the risk of dementia in younger African American patients with type 2 diabetes."

Scherrer has reported no relevant financial relationships.

Ann Fam Med. 2019;17:352-362. Full text

https://wb.md/2M4A2em

'Striking' Benefit of Intranasal Insulin in Slowing Dementia

Daily intranasal insulin may be effective in slowing progression of mild cognitive impairment (MCI) or Alzheimer's disease (AD), new research suggests.

Pauline Anderson

LOS ANGELES — Investigators found intranasal insulin administered via a novel delivery device slowed the rate of cognitive decline by 1 to 2 years. "The magnitude of the benefit is striking," study investigator Suzanne Craft, PhD, professor of gerontology and geriatric medicine at Wake Forest School of Medicine in Winston-Salem, North Carolina, told *Medscape Medical News.* "This is the first trial where a medication has been delivered intranasally to treat AD," said Craft. The findings were presented here at the Alzheimer's Association International Conference (AAIC) 2019.

Protective Effect

Insulin is essential for normal functions in the body and brain. It enhances communication between neurons, increases brain blood flow, and protects against beta-amyloid (Aβ) and abnormal tau.

"One of the things I think is very important for memory is that insulin protects the synapses against amyloid, and also generates new synapses. How well insulin works is the best predictor of how successfully one will age," said Craft.

It appears either patients with AD have low levels of insulin in the brain or the hormone is not working effectively. Boosting insulin levels in the brain might help. However, injecting insulin does not get the hormone straight into the brain, and might lower blood sugar levels, said Craft.

For the study, researchers used a novel mode of delivery — a device that facilitates intranasal applications. The technology involves creating very small aerosol-like droplets of insulin that are driven upwards, directly into the brain and not into the blood stream or lungs, said Craft.

There is growing interest in intranasal delivery of insulin, partly because it is able to penetrate the blood–brain barrier, she said.

The study included 289 patients across 26 sites who had mini-mental state examination (MMSE) scores above 20. Participants were randomly assigned to receive 20 international units (IUs) of insulin or placebo twice daily for 12 months, after which they could opt to receive inulin for 6 months in an open-label phase.

The study began with the Kurve Vianase device, which the researchers had used in all their previous studies. The manufacturer tried to improve the device for this trial, "but unfortunately that improvement resulted in unreliability of that device," said Craft.

She explained that the manufacturer put a new timer switch on the device that "worked erratically," meaning study participants "kept having to replace" the device.

The study then switched to a second delivery system, the Impel Precision Olfactory Device. This meant 49 study subjects were assessed with the first device and 240 with the second device.

There were no safety issues with either device, and there was "respectable compliance" for both, said Craft.

Clinically Significant

The primary outcome was Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), with higher scores indicating worse outcomes. Researchers administered other cognitive and behavioral tests and measured abnormal amyloid and tau proteins — ratios of Aβ42/Aβ40 and Aβ42/tau — in cerebrospinal fluid (CSF) samples.

"These ratios provide an integrated measure of Alzheimer's pathology and have been found to be better predictors than individual biomarkers in some studies," noted Craft.

In the analysis of patients using the second device, both groups worsened cognitively. "So there was no benefit" from the intranasal insulin in either the 12-month trial or this open-label phase, said Craft.

Also in this group, there were no differences between those receiving placebo and those getting insulin in any other measures that researchers incorporated into the study.

However, it was "a different picture" with the first device, said Craft. Here, the insulin group showed an advantage over 12 months, and by 18 months, that group had a 6-point advantage on the ADAS-Cog compared with those who were originally assigned to placebo (P = .018).

"This is a clinically significant effect," said Craft. "We estimate it to be a 1-to-2 year slowing in the rate of disease progression."

Adults with AD typically worsen by about 3 ADAS-Cog points per year, noted Craft.

The Earlier, the Better?

In addition, the CSF biomarker ratios improved with the insulin group using the first device, suggesting a slowing of brain injury associated with AD.

"This showed us that we were affecting the proteins and pathology that is part of Alzheimer's disease, in addition to the cognitive symptoms," said Craft. It is possible the cognitive benefits will increase as more time passes, she added.

The researchers tested the ability of the first device to deliver insulin into the brain. They did so by administering saline and insulin at different times, each followed by a lumbar puncture to assess CSF levels.

"The data are showing that insulin levels were elevated with insulin treatment by that device at every occasion. That was significant; it showed that the device was getting insulin into the brain," said Craft.

The investigators are conducting further analyses to determine whether cognitive worsening of those with higher MMSE scores at baseline slowed more than in participants with lower baseline scores.

"We can't say that's the case yet, but that's what we are thinking is going on — that the earlier you get the insulin, the better," she said.

It's not clear why the two devices produced different results. Craft noted that devices may differ in their ability to deliver insulin to the brain. "All devices are not created equal," she noted.

A phase 3 trial is being planned to confirm the beneficial effects of intranasal insulin in patients with MCI and AD. It is not yet clear which device will be selected for this next study although "we will validate the device prior to the beginning of the study," said Craft.

Potential New Mechanism

Commenting on these findings for *Medscape Medical News*, Rebecca Edelmayer, PhD, director of scientific engagement for the Alzheimer's Association, said the study is "an example of how we're diversifying the clinical trial pipeline with new ideas, of how we are sort of thinking outside the box."

Intranasal insulin may represent a potential new mechanism for treating AD, she said.

"Any type of treatment, whether it be a medicine or a lifestyle intervention, that's going to delay the onset or slow the progression of the disease would be a win for this disease field."

The Alzheimer's Association "wants to continue to make sure" that promising treatments undergo "a rigorous clinical trial," which will be "the next step" for intranasal insulin, said Edelmayer.

Study funding was provided by National Institute on Aging (NIA). Eli Lilly provided placebo for the trial blinded phase, and Humulin-R U100 for the open label extension. Craft and Edelmayer have disclosed no relevant financial relationships.

Alzheimer's Association International Conference (AAIC) 2019: Abstract 35542. Presented July 17, 2019.

http://bit.ly/2GmqTu2

115,000-Year-Old Engraved Bones Found in China

Archaeologists digging at an early hominin site in China have discovered two engraved bone fragments that date back nearly 115,000 years.

by Enrico de Lazaro

The two weathered bone fragments were found at the site of Lingjing in Xuchang county of China's Henan province. The specimens were examined by Dr. Francesco d'Errico from the Universities of Bordeaux and Bergen and his colleagues from China and France.

The researchers found that the bones are rib fragments from adult, large-sized mammals. "The lines on one of the bones were produced by an extremely sharp point, and the prehistoric individual was particularly careful when engraving the first five lines," they said. "To increase the visibility of the subsequent lines, the engraver marked them using multiple strokes."

"Combined, this evidence does not support an interpretation of the lines as evidence of butchery activity, but rather, deliberate engraving of the bone."

Dr. d'Errico and co-authors also found red residue within the incised lines on one of the artifacts.

The Raman spectroscopy analysis of the residue revealed the presence of ochre, a naturally occurring iron oxide pigment.

Photographs of the two engraved bone fragments from the site of Lingjing, China. **Image credit: F. d'Errico & L. Doyon.**

"The fragments were found in the same stratigraphic layer that yielded hominin remains attributed to an archaic population exhibiting a mosaic of anatomical features," the scientists said.

According to the team, the bone fragments were likely engraved symbolically by Denisovans, a mysterious close cousin of Neanderthals.

"A growing body of evidence from Europe and Southeast Asia supports the hypothesis that the cultural adaptations of archaic hominins involved symbolically mediated behavior, thereby challenging the notion that modern cognitive abilities are restricted to *Homo sapiens*," the study authors said.

"While many scholars now agree on this hypothesis with regard to Neanderthals, we offer the first evidence to suggest that the same may also apply to Denisovans — the probable creators of the Lingjing engravings."

The engravings represent the first possible example of such behavior in Eastern Asia to predate 40,000 years ago.

"We are still far from understanding the meaning of these engravings for the archaic human groups living in China during the early Late Pleistocene," the researchers said.

"A recent identification of bone and antler fragments that were used to retouch lithics demonstrates that the Lingjing hominins were familiar with the mechanical properties of weathered bone and considered it to be a suitable raw material for producing artifacts."

"The Lingjing engravings suggest that these populations also saw bone as a medium on which they could permanently record sequential markings and use ochre as a substance to help highlight them."

"Future research may identify spatiotemporal consistencies that could offer clues to help in fully evaluating the significance of these behaviors." The study was published in the journal *Antiquity*.

Zhanyang Li et al. *Engraved bones from the archaic hominin site of Lingjing, Henan Province.* Antiquity, *published online July 8, 2019; doi: 10.15184/aqy.2019.81*

http://bit.ly/2Y8mvoy

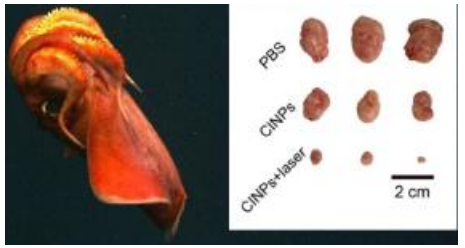
Cuttlefish ink found promising for cancer treatment

Cuttlefish ink contains nanoparticles that strongly inhibit the growth of cancerous tumors in mice

by Lisa Zyga , Phys.org

Researchers have found that cuttlefish ink—a black suspension sprayed by cuttlefish to deter predators—contains nanoparticles that strongly inhibit the growth of cancerous tumors in mice. The nanoparticles consist mostly of melanin by weight, along with amino acids, monosaccharides (simple sugars), metals, and other compounds.

The researchers showed that the nanoparticles modify the immune function in tumors, and when combined with irradiation, can almost completely inhibit tumor growth.



(Left) A cuttlefish. **North Atlantic Stepping Stones Science Party, IFE, URI-IAO; NOAA/OAR/OER.** ***(Right) Comparison of tumor size after 16 days of different treatments, including cuttlefish ink nanoparticles (CINPs) and CINPs with irradiation.*** **Deng et al. ©2019 American Chemical Society**

The researchers, led by Pang-Hu Zhou at the Renmin Hospital of Wuhan University and Xian-Zheng Zhang at the Chemistry Department at Wuhan University, have published a paper on the ability of nanoparticles from cuttlefish ink to inhibit tumor growth in a recent issue of *ACS Nano*.

"We found natural nanoparticles from cuttlefish ink with good biocompatibility that can effectively achieve tumor immunotherapy and photothermal therapy simultaneously," Zhang told *Phys.org*. "This finding might inspire more exploration of natural materials for medical applications."

Tumor immunotherapy involves fighting cancer by stimulating the body's own immune system. One strategy is to target leukocytes, or white blood cells. Macrophages are the predominant leukocyte found in some tumors, and they can take one of two forms: M1 or M2. The M1 phenotype engulfs and destroys tumor cells through the process of phagocytosis and with the activation of T cells (other white blood cells). In the M2 phenotype, on the other hand, this immune function is suppressed, allowing tumor growth to continue unchecked. In tumor environments, the M2 phenotype almost always outnumbers the M1 phenotype.

Recently, researchers have been working on the development of small molecules and antibodies that can convert protumor M2 macrophages to antitumor M1 macrophages. At the same time, they are designing nanoparticles such as photothermal agents that, when exposed to irradiation, locally destroy cancer cells by thermal ablation. These agents can be integrated into synthesized nanoparticles, and then potentially administered to patients. One of the drawbacks, however, is that these synthetic nanoparticles are expensive and require complicated preparation methods.

Due to these costs, some researchers have turned to nature for alternatives. Previous research has shown that certain natural compounds, including those found in brown algae and some bacteria, contain polysaccharides that have the ability to reprogram macrophages from the M2 type to the M1 type.

In the new paper, the researchers found that cuttlefish ink nanoparticles, which are spherical and approximately 100 nm in diameter, also have this ability. After confirming the biocompatibility of these nanoparticles, the researchers performed several experiments both *in vitro* with tumor cells and *in vivo* with tumor-afflicted mice. In the *in vitro* experiments, the researchers found that irradiating the nanoparticles with near-infrared irradiation killed approximately 90% of tumor cells, although the nanoparticles displayed almost no cytotoxicity without irradiation. The researchers explained that the high melanin content of the nanoparticles plays a key role in the irradiation process, as melanin has an intrinsically good photothermal conversion ability.

In mice, nanoparticle treatment proved to be effective both alone and in combination with irradiation, although irradiation further improved the outcome. Bioluminescent imaging revealed that treated mice exhibited significantly lower tumor bioluminescence compared to controls, indicating greatly reduced metastases on internal organs. Mice treated with both nanoparticles and irradiation exhibited a nearly complete inhibition of tumor growth.

By performing a gene analysis, the researchers identified 194 differentially expressed genes involved in immune functions that were associated with the regulation of the inflammatory response and cell killing, and which were either up- or down-regulated by the treatment. The analysis indicated that a certain signaling pathway is responsible for the conversion of M2 macrophages to M1 macrophages. This mechanism not only leads to phagocytosis of tumor cells, but also stimulates the immune system to produce various antitumor factors, all of which play a role in inhibiting tumor growth.

In the future, the researchers plan to explore other natural materials that have anti-cancer properties.

"Our research team is currently studying the biomedical potential of natural materials such as hair, cuttlefish ink, bacteria, fungi, and even the cells of the human body as a therapeutic drug carrier," Zhang said. "By drawing inspiration from nature and taking advantage of its own characteristics, we expect to find some valuable research that will provide new and effective solutions for the treatment of clinical diseases."

More information: *Rong-Hui Deng. Mei-Zhen Zou, Diwei Zheng, Si-Yuan Peng, Wenlong Liu, Xue-Feng Bai, Han-Shi Chen, Yunxia Sun, Pang-Hu Zhou, and Xian-Zheng Zhang. "Nanoparticles from Cuttlefish Ink Inhibit Tumor Growth by Synergizing Immunotherapy and Photothermal Therapy." ACS Nano. DOI: 10.1021/acsnano.9b02993*

http://bit.ly/2K8zTEn

Researchers Testing New Honeybee Sting Vaccine

A research team led by Flinders University's Professor Nikolai Petrovsky has completed a human clinical trial on an adjuvant vaccine designed to eliminate the risk of an allergic reaction to European honeybee stings.

by News Staff / Source

Allergic reactions to bee stings remain a major global clinical problem. Although venom immunotherapy can be effective at preventing life-threatening reactions to future stings, it can itself cause severe and even — although rare — life-threatening reactions.

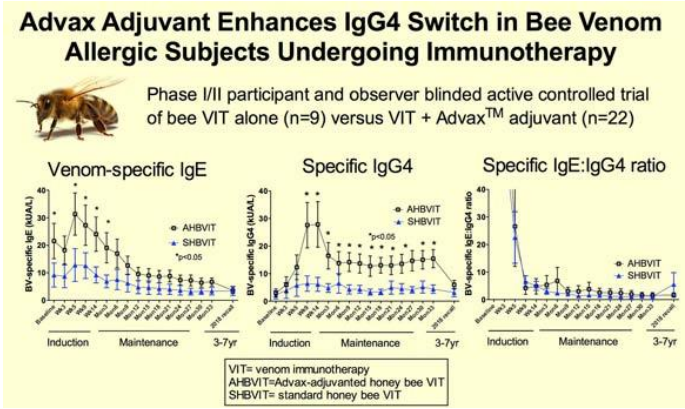
"While a commercial bee venom therapy is already available, it requires patients to have over 50 injections over a three-year period to build up their immune system," said Dr. Anthony Smith, a researcher at Flinders Medical Centre.

The clinical trial included 27 healthy adults with a history of rapid-onset systemic allergic reactions to bee stings.

The vaccine used in the trial contained the Advax adjuvant, a new adjuvant derived from the natural plant-based polysaccharide delta inulin.

This ingredient, developed by Vaxine Pty Ltd in Adelaide, Australia, helps the body neutralize the bee venom at a faster rate.

"The aim was to see if the Advax adjuvant would safely speed up and improve bee sting immunotherapy," said Dr. Robert Heddle, a researcher at the University of Adelaide, Royal Adelaide Hospital and Flinders University.



The Advax adjuvant favorably enhanced the immunogenicity of the honeybee venom immunotherapy, with an early and prolonged switch to specific IgG4 production. **Heddle *et al*, doi: 10.1016/j.jaci.2019.03.035.**

"Our technology is like adding a turbocharger to a car and in this case makes the bee allergy vaccine much more powerful, allowing the immune system to better neutralize the bee venom and prevent allergic symptoms," Professor Petrovsky added.

"Our results are very promising and confirmed the safety of this approach to improving bee sting immunotherapy," Dr. Heddle said.

"The current treatment option for serious bee venom allergies is lengthy and cumbersome, so I hope this enhanced bee venom therapy brings about faster, but longer lasting protection to bee stings for allergic individuals," Dr. Smith said.

The findings were published in the *Journal of Allergy and Clinical Immunology*.

Robert Heddle et al. *Randomized controlled trial demonstrating the benefits of delta inulin adjuvanted immunotherapy in patients with bee venom allergy.* Journal of Allergy and Clinical Immunology, *published online July 9, 2019; doi: 10.1016/j.jaci.2019.03.035*