

<http://www.bbc.co.uk/news/health-26191713>

The medicine in our minds

They are the miracle pills that shouldn't really do anything. Placebos come in all shapes and sizes, but they contain no active ingredient. And yet, mysteriously, they often seem to work.

By Olly Bootle BBC's Horizon programme

Over the last couple of decades, there has been a huge amount of research into what dummy pills can do and how they work. We know that in the right situations, they can be very effective at relieving self-reported conditions like pain and depression. But the latest research suggests they might even be able to help relieve the symptoms of a major neurological disorder, as Paul Pattison found out.

Medication need

In many ways, Paul is just like anyone else with a love of the outdoors. He spends much of his spare time cycling in the hills on the outskirts of Vancouver, where he lives. And every day, he walks his dog through the pine forest that starts where his garden ends. But there's one big difference between Paul and your average outdoorsy type. Whether he's walking or cycling, Paul needs medication to help him do it, because he has Parkinson's Disease. Without his drugs, even walking can be a major struggle.

Parkinson's is caused by an inability of the brain to release enough dopamine, a neurotransmitter that affects our mood, but is also essential for regulating movement. Luckily for Paul, his medication can give him the dopamine he needs to keep his symptoms under control. Given everything we know about the disease, it's hard to believe that a placebo - a 'dummy pill' with no active ingredients - could do anything to help someone with Parkinson's. And that makes Prof Jon Stoessl's experiments all the more remarkable. He is the director of the Pacific Parkinson's Research Centre at the University of British Columbia, in Vancouver.

A few years ago, Paul took part in a trial that Prof Stoessl was conducting. It required him to stop taking his medication. The next day he headed into hospital, his symptoms in full flare-up.

He explains: "That's when they gave me this capsule, and they gave you a half-hour... a normal period of time for the meds to kick in. And boom! "I was thinking this is pretty good, my body becomes erect, my shoulders go back. There's no way that I could be like this without having had my medication."

Except that Paul hadn't been given his medication - he'd been given a placebo.

Placebo 'is a trigger'

"I was in a state of shock. There are physical things that change in me when I take my meds so how could a blank thing, a nothing, create those same feelings?"

Prof Stoessl has conducted numerous experiments with dozens of patients, and is in no doubt that a placebo can sometimes relieve the symptoms of Parkinson's. "In Parkinson's, as in many other conditions, there is an important placebo response and that can be measured with clinical outcomes."

What is new about Prof Stoessl's work though is that, by scanning the brains of people with Parkinson's disease when they experience a placebo effect, he's been able to shed light on how a dummy pill can possibly make a difference. He has found that when someone like Paul responds well to a placebo, it isn't the case that he's simply coping better with his symptoms, or somehow battling through them. Instead, the placebo is triggering the release of dopamine in his brain.

And it isn't a small amount of dopamine that a placebo can release: "What we found is that in somebody with Parkinson's disease, a placebo can release as much dopamine as amphetamine or speed can in somebody with a healthy dopamine system. So it's a very dramatic response."

'Brain's own morphine'

That dramatic response only appears to last for a short while - a placebo certainly isn't a miracle cure.

And even if it was, doctors could hardly start lying to their patients and replacing real drugs with placebo pills.

It's also unclear exactly how a placebo is able to spur the brain into producing more dopamine, given that Parkinson's is caused by an apparent inability of the brain to produce enough.

But what is certainly clear is that the dopamine isn't coming from the placebo pill itself: there's nothing in it.

The dopamine is coming from our brains. And that goes to the heart of how a placebo works. There's now a strong body of evidence that a dummy pill can activate the brain's natural ability to produce the chemicals that we need.

Prof Tor Wager at the University of Colorado is a neuroscientist who studies what happens in the brain when people receive a placebo that they think is a painkiller. "When we've given people a placebo treatment what we see is the release of endogenous opioids, which is the brain's own morphine. "What that means is that the placebo effect is tapping into the same pain control circuitry as opiate drugs like morphine."

Research 'in infancy'

It seems that a dummy pill can do different things according to what you expect it to do.

It can potentially encourage the release of dopamine if you think it's a dopamine-boosting Parkinson's drug; or it can relieve pain if you think it's a painkiller.

In many ways of course our brains are natural pharmacies, constantly giving us chemical hits of one form or another - to stop pain, or to feel it; to energise us, or to calm us down, and it seems to be this in-built pharmacy that a placebo can trigger. In fact, the drugs that we buy in a real pharmacy are often mimicking the chemicals that our brains produce themselves.

As Prof Wager puts it, "The placebo effect taps into our natural pharmacy. "Drugs work because we have receptors for the drugs, and that means that there's some endogenous chemicals that our brains are producing that act on those receptors - the receptors evolved to respond to those natural chemicals."

Research into the power of the placebo is still in its infancy.

'Quantifiable'

There is still an enormous amount that we don't know: what exactly are the mechanisms by which it works? Why do placebos work on some people and not others? But research in the field of placebo studies has boomed over the last decade, and the evidence is growing that a placebo effect can be a powerful thing. Prof Stoessl says: "The placebo effect is real, quantifiable and in fact you're doing quite well with an active therapy if you can get as good a response as the placebo response." And the more we understand it, the better our chances of harnessing the placebo effect, and making the most of the medicine in our minds.

Horizon's The Power of the Placebo will be on BBC2 on Monday 17 February at 2100GMT.

http://www.eurekalert.org/pub_releases/2014-02/uom-hes021314.php

How evolution shapes the geometries of life

University of Maryland physicist and colleagues solve a longstanding biological puzzle

Why does a mouse's heart beat about the same number of times in its lifetime as an elephant's, although the mouse lives about a year, while an elephant sees 70 winters come and go? Why do small plants and animals mature faster than large ones? Why has nature chosen such radically different forms as the loose-limbed beauty of a flowering tree and the fearful symmetry of a tiger?

These questions have puzzled life scientists since ancient times. Now an interdisciplinary team of researchers from the University of Maryland and the University of Padua in Italy propose a thought-provoking answer based on a famous mathematical formula that has been accepted as true for generations, but never fully understood. In a paper published the week of Feb. 17, 2014 in the Proceedings of the National Academy of Sciences, the team offers a re-thinking of the formula known as Kleiber's Law. Seeing this formula as a mathematical expression of an evolutionary fact, the team suggests that plants' and animals' widely different forms evolved in parallel, as ideal ways to solve the problem of how to use energy efficiently.

If you studied biology in high school or college, odds are you memorized Kleiber's Law: metabolism equals mass to the three-quarter power. This formula, one of the few widely held tenets in biology, shows that as living things get larger, their metabolisms and their life spans increase at predictable rates. Named after the Swiss biologist Max Kleiber who formulated it in the 1930s, the law fits observations on everything from animals' energy intake to the number of young they bear. It's used to calculate the correct human dosage of a medicine tested on mice, among many other things.

But why does Kleiber's Law hold true? Generations of scientists have hunted unsuccessfully for a simple, convincing explanation. In this new paper, the researchers propose that the shapes of both plants and animals evolved in response to the same mathematical and physical principles. By working through the logic underlying Kleiber's mathematical formula, and applying it separately to the geometry of plants and animals, the team was able to explain decades worth of real-world observations.

"Plant and animal geometries have evolved more or less in parallel," said UMD botanist Todd Cooke. "The earliest plants and animals had simple and quite different bodies, but natural selection has acted on the two groups so the geometries of modern trees and animals are, remarkably, displaying equivalent energy efficiencies. They are both equally fit. And that is what Kleiber's Law is showing us."

Picture two organisms: a tree and a tiger. In evolutionary terms, the tree has the easier task: convert sunlight to energy and move it within a body that more or less stays put. To make that task as efficient as possible, the tree has evolved a branching shape with many surfaces – its leaves.

"The tree's surface area and the volume of space it occupies are nearly the same," said physicist Jayanth Banavarr, dean of the UMD College of Computer, Mathematical, and Natural Sciences. "The tree's nutrients flow at a constant speed, regardless of its size."

With these variables, the team calculated the relationship between the mass of different tree species and their metabolisms, and found that the relationship conformed to Kleiber's Law.

To nourish its mass, an animal needs fuel. Burning that fuel generates heat. The animal has to find a way to get rid of excess body heat. The obvious way is surface cooling. But because the tiger's surface area is proportionally smaller than its mass, the surface is not up to the task. The creature's hide would get blazing hot, and its coat might burst into flames.

So as animals get larger in size, their metabolism must increase at a slower rate than their volume, or they would not be able to get rid of the excess heat. If the surface area were the only thing that mattered, an animal's metabolism would increase as its size increased, at the rate of its mass to the two-thirds power. But Kleiber's Law, backed by many sets of observations, says the actual rate is mass to the three-quarters power.

Clearly there's a missing factor, and scientists have pored over the data in an attempt to find out what it is.

Some have proposed that the missing part of the equation has to do with the space occupied by internal organs. Others have focused on the fractal, or branching, form that is common to tree limbs and animals' blood vessels, but added in new assumptions about the volume of fluids contained in those fractal networks.

The UMD and University of Padua researchers argue a crucial variable has been overlooked: the speed at which nutrients are carried throughout the animals' bodies and heat is carried away. So the team members calculated the rate at which animals' hearts pump blood and found that the velocity of blood flow was equal to the animals' mass to the one-twelfth power.

"The information was there all along, but its significance had been overlooked," said hydrologist Andrea Rinaldo of Italy's University of Padua and Switzerland's Ecole Polytechnique Federale. "Animals need to adjust the flow of nutrients and heat as their mass changes to maintain the greatest possible energy efficiency. That is why animals need a pump – a heart – and trees do not." Plugging that information into their equation, the researchers found they had attained a complete explanation for Kleiber's Law.

"An elegant answer sometimes is the right one, and there's an elegance to this in the sense that it uses very simple geometric arguments," said physicist Amos Maritan of the University of Padua. "It doesn't call for any specialized structures. It has very few preconditions. You have these two lineages, plants and animals, that are very different and they arrive at the same conclusion. That is what's called convergent evolution, and the stunning result is that it's being driven by the underlying physics and the underlying math."

http://www.eurekalert.org/pub_releases/2014-02/uosd-too021414.php

Theory on origin of animals challenged: Animals needs only extremely little oxygen

Studies of a small sea sponge shows that complex life does not need high levels of oxygen

One of science's strongest dogmas is that complex life on Earth could only evolve when oxygen levels in the atmosphere rose to close to modern levels. But now studies of a small sea sponge fished out of a Danish fjord shows that complex life does not need high levels of oxygen in order to live and grow.

The origin of complex life is one of science's greatest mysteries. How could the first small primitive cells evolve into the diversity of advanced life forms that exists on Earth today? The explanation in all textbooks is: Oxygen. Complex life evolved because the atmospheric levels of oxygen began to rise app. 630 – 635 million years ago. However new studies of a common sea sponge from Kerteminde Fjord in Denmark shows that this explanation needs to be reconsidered. The sponge studies show that animals can live and grow even with very limited oxygen supplies. In fact animals can live and grow when the atmosphere contains only 0.5 per cent of the oxygen levels in today's atmosphere.

"Our studies suggest that the origin of animals was not prevented by low oxygen levels", says Daniel Mills, PhD at the Nordic Center for Earth Evolution at the University of Southern Denmark.

Together with Lewis M. Ward from the California Institute of Technology he is the lead author of a research paper about the work in the journal PNAS.

A little over half a billion years ago, the first forms of complex life - animals - evolved on Earth. Billions of years before that life had only consisted of simple single-celled life forms. The emergence of animals coincided with a significant rise in atmospheric oxygen, and therefore it seemed obvious to link the two events and conclude that the increased oxygen levels had led to the evolution of animals.

"But nobody has ever tested how much oxygen animals need – at least not to my knowledge. Therefore we decided to find out", says Daniel Mills.

The living animals that most closely resemble the first animals on Earth are sea sponges. The species *Halichondria panicea* lives only a few meters from the University of Southern Denmark's Marine Biological Research Centre in Kerteminde, and it was here that Daniel Mills fished out individuals for his research.

"When we placed the sponges in our lab, they continued to breathe and grow even when the oxygen levels reached 0.5 per cent of present day atmospheric levels", says Daniel Mills.

This is lower than the oxygen levels we thought were necessary for animal life.

The big question now is: If low oxygen levels did not prevent animals from evolving – then what did? Why did life consist of only primitive single-celled bacteria and amoebae for billions of years before everything suddenly exploded and complex life arose?

"There must have been other ecological and evolutionary mechanisms at play. Maybe life remained microbial for so long because it took a while to develop the biological machinery required to construct an animal. Perhaps the ancient Earth lacked animals because complex, many-celled bodies are simply hard to evolve", says Daniel Mills.

His colleagues from the Nordic Center for Earth Evolution have previously shown that oxygen levels have actually risen dramatically at least one time before complex life evolved. Although plenty of oxygen thus became available it did not lead to the development of complex life. Read more about this work here:

http://sdu.dk/en/Om_SDU/Fakulteterne/Naturvidenskab/Nyheder_2013/2013_10_16_oxygenfossil.

The link for the news story will be available when the embargo lifts and it will be this:

http://www.sdu.dk/en/Om_SDU/Fakulteterne/Naturvidenskab/Nyheder/2014_02_17_sponge_oxygen

TV clip is available here: <http://youtu.be/tPBvsA3J0C>

<https://filesender.deic.dk/filesender/?vid=33c8961e-2613-68c9-fac6-00004c330e50>

Ref article: *PNAS: The oxygen requirements of the earliest animals.* Daniel B. Mills, Lewis M. Ward, CarriAyne Jones, Brittany Sweeten, Michael Forth, Alexander H. Treusch and Donald E. Canfield. February 17, 2014.

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

'Prostate cancer test has been misused for money'

Pathologist Richard Ablin discovered the PSA antigen 40 years ago. He says it should never have been used as a cancer screening tool for all men

17 February 2014 by Tiffany O'Callaghan

Your book condemns the use of PSA for cancer screening. What do you hope to accomplish?

I hope to expose how the urology community and drug industry misused the PSA test, putting money over the best interests of patients. I also want to show how the US Food and Drug Administration failed in its duty to the public: its advisers warned that routine PSA screening would cause a public health disaster, but it was approved under pressure from advocacy groups and drug companies.

How did you discover PSA back in 1970?

In animals, freezing prostate tissue in situ produced an immune response – antibodies to proteins in the tissue. We did a trial of the freezing technique in men with prostate cancer that had spread, and saw regression. I wondered if freezing spurred an immune response by releasing a cancer-specific antigen, or protein, from the prostate tissue. So I studied prostate tissue and I found an antigen, but it was characteristic of normal and malignant tissue – specific to the prostate, not to the cancer.

That is one of four major concerns you highlight about PSA. What are the others?

So, first is that PSA is not cancer-specific. Second, the level of PSA deemed worrying is arbitrary – 4 nanograms per millilitre or higher. As PSA is not cancer-specific, no level is diagnostic. Third, prostate cancer can be aggressive or, more often, very slow-growing. We can't tell which is which.

Last, many men will develop prostate cancer by age 70. If an older man has a PSA level that prompts a biopsy, it is likely you will find cancer. Since you can't tell if it's aggressive, many men get treated unnecessarily – and risk life-altering side effects including impotence and incontinence.

But surely PSA has its diagnostic uses?

PSA can be a useful predictor of recurrence; after treatment for prostate cancer, if the PSA level increases it can indicate they didn't get all the tissue, or that cancer that began in the prostate has spread. But that is not how it is primarily used.

You note that men with a family history of the disease may benefit from PSA tests to watch for major changes. As your father died of prostate cancer, does that include you?

If your father had prostate cancer, your chances are 2:1, so theoretically you may benefit from PSA monitoring. But the decision depends on how well you deal with risk. My father was diagnosed at 67. He died a year later. I am 73. If I had a biopsy today, there's an 80 per cent chance that I would have prostate cancer. But the data show that at my age treatment wouldn't extend my life, and it would be likely to leave me with debilitating side effects.

What do you advise men grappling with this?

Ideally, it should be an informed decision between a man and his doctor. The unfortunate reality is that no current data show that men who undergo PSA screening live longer than men who decide against it. So if you have no symptoms, no family history of prostate cancer, and a normal digital rectal exam, I would say, do nothing. Because once you're on that train, it's hard to get off.

Profile

Richard Ablin is professor of pathology at the University of Arizona. He discovered PSA in 1970, and co-wrote *The Great Prostate Hoax: How big medicine hijacked the PSA test and caused a public health disaster* (Palgrave Macmillan)

<http://phys.org/news/2014-02-japan-relationship-based-police-style-results.html>

Research in Japan suggests that a 'relationship-based' police interviewing style gets the best results

Research in Japan suggests that a 'relationship-based' police interviewing style gets the best results

Award-winning research into police interviewing techniques in Japan reveals that a 'relationship-based' style may be particularly effective in eliciting true confessions. The research included the first ever study of Japanese offenders' views about police interrogation.

In 1995 members of a religious cult called Aum Shinirikyo carried out a Sarin gas attack on the Tokyo subway that killed two station staff and injured several hundred people. One of those questioned by the police as a member of the cult was Dr Hayashi Ikuo. During interviews, Ikuo made a voluntary decision to confess his involvement in the attack. He was later sentenced to indefinite imprisonment.

In an autobiography written in prison, Ikuo described his feelings about his interrogation by police before standing trial: "At that time, I felt reassured by the fact that I had someone who would understand my true intentions without prejudice. I thought I could trust Mr I and Mr F [police interrogators]. I made up my mind to tell them everything I knew."

Prize-winning research undertaken in Japan by Dr Taeko Wachi, while a PhD candidate in the Department of Psychology at the University of Cambridge, suggests that a 'relationship-based' interviewing style in which interrogators listen closely and attempt to form good relationships with suspects is more likely to elicit true confessions than other styles.

Dr Wachi's research comprised three studies of attitudes to, and experiences of, police interviewing in Japan. The first study explored information on interrogation techniques gathered from almost 280 police officers. The analysis of questionnaires led to the identification of four interview styles: evidence-focused, confrontational, undifferentiated and relationship-focused.

The second study was a 'crime experiment' in which more than 230 members of the public took part. It was designed to reveal which of the interviewing techniques identified in the first study were most likely to elicit true confessions and prevent false confessions. Overall, 74 out of 114 'guilty' participants confessed to their notional 'crime' but none of the 'innocent' participants made false confessions. Relationship-focused interviewing was most likely to elicit a confession.

The third study examined questionnaires from more than 290 offenders in 36 prisons. All of them had been convicted of serious crimes including murder, rape and kidnapping. This third study – which was administered by means of a questionnaire – was the first of its kind in Japan and thus broke new ground in terms of identifying which interviewing styles led offenders to confess.

Again, relationship-focused interviewing was particularly effective in eliciting confessions from suspects who had not decided, before interrogation, whether or not to confess their crimes or had decided to deny the allegations against them.

The research suggested that the relationship-based interviewing style has a positive effect on both police officers' and suspects' feelings after interrogation. Those offenders who confessed to crimes during a relationship-based interview did so as the result of internal pressures, such as "I confessed because I felt guilty about the crime", rather than external pressures, such as "I confessed because of police pressure during the interview".

In view of the lack of in-depth research into investigative interviewing techniques in Japan, Dr Wachi's work makes a significant contribution to understanding the wide number of factors that affect this complex process. It should be noted, however, that most participants in the study were male.

As Dr Wachi points out, there are significant differences, as well as similarities, between the structure of criminal processes in Japan and those in Western Europe and the USA. In Japan the law allows for suspects to be held for 23 days before initiating prosecution: this maximum detention period contrasts with 24 hours (generally) in the UK, 48 hours in Hong Kong and just four hours in Australia.

It has thus been argued that interrogations play a much more important role in Japanese criminal investigations than in other countries. In recent years, several high-profile false confessions have drawn attention to the possible impact of interviewing techniques on suspects' feelings and decisions about confessions and denials. Training of police officers in interviewing is being stepped up.

Interestingly, the Japanese public (in addition to crime victims and their families) exhibits a strong desire for offenders to talk about their criminal motives and explain their criminal acts. Interrogation meets this public interest by helping offenders to give accounts of their cases in detail.

Last month it was announced that Dr Wachi had won first place in the 2013 American Psychology-Law Society Dissertation Awards. As part of her prize she is invited to attend, and present a poster at, the AP-LS Conference in New Orleans, Louisiana in March, 2014. The AP-LS committee reviewers described her dissertation as "highly original... because of the breadth of interrogation factors it addresses".

An impressive aspect of the research was Dr Wachi's design and implementation of a crime experiment which was tested on a range of people recruited from the general public, widely varying in age and from a diversity of backgrounds. In contrast, previous crime experiments have used university students who tend to be from a narrow age range and educational level.

At Cambridge, Dr Wachi's research was supervised by Professor Michael Lamb of the Department of Psychology. He said: "I was delighted to hear that Taeko had won this award. Her persuasive study was comprehensive and very significant, especially because we are increasingly aware of the risks that false confessions may lead to the conviction and incarceration of innocent people. Taeko's findings add to the growing body of evidence that more humane rather than coercive interviewing practices are likely to elicit confessions from guilty individuals, a pattern evident in Western countries, too."

Dr Wachi has been working for the National Research Institute of Police Science (attached to the National Police Agency, Japan) since 2005. She was able to study for a PhD at Cambridge thanks to a scholarship from the Japanese Government Long-Term Overseas Fellowship Program.

Her background gave her the advantage of an in-depth understanding of, and close working relationship with, the National Police Agency, Supreme Public Prosecutors' Office and Ministry of Justice, which enabled her to conduct the studies of police officers and prisoners.

Dr Wachi is currently conducting research into interrogations of those with learning disabilities as well as on public opinions about interviewing techniques. She intends to continue her research into criminal investigation on behalf of the National Police Agency by providing scientific findings about interrogations of various types of suspects.

<http://bit.ly/1c4uUuR>

Spit test could allow depression screening at school

A few globs of spit and a questionnaire could be all that's needed to identify some teenagers who have a high risk of developing depression.

20:00 17 February 2014 by Catherine de Lange

That is the upshot of a study finding that teenage boys with elevated levels of the stress hormone cortisol, as well as depressive symptoms, can be 14 times more likely to become depressed later on.

It's the first biological flag to accurately predict the risk of an individual going on to develop depression, says Barbara Sahakian at the University of Cambridge, one of the study's authors.

The finding could lead to new pharmacological treatments for depression and could change the way schools deal with the condition. Teenagers could be screened for the biomarker and those at risk provided with targeted treatments.

Early predictor

Around the world, depression is one of the leading causes of disability. It takes hold early in life: half of all cases begin by age 14, three-quarters by 24.

"Given that we know more teenagers are getting depressed, we should be looking actively for people who are developing problems and treating them early and effectively," Sahakian says.

Her team measured morning levels of cortisol over three days in 660 teenagers aged between 13 and 18.

Elevated levels of this hormone have previously been implicated in depression. The team also recorded any pre-clinical depressive symptoms the teens reported over a year, such as tearfulness or lack of motivation. The study was later repeated in a group of about 1200 teens.

Teenage boys who reported high levels of depressive symptoms, and had high levels of cortisol, were more likely to have become clinically depressed over the next three years than any other combination. Those in this high risk group were 14 times more likely to go on to develop depression than the lowest-risk group, those who had neither high levels of cortisol nor depressive symptoms. Seventeen per cent of teens fell into this group but cortisol levels were not more useful than depression symptoms alone in pinpointing at-risk girls.

School intervention

Sahakian says screening pupils would be easy to do and beneficial, even if there were social stigma associated with identifying people who had a high risk of developing depression. "It's better than leaving them alone in

their bedrooms to get worse and worse," she says. Screening could be carried out using saliva samples collected over a few days and students could fill out the questionnaire by themselves.

A study in the BMJ in 2012 found that having a professional therapist teach cognitive behavioural therapy (CBT) techniques to an entire class was no more effective than having the teacher give their usual personal social and health education classes, in terms of the effect on pupils' well-being. But the hope is that screening would allow for targeted treatment. Talking therapies such as CBT may also not be the best thing for boys, says Sahakian, because boys tend to respond better to visual techniques.

Screening could be a better way to allocate limited resources, says Carmine Pariante of the Institute of Psychiatry at King's College London. Teenage years are a time of emotional turmoil, when pre-clinical symptoms of depression are likely to be common. "If you help all of the [people you see like this] you end up giving treatment and emotional support to those who might be alright," he says.

And what of those not identified by the questionnaire and cortisol biomarker combination? Depression is more common among teenage girls than boys, yet they are not picked out by this test – possibly because they naturally have higher levels of cortisol than boys. "We need to do more research and find an equivalent for the girls," Pariante says.

Sahakian agrees that other subtypes of depression are likely to be identified with different biomarkers. At one time it was thought cancer was all one disease, she says, but understanding the different types led to better treatments. *Journal reference: PNAS, DOI: 10.1073/pnas.1318786111*

<http://www.medscape.com/viewarticle/820699?src=rss>

Intracranial Atherosclerosis a Major Stroke Risk in Whites

Although intracranial carotid artery calcification (ICAC) is a recognized risk factor for stroke in African Americans and Asians, a new study shows that it is also an important cause of strokes among whites.

The association between ICAC and stroke shown in the study was independent of conventional cardiovascular risk factors and of calcification in other vessel beds, the researchers note.

"The results highlight the importance of physicians being aware that even their white patients can have intracranial calcification," study author Arfan Ikram, MD, PhD, Departments of Epidemiology, Radiology, and Neurology, Erasmus Medical Center, Rotterdam, the Netherlands, told Medscape Medical News.

"And if doctors are screening for any patient's cardiovascular risks, they should consider intracranial calcification," he added. "The study also underlines the importance of carrying out more research into treating ICAC or preventing it in the first place." The study was published online February 17 in JAMA Neurology.

Rotterdam Study

The analysis included 2323 exclusively white participants in the Rotterdam Study, a prospective, population-based study investigating determinants of chronic diseases in the elderly. The mean age of study participants was 69.5 years, and 52.2 % were women.



Red circles indicate ICAC on CT scan.

During examinations at baseline, researchers verified through medical records that study participants did not have a history of stroke. Linkage of the study database with general practice files allowed for continuous monitoring of participants for incident strokes. These were verified by an experienced stroke neurologist and were categorized as ischemic or hemorrhagic. Also through interviews, as well as physical examinations and blood samples, investigators collected information on cardiovascular risk factors, including obesity, diabetes, hypertension, hypercholesterolemia, and smoking.

Using nonenhanced computerized tomography (CT), researchers scanned the coronary arteries, aortic arch, extra-cranial carotid arteries, and intracranial carotid arteries. To measure atherosclerosis, they calculated calcification volume (expressed in number of cubic millimeters).

The researchers did not collect data on the size, location, or vascular territory of brain infarcts.

Although CT is an ideal tool to visualize calcification, which is a key property of atherosclerosis, and to calculate volume, this technology is limited in that it does not show the entire atherosclerotic process or atherosclerotic plaque. "This means that the true volume of atherosclerosis would likely be higher than the numbers we got," said Dr. Ikram.

And for intracranial arteries, the scans can only be useful when taken at the point where the artery enters the skull. "Ideally, you would visualize the artery further inside the skull, closer to the brain, where the artery is even smaller, but this can't be visualized on nonenhanced CT, as it becomes difficult to distinguish calcification," said Dr. Ikram. He added that his "gut feeling" is that more calcification would have been picked up in areas closer to the brain, which would make ICAC an even more important stroke risk factor.

Stroke Risk

During a mean follow up of 6.1 years, 91 patients suffered a stroke (71 ischemic, 10 hemorrhagic, and 7 unspecified). The researchers found that larger ICAC volumes were associated with a higher risk for all strokes and for ischemic stroke. Adjustment for cardiovascular risk factors did not change these results.

After additional adjustment for ultrasound carotid plaque score and calcification volumes in other vessel beds, the association remained significant for all strokes (hazard ratio per increase of 1 standard deviation in ICAC volume: 1.43; 95% confidence interval [CI], 1.04 - 1.96), and for ischemic stroke (HR, 1.39; 95% CI, 0.98 - 1.99).

There was no association between coronary artery calcification and stroke, after adjusting for ICAC. This, said Dr. Ikram, indicates that although coronary calcification may be a major risk factor for myocardial infarction, it is atherosclerosis of arteries in the brain that poses the main risk for stroke.

The results show that ICAC played a role in up to 75% of strokes. Dr. Ikram stressed that almost all strokes have more than 1 cause. "That 75% is the upper limit of the number of cases in which ICAC could have played a role; it doesn't mean it was the only cause," he said.

Other research shows that ICAC is involved in up to 50% of strokes in populations of African and Asian descent. But this does not necessarily mean that ICAC is less of a stroke risk factor in these populations, because different methodologies and definitions could have been used, the researchers note.

For aortic arch calcification and calcification in the extracranial carotid artery, ICAC played a role in up to 45% and 25% of all strokes, respectively.

The study measured calcification but not stenosis. Dr. Ikram stressed that he and his colleagues did not use atherosclerosis threshold levels because they were looking at contributing factors, not just a main cause.

"In other studies, researchers assign a stroke to the ICAC category only if the calcification exceeds a certain threshold," explained Dr. Ikram. "It's possible that ICAC in the artery that we studied was contributing to the stroke even though it didn't yet exceed a threshold."

The study could not determine whether the stroke risk centered on the atherosclerosis in a particular location or whether the calcification measurement taken in that location was indicative of the total atherosclerotic burden of the brain. Also, it is possible that it was not only the calcification that caused the stroke but also the combination of calcification and thromboembolism.

To illustrate this, Dr. Ikram used the example of a patient whose carotid artery is narrowed, but not enough to cause a stroke. That patient develops atrial fibrillation that leads to an embolus.

"That embolus gets stuck in that narrowed artery, and at that moment the patient suffers a stroke. The question is, is this stroke due to the embolus from the heart or is it due to narrowing of the arteries? Had that artery not been narrowed, the embolus would not have gotten stuck or would have dissolved or just passed through."

Atherosclerosis, of course, occurs in coronary as well as carotid and other arteries, with hypertension, diabetes, and high cholesterol among the risk factors for all atherosclerosis. It is not known whether some risk factors cause atherosclerosis only in carotid arteries, said Dr. Ikram.

Approaches to prevent ICAC are the same as those to reduce overall cardiovascular burden — management of diabetes, control of hypertension, smoking cessation, and lowering of cholesterol levels, he said.

Trials investigating aggressive therapy with antithrombotics and surgery "have not shown a clear-cut pattern of what the best treatment is," said Dr. Ikram. Angioplasty in the large carotid artery has been shown to be effective, but it has been difficult to stent the smaller arteries, he said.

Reawakens Interest

This new study "raises important questions" about the role of calcification in the pathophysiology of intracranial atherosclerosis and should "reawaken interest" in intracranial atherosclerosis as a cause of stroke in white individuals, according to an accompanying editorial by Marc I. Chimowitz, MBChB, Medical University of South Carolina, Charleston, and Louis R. Caplan, MD, Beth Israel Deaconess Medical Center, Boston. Dr. Chimowitz and Dr. Caplan noted, however, that the study does not establish a pathophysiologic, causal relationship between intracranial carotid calcification and stroke.

"Establishing this will require further prospective studies that correlate the association between intracranial arterial calcification and stenosis more clearly, identify atherosclerotic plaque features associated with calcification that may be associated with a high risk for distal embolism, and classify ischemic strokes that occur in patients with intracranial carotid calcification according to size, location (cortical or subcortical), vascular territory, and the coexistence of other potential causes," they conclude.

The Rotterdam Study is supported by the Erasmus Medical Center and Erasmus University, Rotterdam, the Netherlands; the Organization for Scientific Research; the Netherlands Organization for Health Research and Development; the Research Institute for Diseases in the Elderly; the Netherlands Genomics Initiative; the Ministry of Education, Culture, and Science; the

Ministry of Health, Welfare, and Sports; the European Commission (DG XII); the Municipality of Rotterdam, as well as grants to individual investigators from the Alzheimer's Association, the International Alzheimer Research Foundation, and Erasmus Medical Center. No relevant financial relationships have been disclosed.
JAMA Neurol. Published online February 17, 2014. [Abstract](#), [Editorial](#)

<http://nyti.ms/1fBYdG3>

From India, Proof That a Trip to Mars Doesn't Have to Break the Bank

While India's recent launch of a spacecraft to Mars was a remarkable feat in its own right, it is the \$75 million mission's thrifty approach to time, money and materials that is getting attention.

By SARITHA RAIFEB. 17, 2014

BANGALORE, India - Just days after the launch of India's Mangalyaan satellite, NASA sent off its own Mars mission, five years in the making, named Maven. Its cost: \$671 million. The budget of India's Mars mission, by contrast, was just three-quarters of the \$100 million that Hollywood spent on last year's space-based hit, "Gravity." "The mission is a triumph of low-cost Indian engineering," said Roddam Narasimha, an aerospace scientist and a professor at Bangalore's Jawaharlal Nehru Center for Advanced Scientific Research.

"By excelling in getting so much out of so little, we are establishing ourselves as the most cost-effective center globewide for a variety of advanced technologies," said Mr. Narasimha.

India's 3,000-pound Mars satellite carries five instruments that will measure methane gas, a marker of life on the planet. Maven (for Mars Atmosphere and Volatile Evolution), weighs nearly twice as much but carries eight heavy-duty instruments that will investigate what went wrong in the Martian climate, which could have once supported life.

"Ours is a contrasting, inexpensive and innovative approach to the very complex mission," said K. Radhakrishnan, the chairman of the Indian Space Research Organization, or ISRO, in an interview at the space agency's heavily guarded Bangalore headquarters. "Yet it is a technically well-conceived and designed mission," he said. Wealthier countries may have little incentive to pursue technological advances on the cheap, but not a populous, resource-starved country. So jugaad, or building things creatively and inexpensively, has become a national strength. India built the world's cheapest car (\$2,500), the world's cheapest tablet (\$49), and even quirkier creations like flour mills powered by scooters.

"If necessity is the mother of invention, constraint is the mother of frugal innovation," said Terri Bresenham, the chief executive of GE Healthcare, South Asia, who is based in Bangalore. GE Healthcare has the largest research and development operations in India and has produced low-cost innovations in infant health, cancer detection and heart disease treatment. In India, even a priority sector like space research gets a meager 0.34 percent of the country's total annual outlay. Its \$1 billion space budget is only 5.5 percent of NASA's budget. ISRO has learned to make cost-effectiveness a daily mantra. Its inexpensive but reliable launch capabilities have become popular for the launches of small French, German and British satellites. Although the space agency had to build ground systems from scratch, its Chandrayaan moon mission in 2008 cost one-tenth what other nations' moon shots cost, said Myswamy Annadurai, mission director.

The most obvious way ISRO does it is low-cost engineering talent, the same reason so many software firms use Indian engineers. India's abundant supply of young technical talent helped rein in personnel costs to less than 15 percent of the budget. "Rocket scientists in India cost very little," said Ajey Lele, a researcher at a New Delhi think tank, the Institute for Defense Studies and Analyses, and author of "Mission Mars: India's Quest for the Red Planet."

The average age of India's 2,500-person Mars team is 27. "At 50, I am the oldest member of my team; the next oldest is 32," said Subbiah Arunan, the project's director. Entry-level Indian space engineers make about \$1,000 a month, less than a third of what their Western counterparts make.

The Indians also had a short development schedule that contributed heavily to the mission's low cost, said Andrew Coates, planetary scientist at University College London and a leader of the European ExoMars expedition planned for 2018. The engineers had to compress their efforts into 18 months (other countries' space vehicles have taken six years or more to build). It was either launch by November 2013 or wait another 26 months when the geometry of the sun, Mars and Earth would again be perfect for a launch.

"Since the time was so short, for the first time in the history of such a project, we scheduled tasks by the hour — not days, not weeks," said Mr. Arunan. Mr. Radhakrishnan added: "Could we pull it off in less than two years' time? Frankly, I doubted it."

The modest budget did not allow for multiple iterations. So, instead of building many models (a qualification model, a flight model and a flight spare), as is the norm for American and European agencies, scientists built the final flight model right from the start. Expensive ground tests were also limited. "India's 'late beginner' advantage was that it could learn from earlier mission failures," said Mr. Lele.

"It is a question of philosophy, and each country has its own," explained Mr. Radhakrishnan. "The Russians, for example, believe in putting large amounts of time and resources into testing so that the systems are robust." His agency curbed costs by another technique familiar to businesses in India: transforming old technology into new. The launch vehicle was first developed in the late 1970s and was augmented several times to become the solid propulsion system currently used in its latest Geosynchronous Satellite Launch Vehicle launcher.

The G.S.L.V.'s engine also dates back to the early 1970s, when ISRO engineers used technology transferred from France's Ariane program. The same approach, which the Indian scientists call modularity, extended to building spacecraft and communication systems. "We sometimes have to trade off an ideal configuration for cost-effectiveness, but the heritage is being improved constantly," said Mr. Radhakrishnan.

Cost savings also came from using similar systems across a dozen concurrent projects. Many related technologies could be used in the Mars project; Astrosat, an astronomy mission to be launched in late 2014; the second moon mission, which is two years away; and even Aditya, a solar mission four years out.

Systems like the attitude control, which maintains the orientation of the spacecraft; the gyro, a sensor that measures the satellite's deviation from its set path; or the star tracker, a sensor that orients the satellite to distant objects in the celestial sphere, are the same across several ISRO missions.

"The building blocks are kept the same so we don't have to tailor-make for each mission," said Mr. Annadurai of the moon mission. "Also, we have a ready backup if a system fails."

Teams also did the kind of thing engineers working on missions do around the world. They worked through weekends with no overtime pay, putting in more hours to the dollar. Mr. Arunan slept on the couch in his office through the 18 months, rereading his favorite P. G. Wodehouse novels to relieve stress. "This is the Indian way of working," said Mr. Annadurai.

Despite its cost-effectiveness, many have argued that India's extraterrestrial excursions are profligate in a country starved of even basic necessities like clean drinking water and toilets. Millions sleep hungry at night, critics have emphasized. They condemn the Mars mission as nothing more than showing off.

But scientists have argued that early Indian satellites paved the way for today's advanced disaster management systems and modern telecom infrastructure. In the 1970s, cyclones killed tens of thousands of people. Last year, when Cyclone Phailin struck India's east coast, the casualties were in the single digits. In the 1980s, television broadcasts were available in only four Indian cities, but today they are found countrywide.

The Mars mission is also having a multiplier effect on Indian industry. Companies like Larsen & Toubro and Godrej & Boyce, which built vital parts for the satellite, will use this high-tech expertise to compete for global aerospace, military and nuclear contracts worth billions of dollars. Godrej, for example, has begun making engine parts for Boeing.

Scientists have also said that space exploration and the alleviation of poverty need not be mutually exclusive. "If the Mars mission's \$75 million was distributed equally to every Indian, they would be able to buy a cup of roadside chai once every three years," said Mr. Narasimha, the aerospace scientist, referring to the tea that many Indians drink. "My guess is that even the poorest Indians will happily forgo their chai to be able to see their country send a rocket all the way to Mars."

<http://phys.org/news/2014-02-scientists-exact-source-stonehenge.html>

Scientists pinpoint the exact source of many of the rocks used to build Stonehenge

Scientists pinpoint the exact source of many of the rocks used to build Stonehenge

A new study, published in the Journal of Archaeological Science, suggests that the site researchers had previously thought was the starting place of many of Stonehenge's rocks may not have been the source after all. Instead, it looks like the rocks actually come from a different site three kilometres away.

The findings, bring into question the long-standing theory that people transported the rocks from Wales to Wiltshire in order to build the monument.

The research focused on the smaller stones at Stonehenge, called bluestones. The chemistry of these rocks varies, but they all originate from the Preseli Hills in Wales and are thought to have been transported to the Stonehenge site over 4000 years ago.

By confirming the source of the rocks, the researchers hope to help answer the long standing question of how around 80 of these bluestones, weighing up to three tonnes each, were transported 250 kilometres from southwest Wales to Wiltshire.

'The Holy Grail question is how were the stones moved and why,' explains Dr Richard Bevins of National Museum of Wales who led the research. 'Many people think humans transported the stones south, down from the Preseli Hills and then up the Bristol Channel on rafts. But a second school of thought says these rocks are glacial erratics that were transported by ice to Salisbury Plain and so were available in the local environment.'

'We're trying to discover the source of the stones so archaeologists can excavate sites in order to see if they can find evidence for people working the source stones,' he continues.

Scientists have known the bluestones originated from the Preseli Hills since 1923, when H. H. Thomas from NERC's British Geological Survey recognised the distinctive dark grey spotty rocks, known as spotted dolerites, during fieldwork. Further work in the early 1990s then tried to tie down the specific locations of the rocks' origin by matching the chemistry of the Stonehenge bluestones with those at the proposed origin site.

'The earlier research looked at the source of one of the spotted dolerites and tied it down to a specific outcrop, Carn Meini. It seems Thomas wanted all of the bluestones to also come from that same small area so he argued the rhyolites came from a nearby outcrop, Carn Alw. When we looked at it again we realised the descriptions of the rhyolites from Carn Alw and those at Stonehenge didn't look the same at all,' says Bevins.

The team took images showing the rocks at Stonehenge and the rocks at Carn Alw. They then asked members of the public with no geological background whether they looked the same.

'We asked people "does A look like B?" and everyone said no,' Bevins continues. 'This is astonishing because this has not been questioned since the original publication by Thomas in 1923.'

The team used a new method of identifying the chemical makeup of the rocks, to match the rocks with their origin. They believe that they have now identified Carn Goedog as the source of at least 55 per cent of the spotted dolerite bluestones at Stonehenge.

'If Carn Goedog is the true origin of the dolerites, and Craig Rhos-y-felin is a source of the rhyolitic bluestones then it does bring into question the stones being transported by rafts down to the Bristol Channel, because both of these outcrops lie on the northern side of the Preseli Hills. The rocks would have had to be dragged up the hills, across the summits and back down again before they even reached the waterways. It's just not likely,' Bevins concludes.

<http://www.wired.com/wiredscience/2014/02/reassuring-trunk-evidence-consolation-elephants/>

A Reassuring Trunk: Evidence of Consolation in Elephants

Asian elephants console others who are in distress with vocalizations and gentle touches, according to a new report published in the journal PeerJ.

By Mary Bates

Anecdotal reports of elephants behaving reassuringly towards each other are common, but this is the first empirical evidence of consolation in elephants.

Joshua Plotnik, a lecturer in conservation biology at Mahidol University in Thailand and CEO of Think Elephants International, and Frans de Waal, of Emory University, observed a group of 26 captive Asian elephants at an elephant park in Thailand. These were mostly unrelated elephants who spent most of their social time together under the guidance of their mahouts, or handlers.

The researchers observed the group for nearly a year, recording what happened when one of the elephants became distressed. This could be triggered by events such as a dog walking past, a snake in the grass, or the presence of another, unfriendly elephant. Elephants signal distress by pointing their ears forward, sticking their tails out erect, and letting out a low-frequency rumble, trumpet, or roar.

Plotnik and de Waal found that nearby elephants used both touching and vocalizations to reassure distressed individuals. The contact was usually initiated by the elephant doing the consoling, not the distressed individual. In the most typical type of physical contact observed by the researchers, the consoling elephant would approach the distressed elephant and put its trunk around or inside its mouth. Reassuring elephants would also vocalize, often making a high-pitched chirping sound.

Elephants also responded to distress signals of other elephants with distress signals of their own, taking on the emotional state of their companion. This is a phenomenon known as "emotional contagion," which is thought to be linked to empathy. If you've ever cried while watching a tear-jerker movie, you've experienced emotional contagion.

Empathic Elephants

Several years ago, while Plotnik was earning his PhD at Emory University, he and de Waal showed that Asian elephants could recognize themselves in a mirror. Often regarded as a test for self-awareness, mirror self-recognition is sometimes considered a potential prerequisite for complex empathy. "In other words, you must be able to see yourself as separate from others in order to show complex empathy towards them," Plotnik says. Demonstrations of true consolation in animals are rare. The behavior has only been documented in the great apes, canines, and some corvids. This might be because complex cognitive abilities are required for consolation, such as the ability to empathically take the perspective of another.

Elephants are known for their complex social behavior and close bonding with family members. In the wild, researchers have observed targeted helping among elephants — directed assistance that takes into account the

specific needs of others. For instance, elephants will help lift an injured or incapacitated family member.

Targeted helping is another rare behavior, and is viewed as a sign of empathic perspective-taking.

In addition to shedding light on the convergent evolution of intelligence in elephants and primates, Plotnik also sees his research as playing a role in elephant conservation. "In Asia, we are faced with large-scale human/elephant conflict issues, and real frustration with the lack of understanding of how and why elephants are attacking people and raiding crops," Plotnik says. "Although we know that loss of natural habitat is a real instigator of these problems, a better understanding of elephant physical and social intelligence could really help us develop comprehensive conservation protocols that take the elephants' perspective into account." Plotnik founded Think Elephants International with the aim of linking the study of elephant behavior with conservation education. The nonprofit works to teach young people in Thailand about elephants and their plight by engaging them directly in scientific research. "If we can change the way in which young people think about these animals, we have a real chance to protect them for the next generation," Plotnik says.

Plotnik, J. M. and de Waal, F. B. M. (2014). Asian elephants (*Elephas maximus*) reassure others in distress. *PeerJ* 2:e278. doi: 10.7717/peerj.278.

http://www.eurekalert.org/pub_releases/2014-02/uom-hdu021714.php

HIV drug used to reverse effects of virus that causes cervical cancer

A commonly-used HIV drug has been shown to kill-off the human papilloma virus that leads to cervical cancer in a world-first clinical trial led by The University of Manchester with Kenyatta National Hospital in Nairobi

A commonly-used HIV drug has been shown to kill-off the human papilloma virus (HPV) that leads to cervical cancer in a world-first clinical trial led by The University of Manchester with Kenyatta National Hospital (KNH) in Nairobi.

Drs Ian and Lynne Hampson, from the University's Institute of Cancer Sciences and Dr Innocent Orora Maranga, Consultant in Obstetrics and Gynaecology at KNH in Nairobi examined Kenyan women diagnosed with HPV positive early stage cervical cancer who were treated with the antiviral HIV drug lopinavir in Kenya. The study looked at 40 women with both high and low-grade pre-cancerous disease of the cervix and the antiviral drug, normally used orally to treat HIV, was self-applied directly to the cervix as a pessary.

The results, due to be presented at two international scientific conferences later this month and next, showed a high proportion of women diagnosed with HPV positive high-grade disease returned to normal following a short course of the new treatment.

The findings build on previous peer-reviewed laboratory based research carried out by Drs Hampson and will be submitted to a journal soon. They have been described by an independent leading specialist in gynaecological cancer as very impressive.

The 40 women, who were all HPV positive with either high-grade, borderline or low grade disease, were treated with one capsule of the antiviral drug twice a day for 2 weeks. Repeat cervical smears showed a marked improvement within one month of the treatment although after three months, there was a definite response. Out of 23 women initially diagnosed with high-grade disease, 19 (82.6%) had returned to normal and two now had low-grade disease giving an overall positive response in 91.2% of those treated. Furthermore the 17 women initially diagnosed with borderline or low-grade disease also showed similar improvement.

Photographic images of the cervix before and after treatment showed clear regression of the cervical lesions and no adverse reactions were reported.

Dr Ian Hampson said: "For an early stage clinical trial the results have exceeded our expectations. We have seen women with high-grade disease revert to a normal healthy cervix within a comparatively short period of time. "We are convinced that further optimisation of the dose and treatment period will improve the efficacy still further. "It is our hope that this treatment has the potential to revolutionise the management of this disease most particularly in developing nations such as Kenya."

Cervical cancer is caused by infection with human papilloma virus (HPV) and is more than five times more prevalent in East Africa than the UK. In many developing countries, HPV-related cervical cancer is still one of the most common women's cancers accounting for approximately 290,000 deaths per year worldwide. The same virus also causes a significant proportion of cancers of the mouth and throat in both men and women and this disease is showing an large increase in developed countries, such as the UK, where it is now more than twice as common as cervical cancer.

Dr Lynne Hampson said: "Current HPV Vaccines are prophylactics aimed at preventing the disease rather than curing or treating symptoms. Other than surgery, as yet there is no effective treatment for either HPV infection or the pre-cancerous lesion it causes which is why these results are so exciting. "Further work is needed but it looks as though this might be a potential treatment to stop early stage cervical cancer caused by HPV."

On a global scale HPV is the most common sexually transmitted disease. Although in the developed world vaccination programmes against HPV are well underway, these are not effective in women already infected with the virus. The current vaccines do not protect against all types of HPV and they are expensive, which can limit their use in countries with low resources.

The researchers believe their findings offer a potential cheap and preferably self-administered treatment that could eliminate early-stage HPV infections before these have developed into cancers would therefore have distinct health advantages. Approximately 300,000 women are dying from cervical cancer per annum which is equivalent to 800 per day, one every two minutes mostly in low resource settings.

The research has been backed by Lord Saatchi, whose wife novelist Josephine Hart died of ovarian cancer and has submitted a Private Member's Medical Innovation Bill to Parliament which he argues would promote "responsible" innovation for medics to try new treatments without the fear of negligence claims. The bill comes amid claims there is currently an estimated average time lag of 17 years for a new treatment or research evidence to reach clinical practice in the UK.

Lord Saatchi said: "What Drs Lynne and Ian Hampson have done is amazing – a classic case of innovation. The fact that they needed to run their trial in Nairobi and that even now there is no guarantee the treatment will be available in the UK any time soon, is a source of immense frustration."

Dr Ian Hampson added: "This is not something we could have done in the UK due to the associated costs and red tape. We have full ethical approval in Kenya and chose to conduct the trial there because of the extreme need for a self-applied treatment for early stage cervical cancer.

"During the trial we provided 820 women with free cervical smear testing in addition to a range of other free medical tests that are not routinely available in Kenya. This was essential in order to identify women with HPV related cervical disease so that we could treat them with lopinavir. It is very significant that during this process we also identified five women who already had invasive cervical cancer and these were immediately referred for surgery."

The research was funded by the UK Philanthropist Mr Ken Chorlton, the Caring Cancer Trust, United in Cancer Charitable Trust, The Humane Research Trust, Quest Cancer, the Cancer Prevention Research Trust and Hologic.

Professor Pierre Martin-Hirsh, Consultant in Gynaecological and Oncologist and Associate Editor in Chief, the British Journal of Obstetrics and Gynaecological, has described the research as very impressive.

http://www.eurekalert.org/pub_releases/2014-02/asu-alj021814.php

Artificial leaf jumps developmental hurdle

In a recent early online edition of Nature Chemistry, ASU scientists, along with colleagues at Argonne National Laboratory, have reported advances toward perfecting a functional artificial leaf.

Designing an artificial leaf that uses solar energy to convert water cheaply and efficiently into hydrogen and oxygen is one of the goals of BISfuel – the Energy Frontier Research Center, funded by the Department of Energy, in the Department of Chemistry and Biochemistry at Arizona State University.

Hydrogen is an important fuel in itself and serves as an indispensable reagent for the production of light hydrocarbon fuels from heavy petroleum feed stocks. Society requires a renewable source of fuel that is widely distributed, abundant, inexpensive and environmentally clean.

Society needs cheap hydrogen.

"Initially, our artificial leaf did not work very well, and our diagnostic studies on why indicated that a step where a fast chemical reaction had to interact with a slow chemical reaction was not efficient," said ASU chemistry professor Thomas Moore. "The fast one is the step where light energy is converted to chemical energy, and the slow one is the step where the chemical energy is used to convert water into its elements viz. hydrogen and oxygen."

The researchers took a closer look at how nature had overcome a related problem in the part of the photosynthetic process where water is oxidized to yield oxygen. "We looked in detail and found that nature had used an intermediate step," said Moore. "This intermediate step involved a relay for electrons in which one half of the relay interacted with the fast step in an optimal way to satisfy it, and the other half of the relay then had time to do the slow step of water oxidation in an efficient way."

They then designed an artificial relay based on the natural one and were rewarded with a major improvement. Seeking to understand what they had achieved, the team then looked in detail at the atomic level to figure out how this might work. They used X-ray crystallography and optical and magnetic resonance spectroscopy techniques to determine the local electromagnetic environment of the electrons and protons participating in the relay, and with the help of theory (proton coupled electron transfer mechanism), identified a unique structural feature of the relay. This was an unusually short bond between a hydrogen atom and a nitrogen atom that facilitates the correct working of the relay.

They also found subtle magnetic features of the electronic structure of the artificial relay that mirrored those found in the natural system.

Not only has the artificial system been improved, but the team understands better how the natural system works. This will be important as scientists develop the artificial leaf approach to sustainably harnessing the solar energy needed to provide the food, fuel and fiber that human needs are increasingly demanding.

ASU chemistry professors involved in this specific project include Thomas Moore, Devens Gust, Ana Moore and Vladimiro Mujica. The department is a unit of the College of Liberal Arts and Sciences. Key collaborators in this work are Oleg Poluektov and Tijana Rajh from Argonne National Laboratory.

This work would not have been possible without the participation of many scientists driven by a common goal and coordinated by a program such as the Energy Frontier Research Center to bring the right combination of high-level skills to the research table.

<http://www.medscape.com/viewarticle/820787?src=rss>

Referrals and Word of Mouth Trump Online Doctor Ratings

Word-of-mouth recommendations and referrals from other physicians nevertheless matter more to Americans when they select a clinician

Robert Lowes

Patients increasingly use physician rating Web sites such as [Vitals](#) and [Healthgrades](#), but word-of-mouth recommendations and referrals from other physicians nevertheless matter more to Americans when they select a clinician, according to a research letter published online today in the *Journal of the American Medical Association (JAMA)*.

Lead author David Hanauer, MD, and coauthors also write that Americans consider online ratings for cars, movies, books, electronics, and appliances more helpful than those for physicians.

Then again, Web sites that review consumer goods and entertainment have been at it longer, said John Santa, MD, MPH, medical director of Consumer Reports Health, which has gotten into the [physician rating](#) business itself. "The influence of physician ratings will go up," Dr. Santa told *Medscape Medical News*. "This is a science and endeavour that is in its infancy."

Dr. Hanauer and coauthors gleaned their findings from an online survey conducted in September 2012 that yielded 2137 responses. When it came to selecting a primary care physician, the factor most frequently rated as very important was "accepts my health insurance" (89%) followed at a distance by "convenient office location" (59%). Online ratings ranked last, with 41% flat-out calling them "not important."

The results don't surprise Dr. Hanauer, an associate professor of pediatrics at the University of Michigan Medical School.

Table 1. What Matters Most to Americans in Selecting a Physician

"Financial issues are so key today," said Dr. Hanauer, referring to health-plan acceptance, the top-ranked factor. "And I think people generally do trust family and friends as a reliable source of information."

Of survey-takers who had never used a physician rating Web site, 43% said they didn't trust the information there. "You don't know who left the comments, and you can't ask questions or have a back-and-forth conversation," Dr. Hanauer explained.

Factor in selecting a primary care physician	Very important	Somewhat important	Not important
<i>Accepts my health insurance</i>	89%	6%	5%
<i>Convenient office location</i>	59%	36%	5%
<i>Physician's years of experience</i>	46%	46%	8%
<i>Part of a trusted group practice</i>	44%	37%	19%
<i>Word of mouth (from family/friends)</i>	38%	47%	15%
<i>Referral from another physician</i>	34%	46%	19%
<i>Physician's rating on Web sites</i>	19%	40%	41%

Source: *Public Awareness, Perception, and Use of Online Physician Rating Sites*. JAMA. 2014;311:734-735.

Fear of Physician Reprisal

The relative lack of importance assigned to online physician ratings may reflect how much the public knows about them. Sixty-five percent of respondents said they were aware that such Web sites exist, compared with higher percentages who knew about online ratings for cars (87%), movies or books (82%), and electronics or appliances (81%).

Of Americans who knew about physician rating Web sites, 36% used them at least once in the past year. In contrast, more than half of the respondents who knew about Web sites for movie or books, electronics or appliances, and restaurants were users. Differences between usage rates can be misleading, however, said Dr. Hanauer, because "you might look for a movie every week, but once you find a doctor, you might not go back to the rating site for a long time."

Among all respondents, roughly 23% used a physician rating Web site at least once in the past year. A study by the Kaiser Family Foundation, cited in the research letter, showed that only 6% of Americans used comparative quality data — whether it was online or in print — to choose a physician in 2008.

"Usage is going up," Dr. Hanauer told *Medscape Medical News*. "It could become second-nature someday."

In terms of usefulness, rating Web sites that specialize in physicians compared favorably with other ones. All of them were graded as very or somewhat useful by more than 90% of respondents.

"Among those who sought online physician ratings in the last year, 35% reported selecting a physician based on good ratings, and 37% had avoided a physician with bad ratings," write Dr. Hanauer and coauthors.

Five percent of survey takers said they had rated a physician or wrote a comment online. Of that group, 54% posted a positive rating, 29% a neutral rating, and 19% a negative one. The study suggests that more Americans might disparage their physicians online if they didn't fear repercussions. Roughly one in 3 worried about their identity being disclosed if they said something negative, and one in 4 worried about the physician retaliating.

Dr. Hanauer noted that some physicians require new patients to promise in writing that they will not post a negative review on a rating Web site.

"The Stakes Are Higher"

Physician rating Web sites have come under fire for being unreliable, partly because they usually derive their scores from a handful of patient responses. In addition, such Web sites focus on qualitative issues such as a physician's bedside manner as opposed to quantitative measures of clinical quality, according to critics.

Dr. Santa at Consumer Reports Health said that his organization is taking physician ratings to the next level by including hard data on adherence to practice guidelines for cancer screenings and pneumonia vaccination, and patients' control of blood pressure and hemoglobin A1c, among other measures. *Consumer Reports* currently rates physicians in California Massachusetts, Minnesota, and Wisconsin.

Quantitative measures of clinical performance are valuable, said Dr. Hanauer, but they can be just as unreliable as qualitative measures. For example, someone can grade pediatricians on the percentage of their patients who receive childhood vaccines.

"Some practices fire [parents of] patients who don't get vaccinated so they won't have bad numbers," said Dr. Hanauer. "We have to understand how these numbers can be manipulated."

For some physicians, just the mere thought of being rated online as if they were toasters or plumbers is enough to provoke grumbles. Dr. Santa counters that just because physicians are far more complicated than toasters or plumbers doesn't mean they shouldn't be evaluated.

"The public deserves to have more and better information about doctors," he said. "It's more risky choosing a doctor than a plumber." Dr. Hanauer and his coauthors suggest as much. "The stakes," they write, "are higher."

The authors reported no conflicts of interest. Dr. Santa is an employee of Consumer Reports, which publishes physician ratings online. JAMA. 2014;311:734-735.

http://www.eurekalert.org/pub_releases/2014-02/uonc-mbr021814.php

Medicare beneficiaries return to emergency rooms after nursing home discharge

High percentage of Medicare patients discharged from nursing homes return to the emergency room within 30 days

Nursing homes are widely used by Medicare beneficiaries who require rehabilitation after hospital stays. But according to a recent study led by a researcher at the University of North Carolina at Chapel Hill School of Nursing, a high percentage of Medicare patients who are discharged from nursing homes will return to the hospital or the emergency room within 30 days.

"Nearly two million older adults use this benefit every year," said assistant professor Mark Toles, the first author of the study. "Before this study, we didn't recognize the large number of older adults who require additional acute care after they're discharged from a nursing home."

The study included more than 50,000 Medicare beneficiaries who were treated at skilled nursing facilities in North and South Carolina. Analyses conducted in collaboration with the Carolinas Center for Medical Excellence and investigators at Duke University revealed that approximately 22 percent of beneficiaries required emergency care within 30 days of discharge and 37.5 percent required acute care within 90 days.

Toles and his colleagues also examined whether factors such as race and diagnosis increased the likelihood that older adults discharged from a nursing facility would return to the hospital. They found that men and African Americans were more likely to need additional acute care along with older adults with cancer or respiratory diseases. Other factors associated with a higher need for acute care included a high number of previous hospitalizations, comorbid conditions, and receiving care from a for-profit facility.

Toles explained that researchers currently don't know how many of these rehospitalizations and emergency room visits are preventable. Because the Affordable Care Act penalizes hospitals for readmitting Medicare

patients, there has been more focus on improving patients' transition from the hospital to their home. Toles hopes this study will convince decision makers to pay attention to transitions from nursing facilities as well. "The role of nursing homes in communities has changed," he said. "These facilities are increasingly dedicated to transitioning older adults from the hospital back to their own homes. Short-term use of nursing facilities has grown tremendously over the past ten years and we have to examine interventions that will improve that transition."

The study was published in the January 2014 issue of the Journal of the American Geriatrics Society. Funding was provided by the John A. Hartford Foundation, the National Institute for Nursing Research, and pilot funding from the NewCourtland Center for Transitions and Health and the Center for Integrative Science in Aging.

Co-authors include Ruth A. Anderson from the Duke University School of Nursing, Mark Massing from the Carolinas Center for Medical Excellence, Mary D. Naylor from the University of Pennsylvania School of Nursing, and Erick Jackson and Sharon Peacock-Hinton from the Carolinas Center for Medical Excellence. The senior author of the study is Cathleen Colon-Emeric from the Duke University School of Medicine.

http://www.eurekalert.org/pub_releases/2014-02/sip-esi021814.php

Evolution stuck in slime for a billion years

Tasmanian researchers have revealed ancient conditions that almost ended life on Earth, using a new technique they developed to hunt for mineral deposits

The first life developed in the ancient oceans around 3.6 billion years ago, but then nothing much happened. Life remained as little more than a layer of slime for a billion years. Suddenly, 550 million years ago, evolution burst back into action – and here we are today. So what was the hold-up during those 'boring billion' years? According to University of Tasmania geologist Professor Ross Large and his international team, the key was a lack of oxygen and nutrient elements, which placed evolution in a precarious position. "During that billion years, oxygen levels declined and the oceans were losing the ingredients needed for life to develop into more complex organisms."

By analysing ancient seafloor rocks, Ross and his Australian, Russian, US and Canadian colleagues were able to show that the slowdown in evolution was tightly linked to low levels of oxygen and biologically-important elements in the oceans.

"We've looked at thousands of samples of the mineral pyrite in rocks that formed in the ancient oceans. And by measuring the levels of certain trace elements in the pyrite, using a technique developed in our labs, we've found that we can tell an accurate story about how much oxygen and nutrients were around billions of years ago." Their research will be published in the March issue of the journal *Earth and Planetary Science Letters*.

The red line represents the estimated oxygenation curve based on the abundance of the trace element selenium (Se) in pyrite samples. Oxygen levels are presented as %PAL (Present Atmospheric Levels), where 100% PAL represents the Earth's atmospheric oxygen at the present day. University of Tasmania

"We were initially looking at oxygen levels in the ancient oceans and atmosphere to understand how mineral deposits form, and where to look for them today. That's a focus of the Centre for Ore Deposit and Exploration Science (CODES), which we established with ARC and industry funding at UTAS in 1989," Ross explains. "But the technology we have developed to find minerals can also tell us much about the evolution of life." After an initial burst of oxygen, the study plots a long decline in oxygen levels during the 'boring billion' years before leaping up about 750-550 million years ago. "We think this recovery of oxygen levels led to a significant increase in trace metals in the ocean and triggered the 'Cambrian explosion of life'.

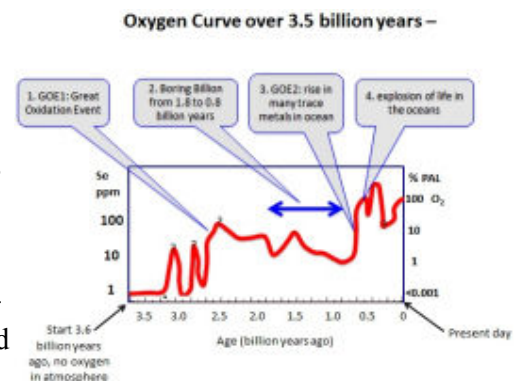
"We will be doing much more with this technology, but it's already becoming clear that there have been many fluctuations in trace metal levels over the millennia and these may help us understand a host of events including the emergence of life, fish, plants and dinosaurs, mass extinctions, and the development of seafloor gold and other ore deposits," says Ross.

<http://scitechdaily.com/researchers-develop-graphene-membrane-water-filters/>

Researchers Develop Graphene Membrane Water Filters

Scientists at the University of Manchester have developed graphene membrane water filters that offer precise and fast sieving of salts and organic molecules.

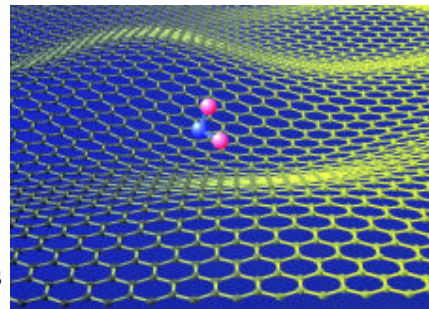
Graphene has proven itself as a wonder material with a vast range of unique properties. Among the least-known marvels of graphene is its strange love affair with water. Graphene is hydrophobic – it repels water – but narrow capillaries made from graphene vigorously suck in water allowing its rapid permeation, if the water



layer is only one atom thick – that is, as thin as graphene itself. This bizarre property has attracted intense academic and industrial interest with intent to develop new water filtration and desalination technologies. One-atom-wide graphene capillaries can now be made easily and cheaply by piling layers of graphene oxide – a derivative of graphene – on top of each other. The resulting multilayer stacks (laminates) have a structure similar to nacre (mother of pearl), which makes them also mechanically strong.

Two years ago, University of Manchester researchers discovered that thin membranes made from such laminates were impermeable to all gases and vapors, except for water. This means that even helium, the hardest gas to block off, cannot pass through the membranes whereas water vapor went through with no resistance.

Now the same team led by Dr Rahul Nair and Prof Andre Geim has tested how good the graphene membranes are as filters for liquid water. The results appear in the latest issue of Science.



Graphene Water Filters NO₂ molecule on graphene surface. The University of Manchester

The researchers report that, if immersed in water, the laminates become slightly swollen but still allow ultrafast flow of not one but two monolayers of water. Small salts with a size of less than nine Angstroms can flow along but larger ions or molecules are blocked. Ten Angstroms is equivalent to a billionth of a metre. The graphene filters have an astonishingly accurate mesh that allows them to distinguish between atomic species that are only a few percent different in size.

On top of this ultraprecise separation, it is also ultrafast. Those ions that can go through do so with such a speed as if the graphene membranes were an ordinary coffee filter. The latter effect is due to a property that the Manchester scientists call “ion sponging”. Their graphene capillaries suck up small ions as powerful hoovers leading to internal concentrations that can be hundreds of times higher than in external salty solutions.

Dr Nair said: “The water filtration is as fast and as precise as one could possibly hope for such narrow capillaries. Now we want to control the graphene mesh size and reduce it below nine Angstroms to filter out even the smallest salts like in seawater. Our work shows that it is possible.”

Dr Irina Grigorieva, a co-author of the study, added: “Our ultimate goal is to make a filter device that allows a glass of drinkable water made from seawater after a few minutes of hand pumping. We are not there yet but this is no longer science fiction”.

The work was done in collaboration with a group led by Hengan Wu from Chinese Academy of Sciences who carried out extensive computer simulations to understand the filtration mechanism.

Publication: R. K. Joshi, et al., “Precise and Ultrafast Molecular Sieving Through Graphene Oxide Membranes,” *Science* 14 February 2014; Vol. 343 no. 6172 pp. 752-754; DOI: 10.1126/science.1245711

PDF Copy of the Study: [Precise and ultrafast molecular sieving through graphene oxide membranes](#)

<http://www.bbc.co.uk/news/health-26224813>

Master monkey's brain controls sedated 'avatar'

The brain of one monkey has been used to control the movements of another, "avatar", monkey, US scientists report.

By James Gallagher Health and science reporter, BBC News

Brain scans read the master monkey's mind and were used to electrically stimulate the avatar's spinal cord, resulting in controlled movement. The team hope the method can be refined to allow paralysed people to regain control of their own body. The findings, published in *Nature Communications*, have been described as "a key step forward".

Damage to the spinal cord can stop the flow of information from the brain to the body, leaving people unable to walk or feed themselves. The researchers are aiming to bridge the damage with machinery.

Match electrical activity

The scientists at Harvard Medical School said they could not justify paralysing a monkey. Instead, two were used - a master monkey and a sedated avatar. The master had a brain chip implanted that could monitor the activity of up to 100 neurons. During training, the physical actions of the monkey were matched up with the patterns of electrical activity in the neurons.

The avatar had 36 electrodes implanted in the spinal cord and tests were performed to see how stimulating different combinations of electrodes affected movement. The two monkeys were then hooked up so that the brain scans in one controlled movements in real time in the other. The sedated avatar held a joystick, while the master had to think about moving a cursor up or down.

In 98% of tests, the master could correctly control the avatar's arm.

One of the researchers, Dr Ziv Williams, told the BBC: "The goal is to take people with brain stem or spinal cord paralysis and bypass the injury. "The hope is ultimately to get completely natural movement, I think it's theoretically possible, but it will require an exponential additional effort to get to that point." He said that giving paralysed people even a small amount of movement could dramatically alter their quality of life.

Reality or science fiction?

The idea of one brain controlling an avatar body is the stuff of blockbuster Hollywood movies. However, Prof Christopher James, of the University of Warwick, dismissed a future of controlling other people's bodies by thought. He said: "Some people may be concerned this might mean someone taking over control of someone else's body, but the risk of this is a no-brainer. "Whilst the control of limbs is sophisticated, it is still rather crude overall, plus of course in an able-bodied person their own control over their limbs remains anyway, so no-one is going to control anyone else's body against their wishes any time soon."

Instead, he said this was "very important research" with "profound" implications "especially for controlling limbs in spinal cord injury, or controlling prosthetic limbs with limb amputees".

Realising that goal will face additional challenges. Moving a cursor up and down is a long way from the dextrous movement needed to drink from a cup.

There are also differences in the muscles of people after paralysis; they tend to become more rigid. And fluctuating blood pressure may make restoring control more challenging.

Prof Bernard Conway, head of biomedical engineering at the University of Strathclyde, said: "The work is a key step forward that demonstrates the potential of brain machine interfaces to be used in restoring purposeful movement to people affected by paralysis. "However, significant work still remains to be done before this technology will be able to be offered to the people who need it."

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

Acid-bath stem cell results called into question

Was it all too good to be true? Concerns have been raised over a paper that claims to have turned adult cells into stem cells with just a 30-minute dip in acid.

18:59 18 February 2014 by Helen Thomson

An investigation has been launched by RIKEN in Japan into the research results of one of their members of staff – Haruko Obokata. At the end of last month, Obokata and her colleagues published two papers in the journal Nature showing that an acidic environment turned adult mouse cells into "totipotent" stem cells. These can become any cell in the body or placenta. Some team members later told New Scientist that they had repeated the experiment using human cells. The technique holds great promise for regenerative medicine because it could be used to create any cell in the body without needing to reprogram genes, or use cells from embryos.

Over the weekend, some blogs reported issues with images in one of the papers. Specifically, two images of different placentas appear very similar, and an image of a genome analysis appears to have another genome analysis spliced into it. Spliced images are sometimes used but should be explained.

Honest mistake

Issues have also been raised over duplicated images in a related paper by Obokata, published in 2011 (Tissue Engineering Part A, DOI: 10.1089/ten.tea.2010.0385). Charles Vacanti at Harvard Medical School, a co-author on all the papers, says he is aware of the mix-up on some images in the 2011 paper. He contacted the journal to request an erratum. He says the mistake did not affect any of the data, conclusions or any other component of the paper, and that it looks like an "honest mistake".

A spokesperson for the journal says it is investigating the latest allegations, and a RIKEN representative says their institution believes that the research results are valid but has launched an investigation and will make their findings public as soon as they are available.

Meanwhile, several researchers have struggled to repeat the stem cell experiments. "We've tried a few times but always unsuccessfully. I have to say, unfortunately, that I am now very sceptical of the published results," says José Silva, a stem cell researcher at the University of Cambridge.

Too little information

It may merely be a case of not enough information: Sally Cowley, head of the James Martin Stem Cell Facility at the University of Oxford, says her lab has not yet attempted to replicate the production of these "STAP" cells because the full protocol is not available. "I emailed Obokata for a detailed protocol, but have had no reply," she says. "It is a failure of the biomedical sciences publishing system in general, in my opinion, that there is rarely enough detail to be able to reproduce procedures accurately," she adds. Cowley hopes this high-profile example will encourage papers to supply detailed protocols as a matter of course.

Vacanti has said that he is happy to make the detailed protocol public.

Teruhiko Wakayama, a co-author on these papers told Nature that even he has had difficulties in reproducing the experiment – although he had repeated it independently before the papers were published.

Obokata has not responded to New Scientist's request for comment.

<http://www.medscape.com/viewarticle/820736?src=rss>

Opposition Growing Against Azithromycin for Infections

Treatment guidelines increasingly recommend that certain antibiotics, particularly the macrolide azithromycin, no longer be used to treat many common infections.

Neil Canavan

NEW YORK CITY - Inappropriate use has led to widespread antibiotic resistance and is contributing to the emergence of super bugs. At least one prominent emergency medicine expert suggests that the drug not be used at all. "If we don't stop, we're not going to have good antibiotics in the future," warned Joseph Lex, MD, from Temple University in Philadelphia, here at the American Academy of Emergency Medicine (AAEM) 20th Annual Scientific Assembly. "Every country that has recommended the use of narrow-spectrum antibiotics instead has seen a fall in their resistance rates. We just have to get to the point where we do the same thing." Dr. Lex is hardly a lone voice in this call to move away from the abuse of broad-spectrum antibiotics. Current guidelines present a chorus of similar opinions.

Azithromycin was developed in 1980 and has been marketed in the United States since 1991. As of 2011, it is the most commonly prescribed antibiotic. The current indications for azithromycin are acute bacterial exacerbations of chronic pulmonary disease, acute bacterial sinusitis, community-acquired pneumonia, pharyngitis, tonsillitis, uncomplicated skin and skin structure infection, urethritis and cervicitis, and genital ulcer disease.

However, just last year, the Canadian Pediatric Society strongly recommended that azithromycin not be used to treat acute pharyngitis, otitis media, or community-acquired pneumonia (Paediatr Child Health. 2013;18:311-313). That guidance did not recommend that clinicians consider not using it — it's recommendation is "do not use," stressed Dr. Lex. The only exceptions for azithromycin use area life-threatening beta-lactam allergy and pneumonia caused by an atypical bacteria.

"The long half-life of azithromycin contributes to the development of resistance," he explained. The way the drug is being used, "you're likely to get a subinhibitory nasal pharyngeal concentration, so these kids actually become carriers of azithromycin-resistant pneumococci."

Alternatives

The data show that macrolides have limited efficacy against 2 of the most common bacterial pathogens associated with acute otitis media — Haemophilus influenzae and Streptococcus pneumoniae.

Macrolide resistance is not a potential, it is a reality, and rates are increasing. "There is a better drug than azithromycin for every one of the indications," Dr. Lex pointed out.

The rhinosinusitis guidelines issued in 2012 by the Infectious Disease Society of America (IDSA) recommend considering antibiotics if symptoms persist beyond 10 days, are severe or worsening, or if there is high fever and nasal discharge for at least 3 days (Clin Infect Dis. 2012;54:1041-1045). Macrolides are not recommended at all. "Roughly 30% of these cases will be resistant to azithromycin," said Dr. Lex.

The acute bacterial sinusitis clinical practice guidelines from the American Academy of Pediatrics recommend amoxicillin with or without clavulanate for patients 1 to 18 years of age (Pediatrics. 2013;132:e262-e280). There is no recommendation for macrolides.

For group A streptococcal pharyngitis, the 2012 IDSA guidelines recommend first-line treatment with penicillin, and macrolides only for patients allergic to penicillin. "In the United States, 5% to 8% of pharyngeal isolates of group A strep are resistant to a macrolide," Dr. Lex reported.

For children older than 2 years of age with bacterial pediatric pneumonia, the 2011 IDSA clinical practice guidelines recommend first-line treatment with amoxicillin with or without clavulanate (Clin Infect Dis. 2011;53:e25-e76). Second-line choices do not include macrolides. "We know that 80% of pediatric pneumonia under the age of 2 is viral," said Dr. Lex, adding that azithromycin has no activity against a virus.

In the 2007 consensus guidelines on the management of community-acquired pneumonia in adults, macrolides in combination with doxycycline can be considered in previously healthy adults who have not recently taken an antibiotic (Clin Infect Dis. 2007;44[Suppl 2]:S27-S72). "This is before our concern about widespread macrolide overuse, and they're still not recommending using a macrolide alone," Dr. Lex noted.

Recently, "there has been a spate of new treatment recommendations that have demoted the use of azithromycin, especially in pediatrics," said Dr. Lex.

"Unfortunately, physicians get into a groove - a habit of prescribing a particular antibiotic for a particular condition. Right now, there's at least a year or 2 of lag time before these recommendations are adopted."

Patient Education

"Part of the reason for the overuse of azithromycin is pressure from the patients," Michael Epter, DO, emergency medicine physician in Las Vegas and education chair for the AAEM, told Medscape Medical News. "Patients come in with the symptomatology of a respiratory tract infection — which is commonly due to virus — yet they will insist on receiving an antibiotic."

When this happens, azithromycin is usually the agent prescribed. "With the once-a-day, 5-day regimen, patient compliance is high. Doctors like that." Even newer-generation macrolides are not as easy to use.

This time of year, "patients come in with your basic winter cold. In the majority of cases, it's a viral-related illness and antibiotics are only effective for their placebo effect," said Dr. Epter.

Azithromycin is also overused in sinusitis, which has repeatedly been shown to be the result of a viral infection. In fact, "94 of 100 patients will show no change in their symptoms when treated with an antibiotic, yet the use of azithromycin in sinusitis is rampant."

But no matter what the data say, it is a hard sell to convince patients to settle for over-the-counter symptom relief. "I try to explain it to them," Dr. Epter lamented, "but it's an uphill battle."

He said he first tries to explain the consequences of antibacterial resistance, and how treatment for a cold can complicate treatment for a more serious subsequent problem, such as pneumonia. Unfortunately, he said, more often than not, patients aren't happy until they get a prescription.

The easiest solution is point-of-care rapid testing to properly identify and narrowly treat the offending bug. However, "that technology is not yet being aggressively adopted in hospitals," said Dr. Epter. "We're still a couple of years away from getting to that point."

Dr. Lex and Dr. Epter have disclosed no relevant financial relationships.

<http://newsonjapan.com/html/newsdesk/article/106597.php>

Tokyo prosecutors raid Novartis Pharma over drug ads

Tokyo prosecutors raid Novartis Pharma over drug ads

Tokyo prosecutors raided Novartis Pharma K.K. on Wednesday over its alleged use of exaggerated advertising for a blood pressure-lowering drug, following a criminal complaint filed by the health ministry last month.

The ministry complained that the ads for the Diovan drug cited clinical study reports by two Japanese universities that contained false data and concluded the drug was more effective than others for reducing the risk of cerebral stroke and angina.

The ministry's investigation panel in a report last September said Novartis Pharma's use of the falsified reports for ads could amount to exaggerated ads banned under the pharmaceutical affairs law.

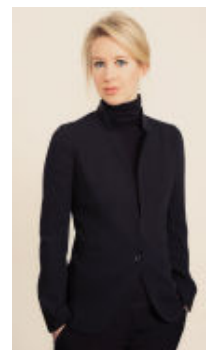
<http://www.wired.com/wiredscience/2014/02/elizabeth-holmes-theranos/>

This Woman Invented a Way to Run 30 Lab Tests on Only One Drop of Blood

Phlebotomy. Even the word sounds archaic—and that's nothing compared to the slow, expensive, and inefficient reality of drawing blood and having it tested.

By Caitlin Roper

As a college sophomore, Elizabeth Holmes envisioned a way to reinvent old-fashioned phlebotomy and, in the process, usher in an era of comprehensive superfast diagnosis and preventive medicine. That was a decade ago. Holmes, now 30, dropped out of Stanford and founded a company called Theranos with her tuition money. Last fall it finally introduced its radical blood-testing service in a Walgreens pharmacy near the company headquarters in Palo Alto, California. (The plan is to roll out testing centers nationwide.) Instead of vials of blood—one for every test needed—Theranos requires only a pinprick and a drop of blood. With that they can perform hundreds of tests, from standard cholesterol checks to sophisticated genetic analyses. The results are faster, more accurate, and far cheaper than conventional methods. The implications are mind-blowing. With inexpensive and easy access to the information running through their veins, people will have an unprecedented window on their own health.



Mathew Scott; Hair and makeup by Raina Antle

And a new generation of diagnostic tests could allow them to head off serious afflictions from cancer to diabetes to heart disease. None of this would work if Theranos hadn't figured out how to make testing transparent and inexpensive. The company plans to charge less than 50 percent of the standard Medicare and Medicaid reimbursement rates. And unlike the rest of the testing industry, Theranos lists its prices on its website: blood typing, \$2.05; cholesterol, \$2.99; iron, \$4.45. If all tests in the US were performed at those kinds of prices, the company says, it could save Medicare \$98 billion and Medicaid \$104 billion over the next decade.

What was your goal in starting a lab-testing company?

We wanted to make actionable health information accessible to people everywhere at the time it matters most. That means two things: being able to detect conditions in time to do something about them and providing access to information that can empower people to improve their lives.

There are a billion tests done every year in the United States, but too many of them are done in the emergency room. If you were able to do some of those tests before a person gets checked into the ER, you'd start to see problems earlier; you'd have time to intervene before a patient needed to go to the hospital. If you remove the biggest barriers to these tests, you'll see them used in smarter ways.

What was your motivation to launch Theranos at the age of 19? What set you on this road?

I definitely am afraid of needles. It's the only thing that actually scares me. But I started this company because I wanted to spend my life changing our health care system. When someone you love gets really sick, most of the time when you find out, it's too late to be able to do something about it. It's heartbreaking.

You're not alone in your fear of needles.

Phlebotomy is such a huge inhibitor to people getting tested. Some studies say that a substantive percentage of patients who get a lab requisition do not follow through because they're scared of needles or they're afraid of worrying, waiting to hear that something is wrong. We wanted to make this service convenient, to bring it to places close to people's homes, and to offer rapid results.

Why the focus on rapid results?

We can get results, on average, in less than four hours. And this can be very helpful for doctors and patients, because it means that someone could, for example, go to a Walgreens in the morning to get a routine test for something their doctor is tracking, and the physician can have the results that afternoon when they see the patient. And we're able to do all the testing using just a single microsample, rather than having to draw a dedicated tube for each type of test.

So if I got a blood test and my doctor saw the results and wanted other tests done, I wouldn't have to have more blood drawn?

Exactly. And on their lab form, the physician can write, "If a given result is out of range, run this follow-up test." And it can all be done immediately, using that same sample.



Todd Tankersley Brown Bird Design

Some conventional tests, like pH assays, can be done quickly. Others, like those that require culturing bacteria or viruses, can take days or even weeks. Are there some tests that take Theranos longer? Can everything really be turned around in four hours?

Yes, we had to develop assays or test methodologies that would make it possible to accelerate results. So we do not do things like cultures. In the case of a virus or bacteria, traditionally tested using a culture, we measure the DNA of the pathogen instead so we can report results much faster.

Where do you see this making a big difference?

Fertility testing is a good example. Most people pay for it out of pocket, and it can cost as much as \$2,000. These tests provide the data you need to figure out someone's fertility, and some women can't afford them. Our new fertility panel is going to cost \$35. That means women will be able to afford the tests. They'll be able to better manage the process and take some of the stress out of trying to conceive.

What are you doing to ensure the accuracy of your testing?

The key is minimizing the variability that traditionally contributes to error in the lab process. Ninety-three percent of error is associated with what's called pre-analytic processing — generally the part of the process where humans do things.

Such as?

Manually centrifuging a sample or how much time elapses before you test the sample, which brings its decay rate into play.

So how do you avoid these potential errors?

There's no manual handling of the sample, no one is trying to pipette into a Nanotainer, no one is manually processing it. The blood is collected and put into a box that keeps it cold. The very next thing that happens is lab processing, and that's done with automated devices at our centralized facility with no manual intervention or operation.

How can improved processes actually save lives?

We've created a tool for physicians to look at lab-test data over time and see trends. We don't usually think about lab data this way today. It's "Are you in range, or are you out of range?" Instead, we like to think,

“Where are you going?” If you showed me a single frame from a movie and asked me to tell you the story, I wouldn’t be able to do it. But with many frames, you can start to see the movie unfold.

How else can you use this technology?

Many, many years of work went into making this possible. We started our business working with pharmaceutical companies. Because we made it possible to get data much faster, they could use our infrastructure to run clinical trials. They were also able to run what’s called an adaptive clinical trial, where based on the data, they could change the dosing for a patient in real time or in a premeditated way, as opposed to waiting a long period and then deciding to change a dose.

In the long run, what impact will your technology have?

The dream is to be able to help contribute to the research that’s going on to identify cancer signatures as they change over time, to help intervene early enough to do something about an illness.

Will people become more used to gathering and examining their own health data?

No one thinks of the lab-testing experience as positive. It should be! One way to create that is to help people engage with the data once their physicians release it. You can’t do that if you don’t really understand why you’re getting certain tests done and when you don’t know what the results mean when you get them back. It drives me crazy when people talk about the scale as an indicator of health, because your weight doesn’t tell you what’s going on at a biochemical level. What’s really exciting is when you can begin to see changes in your lifestyle appear in your blood data. With some diseases, like type 2 diabetes, if people get alerted early they can take steps to avert getting sick. By testing, you can start to understand your body, understand yourself, change your diet, change your lifestyle, and begin to change your life.

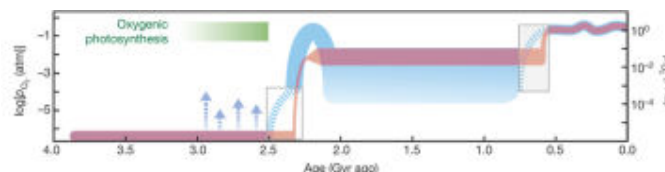
http://www.eurekalert.org/pub_releases/2014-02/uoc--tua021814.php

The ups and downs of early atmospheric oxygen

UC Riverside research team challenges conventional view of a simple two-step rise in early oxygen on Earth; study suggests instead dynamic oxygen concentrations that rose and fell over billions of years

RIVERSIDE, Calif. — A team of biogeochemists at the University of California, Riverside, give us a nontraditional way of thinking about the earliest accumulation of oxygen in the atmosphere, arguably the most important biological event in Earth history.

A general consensus asserts that appreciable oxygen first accumulated in Earth's atmosphere around 2.3 billion years ago during the so-called Great Oxidation Event (GOE). However, a new picture is emerging: Oxygen production by photosynthetic cyanobacteria may have initiated as early as 3 billion years ago, with oxygen concentrations in the atmosphere potentially rising and falling episodically over many hundreds of millions of years, reflecting the balance between its varying photosynthetic production and its consumption through reaction with reduced compounds such as hydrogen gas.



Evolution of Earth’s atmospheric oxygen over time. The faded red curve shows a ‘classical, two-step’ view of atmospheric evolution⁹⁵, while the blue curve shows the emerging model (P_{O_2} , atmospheric partial pressure of O_2).

"There is a growing body of data that points to oxygen production and accumulation in the ocean and atmosphere long before the GOE," said Timothy W. Lyons, a professor of biogeochemistry in the Department of Earth Sciences and the lead author of the comprehensive synthesis of more than a decade's worth of study within and outside his research group.

Lyons and his coauthors, Christopher T. Reinhard and Noah J. Planavsky, both former UCR graduate students, note that once oxygen finally established a strong foothold in the atmosphere starting about 2.3 billion years ago it likely rose to high concentrations, potentially even levels like those seen today. Then, for reasons not well understood, the bottom fell out, oxygen plummeted to a tiny fraction of today's level, and the ocean remained mostly oxygen free for more than a billion years. The paper appears in Nature on Feb. 19.

"This period of extended low oxygen spanning from roughly 2 to less than 1 billion years ago was a time of remarkable chemical stability in the ocean and atmosphere," Lyons said.

His research team envisions a series of interacting processes, or feedbacks, that maintained oxygen at very low levels principally by modulating the availability of life-sustaining nutrients in the ocean and thus oxygen-producing photosynthetic activity. "We suggest that oxygen was much lower than previously thought during this important middle chapter in Earth history, which likely explains the low abundances and diversity of eukaryotic organisms and the absence of animals," Lyons said.

The late Proterozoic—the time period beginning less than a billion years ago following this remarkable chapter of sustained low levels of oxygen—was strikingly different, marked by extreme climatic events manifest in

global-scale glaciation, indications of at least intervals of modern-like oxygen abundances, and the emergence and diversification of the earliest animals. Lyons notes that the factors controlling the rise of animals are under close scrutiny, including challenges to the long-held view that a major rise in atmospheric oxygen concentrations triggered the event.

"Despite the new ideas about animal origins, we suspect that oxygen played a major if not dominant role in the timing of that rise and, in particular, in the subsequent emergence of complex ecologies for animal life on and within the sediment, predator-prey relationships, and large bodies" said Lyons. "But, again, feedbacks always rule the day. Environmental change drives evolution, and steps in the progression of life change the environment."

No single factor is likely to be the whole story, and there is much more to be written in the tale. Lyons and coauthors, along with research groups from around world over, are focusing current efforts on the timing and drivers of oxygenation in the late Proterozoic, favoring a combination of global-scale mountain building, evolutionary controls on the way carbon is cycled in the biosphere, and concomitant climate events.

"We are faced with a lot of chicken-and-egg questions when it comes to unraveling the timing and sequence of oxygenation of the ocean and atmosphere," Lyons said. "But now, armed with new and better data, more sophisticated numerical simulations, and highly integrated investigations in the lab and the field, Earth's oxygenation history seems much longer and more dynamic than envisioned before, and we are getting closer to understanding the mechanisms behind such change."

Reinhard is a postdoctoral fellow at the California Institute of Technology and will join the faculty of the Georgia Institute of Technology as an assistant professor later this year. Planavsky is an assistant professor at Yale University.

The research was supported by an O.K. Earl Postdoctoral Fellowship in the Division of Geological and Planetary Sciences at Caltech to Reinhard, a National Science Foundation Postdoctoral Fellowship to Planavsky, and grants to Lyons from the NSF and NASA.

http://www.eurekalert.org/pub_releases/2014-02/uonh-urm021914.php

UNH research: Most of us have made best memories by age 25

By the time most people are 25, they have made the most important memories of their lives, according to new research from the University of New Hampshire.

DURHAM, N.H. – Researchers at UNH have found that when older adults were asked to tell their life stories, they overwhelmingly highlighted the central influence of life transitions in their memories. Many of these transitions, such as marriage and having children, occurred early in life.

"When people look back over their lives and recount their most important memories, most divide their life stories into chapters defined by important moments that are universal for many: a physical move, attending college, a first job, marriage, military experience, and having children," said Kristina Steiner, a doctoral student in psychology at UNH and the study's lead researcher.

The research team also included David Pillemer, Dr. Samuel E. Paul Professor of Developmental Psychology at UNH; Dorthe Kirkegaard Thomsen, professor of psychology and behavioral sciences at the University of Aarhus (Denmark); and Andrew Minigan, an undergraduate student in psychology at UNH. The researchers present the results of their study, "The reminiscence bump in older adults' life story transitions," in the journal *Memory*.

In the first study to use a naturalistic approach by collecting free-flowing life stories, researchers spoke with 34 members of an active retirement community, ages 59 to 92. All the participants were white, and 76 percent had earned at least an undergraduate degree. Participants were asked to tell their life stories in 30 minutes. One week later, participants divided their life stories into self-defined "chapters."

In the UNH study, researchers found a pronounced "reminiscence bump" between ages 17 and 24, when many people defined chapters of their life story beginning and ending. A reminiscence bump is a period of time between the ages of 15 and 30 when many memories, positive and negative, expected and unexpected, are recalled.

"Many studies have consistently found that when adults are asked to think about their lives and report memories, remembered events occurring between the ages of 15 to 30 are over-represented. I wanted to know why this might be. Why don't adults report more memories from the ages of 30 to 70? What is it about the ages of 15 to 30 that make them so much more memorable?" Steiner asked.

"Our life narratives are our identity. By looking at life narratives, researchers can predict levels of well-being and psychological adjustment in adults. Clinical therapists can use life narrative therapy to help people work through issues and problems in their lives by helping them see patterns and themes," said Steiner, who studies autobiographical memory.

http://www.eurekalert.org/pub_releases/2014-02/mscc-cts021414.php

Cell therapy shows remarkable ability to eradicate cancer in clinical study

Genetically modified T cells induced complete remissions in 88 percent of advanced leukemia patients treated

NEW YORK - Investigators from Memorial Sloan Kettering Cancer Center have reported more encouraging news about one of the most exciting methods of cancer treatment today. The largest clinical study ever conducted to date of patients with advanced leukemia found that 88 percent achieved complete remissions after being treated with genetically modified versions of their own immune cells. The results were published today in *Science Translational Medicine*.

"These extraordinary results demonstrate that cell therapy is a powerful treatment for patients who have exhausted all conventional therapies," said Michel Sadelain, MD, PhD, Director of the Center for Cell Engineering at Memorial Sloan Kettering and one of the study's senior authors. "Our initial findings have held up in a larger cohort of patients, and we are already looking at new clinical studies to advance this novel therapeutic approach in fighting cancer."

Adult B cell acute lymphoblastic leukemia (B-ALL), a type of blood cancer that develops in B cells, is difficult to treat because the majority of patients relapse. Patients with relapsed B-ALL have few treatment options; only 30 percent respond to salvage chemotherapy. Without a successful bone marrow transplant, few have any hope of long-term survival.

In the current study, 16 patients with relapsed B-ALL were given an infusion of their own genetically modified immune cells, called T cells. The cells were "reeducated" to recognize and destroy cancer cells that contain the protein CD19. While the overall complete response rate for all patients was 88 percent, even those with detectable disease prior to treatment had a complete response rate of 78 percent, far exceeding the complete response rate of salvage chemotherapy alone.

Dennis J. Billy, C.Ss.R, of Wynnewood, Pennsylvania, was one of the first patients to receive this treatment more than two years ago. He was able to successfully undergo a bone marrow transplant and has been cancer-free and back at work teaching theology since 2011. Paolo Cavalli, a restaurant owner from Oxford, Connecticut, remains in complete remission eight months after receiving his personalized T cell treatment.

A History of Scientific Achievements for Cell-Based Therapies

Cell-based, targeted immunotherapy is a new approach to treating cancer that harnesses the body's own immune system to attack and kill cancerous cells. Unlike with a common virus such as the flu, our immune system does not recognize cancer cells as foreign and is therefore at a disadvantage in eradicating the disease. For more than a decade, researchers at Memorial Sloan Kettering have been exploring ways to reengineer the body's own T cells to recognize and attack cancer. In 2003, they were the first to report that T cells engineered to recognize the protein CD19, which is found on B cells, could be used to treat B cell cancers in mice.

"Memorial Sloan Kettering was the first center to report successful outcomes using this CD19-targeted approach in B-ALL patients," said Renier Brentjens, MD, PhD, Director of Cellular Therapeutics at Memorial Sloan Kettering and one of the study's senior authors. "It's extremely gratifying to witness the astonishing results firsthand in my patients, having worked for more than a decade developing this technology from the ground up."

In March 2013, the same team of researchers first reported the results of five patients with advanced B-ALL who were treated with cell therapy. Remarkably, all five patients achieved complete remissions.

Results Demonstrate Potential of New Therapy

In the current study, seven of the 16 patients (44 percent) were able to successfully undergo bone marrow transplantation — the standard of care and the only curative option for B-ALL patients — following treatment. Three patients were ineligible due to failure to achieve a complete remission, three were ineligible due to preexisting medical conditions, two declined, and one is still being evaluated for a potential bone marrow transplant. Historically, only 5 percent of patients with relapsed B-ALL have been able to transition to bone marrow transplantation.

The study also provides guidelines for managing side effects of cell therapy, which can include severe flu-like symptoms such as fever, muscle pain, low blood pressure, and difficulty breathing, referred to as cytokine release syndrome. The researchers developed diagnostic criteria and a laboratory test that can identify which patients are at greater risk for developing this syndrome.

Additional studies to determine whether cell therapy can be applied to other types of cancer are already underway, and studies to test whether B-ALL patients would benefit from receiving targeted immunotherapy as frontline treatment are being planned.

This research was supported by the National Cancer Institute, the Terry Fox Foundation, the American Society of Hematology-Amos Medical Faculty Development Program, the Alliance for Cancer Gene Therapy, the Mallah Foundation, the Majors Foundation, the Damon Runyon Cancer Research Foundation, Kate's Team, Mr. William H. Goodwin and Mrs. Alice Goodwin and the Commonwealth Cancer Foundation for Research, the Carson Family Fund, and the Experimental Therapeutics Center of Memorial Sloan Kettering.

Editor's note: Dr. Sadelain and Dr. Brentjens are co-holders of a patent that covers the technology used to create the modified T cells in this study. The technology was licensed to Juno Therapeutics in December 2013.

http://www.eurekalert.org/pub_releases/2014-02/nu-nsr021414.php

New sitting risk: Disability after 60

Regardless of exercise, too much sedentary time is linked to major disability after 60

CHICAGO - If you're 60 and older, every additional hour a day you spend sitting is linked to a 50 percent greater risk of being disabled -- regardless of how much moderate exercise you get, reports a new Northwestern Medicine® study.

The study is the first to show sedentary behavior is its own risk factor for disability, separate from lack of moderate vigorous physical activity. In fact, sedentary behavior is almost as strong a risk factor for disability as lack of moderate exercise.

If there are two 65-year-old women, one sedentary for 12 hours a day and another sedentary for 13 hours a day, the second one is 50 percent more likely to be disabled, the study found.

"This is the first time we've shown sedentary behavior was related to increased disability regardless of the amount of moderate exercise," said Dorothy Dunlop, professor of medicine at Northwestern University Feinberg School of Medicine and lead author of the study. "Being sedentary is not just a synonym for inadequate physical activity."

Disability affects more than 56 million Americans. It's defined by limitations in being able to do basic activities such as eating, dressing or bathing oneself, getting in and out of bed and walking across a room. Disability increases the risk of hospitalization and institutionalization and is a leading source of health care costs, accounting for \$1 in \$4 spent.

The study will be published February 19 in the *Journal of Physical Activity & Health*.

The finding -- that being sedentary was almost as strong a risk factor for disability as lack of moderate vigorous activity -- surprised Dunlop.

"It means older adults need to reduce the amount of time they spend sitting, whether in front of the TV or at the computer, regardless of their participation in moderate or vigorous activity," she said.

The study focused on a sample of 2,286 adults aged 60 and older from the National Health and Nutrition Examination Survey. It compared people in similar health with the same amount of moderate vigorous activity. Moderate activity is walking briskly, as if you are late to an appointment.

The participants wore accelerometers from 2002 to 2005 to measure their sedentary time and moderate vigorous physical activity. The accelerometer monitoring is significant because it is objective. The older and heavier people are, the more they tend to overestimate their physical activity. Previous research indicated a relationship between sedentary behavior and disability but it was based on self-reports and, thus, couldn't be verified.

Because the study examines data at one point in time, it doesn't definitively determine sedentary behavior causes disability. "It draws attention to the fact that this is a potential problem," said Dunlop, who is doing a longitudinal study on sedentary behavior and disability risk.

Studies with animals have shown immobility is a separate risk factor for negative effects on health. "This is the first piece of objective evidence that corroborates the animal data," Dunlop said.

To cut down on sitting time, Dunlop has the following suggestions:

Stand up when you talk on the phone or during a work meeting.

When you go to grocery store or mall, park in a space farthest away.

When you get up to have glass of water, walk around the house or office.

Walk for short errands instead of taking the car.

Take the stairs instead of the elevator, if you are able.

Dunlop wears a device on her wrist that tracks her steps and is synced to her smartphone and computer. She's created a social circle with her friends and family, so they can keep track of each other's progress.

"It's great reinforcement to keep moving," Dunlop said.

Rowland Chang, M.D., senior associate dean for public health at Feinberg, is a coauthor on the paper.

This study is supported in part by the National Institute for Arthritis and Musculoskeletal Diseases of the National Institutes of Health, grants R01-AR054155, R21-AR059412 and P60-AR064464.

<http://bit.ly/1mt6KUF>

Neutron star spotted moving 5 million mph, trailing particle jet

Jet is the longest collection of high energy particles in the Milky Way.

by John Timmer - Feb 19 2014, 11:00pm TST

Yesterday, the people who run NASA's Chandra X-ray Observatory announced that they had imaged the longest particle jet yet seen in the Milky Way. The jet, seen in the lower right in the image above, has reached this length because its source, a neutron star known as IGR J11014-6103, also happens to be one of the fastest moving neutron stars ever spotted, possibly traveling as fast as eight million kilometers an hour.

Neutron stars are formed in supernova explosions, which are typically symmetrical. As a result, many of them never leave the supernova remnant in which they form. In some cases, however, asymmetries in the explosion give the neutron star a nudge and send it traveling from the site where the exploding star sat.



An extraordinary jet trailing behind a runaway pulsar is seen in this composite image that contains data from Chandra (purple), radio data from the ACTA (green), and optical data from the 2MASS survey (red, green, and blue).

The pulsar and its tail are found in the lower right of this image. Image Credit: NASA/CXC/ISDC

In the case of IGR J11014-6103, the nudge was anything but gentle; preliminary estimates of its speed place it at between four and eight million kilometers an hour, making it one of the fastest moving neutron stars ever spotted.

But the new observations show that, in addition to its high speed, the neutron star has a feature that's less unusual: high-energy particle jets that mark it as a pulsar. In this case, the jets appear to be emitted in a direction that's perpendicular to the neutron star's motion, making them tail off at an angle. In addition, kinks in the jets suggest that the axis of rotation of the neutron star has a significant wobble in it.

Further observations of the system could help clarify the features of the asymmetries that sent the neutron star packing and give us a glimpse into the processes that produce a supernova.

For more details and a higher-resolution image, you can visit the [Chandra site](http://www.nasa.gov).

<http://www.bbc.co.uk/news/technology-26258971>

Screens to replace windows on S-512 supersonic jet

A company building a supersonic jet says it plans to replace cabin windows with thin display screens embedded in the wall.

Cameras recording outside the aircraft will display pictures on the screens. Spike Aerospace, which is designing the plane, says drag will be reduced by removing windows, which "cause significant challenges in designing and constructing an aircraft fuselage". The S-512 supersonic jet is not expected to launch until 2018.

In a blog on its website the company said windows required additional structural support and added weight to the aircraft but these problems could be eliminated by using micro-cameras and flat displays.

Cruising speed

It plans to surround the aircraft with cameras and display the views on the cabin screens. Passengers will be able to dim the screens or change the images.

Dr Darren Ansell, an expert in space and aerospace engineering at the University of Central Lancashire, said that the experience for passengers of being in a plane without windows could be an unusual one. "There will be no natural light - it will all be simulated - so it will be a bit like being in a tube. And how would it work from a safety perspective? If there was an accident how would you know which way the plane was facing, and where you had landed, when the cameras have failed?" he said.

Spike Aerospace is based in Boston in the US and is made up of a team of engineers who have experience of aircraft design and building. In December, it announced plans for the S-512, which it claimed would be the world's first supersonic business jet.



Photo of jet It's claimed that the S-512 will reach speeds of Mach 1.8

Expected to cost \$80m (£48m), the jet will carry 18 passengers and the company claims it will be able to fly from New York to London in three to four hours rather than the six to seven it currently takes. It will have a cruising speed of Mach 1.6 and a maximum speed of Mach 1.8. In comparison, a Boeing 777-300 has a cruising speed of Mach 0.8. Other firms are racing to develop similar supersonic jets, including Aerion and Gulfstream.

<http://scitechdaily.com/new-type-fuel-cell-produces-electricity-directly-biomass/>

New Type of Fuel Cell Produces Electricity Directly from Biomass

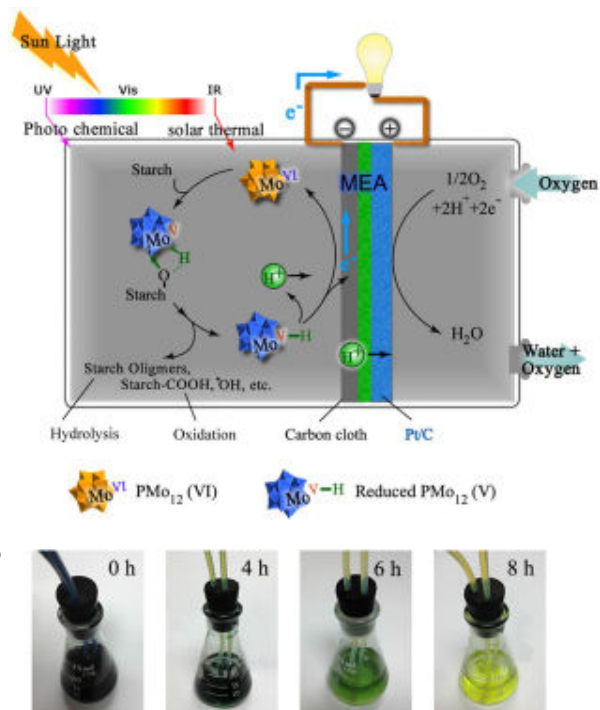
A new solar-induced direct biomass-to-electricity hybrid fuel cell can operate on fuels as varied as powdered wood.

The fuel cell, shown on the right, relies on a polyoxometalate (POM) catalyst (shown in the vials) which changes color as it reacts with light. Scientists at Georgia Tech have developed a new type of low-temperature fuel cell that directly converts biomass to electricity with assistance from a catalyst activated by solar or thermal energy. Although low temperature fuel cells powered by methanol or hydrogen have been well studied, existing low temperature fuel cell technologies cannot directly use biomass as a fuel because of the lack of an effective catalyst system for polymeric materials.

Now, researchers at the Georgia Institute of Technology have developed a new type of low-temperature fuel cell that directly converts biomass to electricity with assistance from a catalyst activated by solar or thermal energy. The hybrid fuel cell can use a wide variety of biomass sources, including starch, cellulose, lignin – and even switchgrass, powdered wood, algae and waste from poultry processing. The device could be used in small-scale units to provide electricity for developing nations, as well as for larger facilities to provide power where significant quantities of biomass are available.

“We have developed a new method that can handle the biomass at room temperature, and the type of biomass that can be used is not restricted – the process can handle nearly any type of biomass,” said Yulin Deng, a professor in Georgia Tech’s School of Chemical and Biomolecular Engineering and the Institute of Paper Science and Technology (IPST). “This is a very generic approach to utilizing many kinds of biomass and organic waste to produce electrical power without the need for purification of the starting materials.”

The new solar-induced direct biomass-to-electricity hybrid fuel cell was described February 7, 2014, in the journal *Nature Communications*.



This schematic illustration shows the working principle of the solar-induced direct biomass-to-electricity hybrid fuel cell. (Courtesy of Yulin Deng)

The challenge for biomass fuel cells is that the carbon-carbon bonds of the biomass – a natural polymer – cannot be easily broken down by conventional catalysts, including expensive precious metals, Deng noted. To overcome that challenge, scientists have developed microbial fuel cells in which microbes or enzymes break down the biomass. But that process has many drawbacks: power output from such cells is limited, microbes or enzymes can only selectively break down certain types of biomass, and the microbial system can be deactivated by many factors.

Deng and his research team got around those challenges by altering the chemistry to allow an outside energy source to activate the fuel cell’s oxidation-reduction reaction.

In the new system, the biomass is ground up and mixed with a polyoxometalate (POM) catalyst in solution and then exposed to light from the sun – or heat. A photochemical and thermochemical catalyst, POM functions as both an oxidation agent and a charge carrier. POM oxidizes the biomass under photo or thermal irradiation, and delivers the charges from the biomass to the fuel cell’s anode. The electrons are then transported to the cathode, where they are finally oxidized by oxygen through an external circuit to produce electricity.

“If you mix the biomass and catalyst at room temperature, they will not react,” said Deng. “But when you expose them to light or heat, the reaction begins. The POM introduces an intermediate step because biomass cannot be directly accessed by oxygen.”

The system provides major advantages, including combining the photochemical and solar-thermal biomass degradation in a single chemical process, leading to high solar conversion and effective biomass degradation. It also does not use expensive noble metals as anode catalysts because the fuel oxidation reactions are catalyzed by the POM in solution. Finally, because the POM is chemically stable, the hybrid fuel cell can use unpurified polymeric biomass without concern for poisoning noble metal anodes.

The system can use soluble biomass, or organic materials suspended in a liquid. In experiments, the fuel cell operated for as long as 20 hours, indicating that the POM catalyst can be re-used without further treatment. In their paper, the researchers reported a maximum power density of 0.72 milliwatts per square centimeter, which is nearly 100 times higher than cellulose-based microbial fuel cells, and near that of the best microbial fuel cells. Deng believes the output can be increased five to ten times when the process is optimized.

"I believe this type of fuel cell could have an energy output similar to that of methanol fuel cells in the future," he said. "To optimize the system, we need to have a better understanding of the chemical processes involved and how to improve them."

The researchers also need to compare operation of the system with solar energy and other forms of input energy, such as waste heat from other processes. Beyond the ability to directly use biomass as a fuel, the new cell also offers advantages in sustainability – and potentially lower cost compared to other fuel cell types.

"We can use sustainable materials without any chemical pollution," Deng said. "Solar energy and biomass are two important sustainable energy sources available to the world today. Our system would use them together to produce electricity while reducing dependence on fossil fuels."

In addition to Deng, the research team included Wei Liu, Wei Mu, Mengjie Liu, Xiaodan Zhang and Hongli Cai, all from the School of Chemical and Biomolecular Engineering or the Institute of Paper Science and Technology at Georgia Tech.

Publication: Wei Liu, et al., "Solar-induced direct biomass-to-electricity hybrid fuel cell using polyoxometalates as photocatalyst and charge carrier," Nature Communications 5, Article number: 3208; doi:10.1038/ncomms4208 Source: John Toon, Georgia Institute of Technology

http://www.eurekalert.org/pub_releases/2014-02/cp-had021114.php

Human and dog brains both have dedicated 'voice areas'

The first study to compare brain function between humans and any nonprimate animal shows that dogs have dedicated voice areas in their brains, just as people do.

Dog brains, like those of people, are also sensitive to acoustic cues of emotion, according to a study in the Cell Press journal *Current Biology* on February 20.

The findings suggest that voice areas evolved at least 100 million years ago, the age of the last common ancestor of humans and dogs, the researchers say. It also offers new insight into humans' unique connection with our best friends in the animal kingdom and helps to explain the behavioral and neural mechanisms that made this alliance so effective for tens of thousands of years.

"Dogs and humans share a similar social environment," says Attila Andics of MTA-ELTE Comparative Ethology Research Group in Hungary. "Our findings suggest that they also use similar brain mechanisms to process social information. This may support the successfulness of vocal communication between the two species."

Andics and his colleagues trained 11 dogs to lay motionless in an fMRI brain scanner. That made it possible to run the same neuroimaging experiment on both dog and human participants—something that had never been done before. They captured both dogs' and humans' brain activities while the subjects listened to nearly 200 dog and human sounds, ranging from whining or crying to playful barking or laughing.

The images show that dog and human brains include voice areas in similar locations. Not surprisingly, the voice area of dogs responds more strongly to other dogs while that of humans responds more strongly to other humans.

The researchers also noted striking similarities in the ways the dog and human brains process emotionally loaded sounds. In both species, an area near the primary auditory cortex lit up more with happy sounds than unhappy ones.

Andics says the researchers were most struck by the common response to emotion across species.

There were some differences, too: in dogs, 48% of all sound-sensitive brain regions respond more strongly to sounds other than voices. That's in contrast to humans, in which only 3% of sound-sensitive brain regions show greater response to nonvocal versus vocal sounds.

The study is the first step toward understanding how it is that dogs can be so remarkably good at tuning into the feelings of their human owners.

"This method offers a totally new way of investigating neural processing in dogs," Andics says. "At last we begin to understand how our best friend is looking at us and navigating in our social environment."

Current Biology, Andics et al.: "Voice-sensitive regions in the dog and human brain are revealed by comparative fMRI."

http://www.eurekalert.org/pub_releases/2014-02/uotm-mar022014.php

MD Anderson researcher uncovers some of the ancient mysteries of leprosy

Research at The University of Texas MD Anderson Cancer Center is finally unearthing some of the ancient mysteries behind leprosy, also known as Hansen's disease, which has plagued mankind throughout history.

The new research findings appear in the current edition of journal PLOS Neglected Tropical Diseases.

According to this new hypothesis, the disease might be the oldest human-specific infection, with roots that likely stem back millions of years.

There are hundreds of thousands of new cases of leprosy worldwide each year, but the disease is rare in the United States, with 100-200 new cases annually. Leprosy is known for attacking a patient's skin and nerves. Effective antimicrobial treatments exist today. However, when misdiagnosed or untreated, the disease can lead to extensive skin lesions, deformities in the patient's face and extremities, disabilities, and even death. Leprosy carries a social stigma and diagnosis is frequently and notoriously delayed.

An incidental yet important discovery

Work led by MD Anderson pathologist Xiang-Yang Han, M.D., Ph.D., a professor in laboratory medicine, resulted in the discovery in 2008 of a new leprosy-causing species, called *Mycobacterium lepromatosis*. Before that time, only one species of bacteria, called *Mycobacterium leprae*, was known to cause leprosy.

In the past several years, Han and other researchers have found the new leprosy agent in patients from Mexico, Canada, Brazil, Singapore, and Myanmar. Han's team, in collaboration with Francisco Silva, an evolutionary geneticist from Spain, analyzed 20 genes of *Mycobacterium lepromatosis* and compared them with those of *Mycobacterium leprae*.

They found the two leprosy bacteria came from a last common ancestor around 10 million years ago. Before the divergence, the common bacteria ancestor had undergone a massive reductive evolution that resulted in inactivation of approximately 40 percent of all the genes in its genome. Those genes went on to become non-functioning pseudogenes or were even lost. This reductive evolution, unique among all pathogenic bacteria known so far, was unearthed from genome sequencing of *Mycobacterium leprae* several years ago before the discovery of *Mycobacterium lepromatosis*, by another research team.

A unifying theory

In the newly published study, Han and Silva came to the hypothesis that leprosy has existed for millions of years. This theory was built by connecting the dots from several known facts and published studies.

One piece of evidence is the fact that leprosy is a strict human disease without other hosts or reservoirs. Once outside of the human body, leprosy bacteria are unable to grow in artificial media. One caveat is that *Mycobacterium leprae* is found in wild armadillos, but only in North America and South America. It's believed the animals likely first acquired the infection from early American explorers a few hundred years ago.

A second piece of evidence suggesting a long history of leprosy lies within the bacterial genome. All worldwide *Mycobacterium leprae* strains analyzed so far, more than 400 in total, have been found to have essentially identical genomes, or be clonal. This suggests human beings carried the leprosy bacteria when departing Africa around 100,000 years ago to populate the rest of the world. It also means that leprosy bacteria are extraordinarily stable within their human hosts, a sign of mature parasitic life far older than 100,000 years.

A third piece of evidence relates to the last common ancestor of the two known leprosy bacteria, which completed reductive evolution around 10 million years ago, resulting in a lean genome and the loss of free-living ability. A well-adapted lean parasite is confined to its specific host species and is unlikely to switch to other host species.

Lastly, the oldest age of the leprosy bacteria's pseudogenes suggest that gene inactivation began approximately 20 million years ago. This is likely the point when the ancestor of leprosy bacteria jumped to our early human ancestors and transitioned from free-living to strictly parasitic. In essence, the theory unifies the reductive evolution of the leprosy bacteria and their strict parasitic lifestyle in humans into a single continuous, long process.

Insights into the pathogenesis of leprosy

Han and Silva also brought human evolution, host genetic diversity, and host immunity into the complex picture of leprosy. Their hypothesis that leprosy existed for millions of years offers new insights into disease pathogenesis. For example, the parasitic adaptation of the leprosy bacteria inside hominid-human hosts is similar to a very long hide-and-seek game. In this scenario, the parasite hides by mutating or removing harmful molecules while retaining protective ones. In the end, this leads to evasion from host immunity, a phenomenon commonly seen in leprosy. Finally, Han and Silva concluded that leprosy can be viewed as a natural consequence of a long parasitism.

Han, a clinical microbiologist, routinely diagnoses secondary infections caused by various kinds of microbes in patients with cancer. "Many patients who come to MD Anderson suspected of having cancer turn out to have infections instead and we make such game-changing diagnoses nearly every day" said Dr. Han.

"Discovering the new leprosy agent *Mycobacterium lepromatosis* was incidental. However, locating this additional leprosy cause significantly adds to our understanding of the ancient disease. In particular, tracing the ultimate origin of leprosy through the parasitic adaptive evolution of the leprosy bacteria is rather insightful, not only for this single disease but also for our better understanding of the mechanism behind other human infections. Medical historians and anthropologists may appreciate this also."

Han's team is currently focused on the decoded genome of *Mycobacterium lepromatosis* and its assembly.

http://www.eurekalert.org/pub_releases/2014-02/fhcr-dpc022014.php

Dismantling pancreas cancer's armor

Immunotherapy against pancreas cancer gains ground as Fred Hutch researchers discover a method that allows native immune cells to launch an attack

SEATTLE – Pancreas cancer is notoriously impervious to treatment and resists both chemotherapy and radiotherapy. It has also been thought to provide few targets for immune cells, allowing tumors to grow unchecked. But new research from Fred Hutchinson Cancer Research Center shows that pancreas cancer "veils" itself from the immune system by recruiting specialized immune suppressor cells. The research team also found that removing these cells quickly triggers a spontaneous anti-tumor immune response.

The findings, published Feb. 20 in *Gut*, give hope for future immunotherapy strategies against this deadly and aggressive cancer.

"The take-home message is that there is a latent immune response against pancreas cancer that can be expressed if we remove its obstacles," said Sunil Hingorani, M.D., Ph.D., an associate member of the Clinical Research Division at Fred Hutch, who led the study. "Removing the suppressor cells creates a context that could enable an adoptive immune cell therapy against pancreas cancer."

An almost uniformly deadly cancer

Pancreas cancer is almost uniformly deadly. About 45,000 people are diagnosed with the disease in the U.S. each year. "The mortality rate is essentially the same as the incidence rate," Hingorani noted. Pancreas cancer "doesn't obey the rules" established for other solid tumors, he said: It metastasizes early, resists traditional treatment, and survives quite well on a diminished blood supply.

The tumor builds a fibrous wall around itself which exerts so much pressure that blood vessels entering the tumor are constricted, which also prevents chemotherapy from entering. In addition, scientists have historically had difficulty stimulating a therapeutic immune response against pancreas tumors because they have identified few molecular targets on which to focus the immune attack.

But as the new findings in a mouse model show, pancreas tumors fly under the radar not because they lack targets for the immune system, but because they recruit suppressor cells that keep immune cells at bay. When these immune suppressor cells are removed, helpful immune cells spontaneously move into the tumor and begin their attack.

Activating a T-cell response against the cancer

Pancreas cancer is nearly always diagnosed at very late stages, which has made its development hard to study. To gain insight into these aggressive tumors, Hingorani's team pioneered the development of a genetic mouse model of pancreas cancer. Previous work in the model led to their discovery of an enzyme that can make pancreas tumors more permeable to chemotherapy. The group turned again to this model to learn more about how pancreas tumors interact with the immune system.

From their earlier work, Hingorani's team knew that several different types of immunosuppressive cells infiltrate pancreas tumors. Together with immunologist Philip Greenberg, M.D., a member of Fred Hutch's Clinical Research Division, they have begun studying ways to target these inhibitory cells. As Ingunn Stromnes, Ph.D., the postdoctoral researcher co-mentored by Hingorani and Greenberg who spearheaded this latest study, watched pancreas tumors develop in mice, she saw that one cell type stood out. Descended from bone marrow cells and dubbed granulocyte-myeloid-derived suppressor cells (Gr-MDSCs), these cells jumped in number as pancreas tumors turned invasive. Stromnes discovered the pancreas tumors were orchestrating the accumulation of these suppressor cells by releasing a protein known as granulocyte macrophage colony-stimulating factor (GM-CSF), which attracted the Gr-MDSCs.

Strikingly, the Gr-MDSCs actively worked against T cells, a class of immune cell central to many immunotherapy strategies. T cells are often harnessed to fight tumors because they can recognize very specific

molecules and destroy any cells expressing those molecules. But Gr-MDSCs prevented T cells from dividing and even induced their death.

Stromnes found this effect could be reversed, however, and the T-cell response activated, by depleting Gr-MDSCs. When she did so, she saw evidence not only that the T cells could now enter the tumors, but also that the tumors showed evidence of the type of cellular damage the T cells are designed to mete out.

"The findings are important because they show that the tumor microenvironment itself, and in particular a specific subset of cells in the tumor, is preventing T cells from trafficking to the tumor and mounting a response," Stromnes said. Importantly, humans also possess cells very similar to Gr-MDSCs, which strengthens the case that similar strategies could impact human pancreas cancer. Additionally, the damage wreaked on Gr-MDSC-depleted tumors appeared to release some of the pressure inside the tumor, allowing crushed blood vessels to open again and providing a potential avenue for chemotherapy.

'We want to put as big a hurt on pancreas cancer as possible'

The results are a backbone on which the team can begin designing a multipronged approach to pancreas cancer therapies, Stromnes noted. The findings show that a T-cell-based therapy alone may not be enough. Researchers must also take into account pancreas cancer's immunosuppressive strategies. "We're trying to get the helpful immune cells into the tumors, and our results show that to do that, we need to get rid of these inhibitory cells the tumors have co-opted," she said.

The team is now working to develop a T-cell therapy to take advantage of their new findings. They plan to test their Gr-MDSC strategy combined with immunotherapy as well as chemotherapy to devise the strongest possible treatment for pancreas cancer.

"Our goal is not incremental advances," Hingorani said. "We want to put as big a hurt on pancreas cancer as possible."

This work was supported by the National Cancer Institute, the Giles W. and Elise G. Mead Foundation, the Safeway Foundation, the Irvington Institute Fellowship Program of the Cancer Research Institute, the Jack & Sylvia Paul Fund to Support Collaborative Immunotherapy Research and the Fred Hutchinson/University of Washington Cancer Consortium.

http://www.eurekalert.org/pub_releases/2014-02/msu-wf1022014.php

With friends like these, who needs democracy?

From Ethiopia to Nicaragua, countries that go through civil war are much less likely to become democratic if the winning side gets help from rival nations, a Michigan State University political scientist argues.

EAST LANSING, Mich. - In a new study examining democratization after civil wars since World War II, Michael Colaresi found the majority of groups that eventually took power failed to establish democratic governments if those groups took money or weapons from a foreign enemy during the war. Receiving such aid can create mistrust among the nation's citizens and make it more difficult for the new regime to institute a democracy, which requires public consent for effective governance, said Colaresi, professor of political science.

"Leaders want to stay in power," Colaresi said. "If they try to build democratic institutions, they would then need public support and trust to continue to govern, which is no easy task if you have received support from enemies the public does not trust."

The study, published in the *Journal of Peace Research*, is the first to show which events within a civil war can help to systematically forecast where post-conflict democratization is likely or unlikely to occur. Past research looked at factors such as the destructiveness of the war and whether the rebel group won, but failed to make a connection to future democracies.

Colaresi studied 136 civil wars from 1946 to 2009, 34 of which involved rivals aiding the winning side. Of those 34 countries, only one – Algeria – bucked the trend by becoming significantly more democratic over the next decade. The others either remained undemocratic or became substantially more repressive after the civil war.

This logic holds even if the public was unaware of the aid during the civil war. Colaresi noted that democracy in most cases involves greater transparency, holding elections, having a free press and an active legislature, meaning those previous unpopular ties eventually would become public – a disincentive to democratize.

In addition, anti-democratic effects of aid hold when the state providing support is itself democratic, such as the United States. "A tie to an unpopular external democracy," Colaresi said, "is still a potential electoral problem." The findings have implications for world leaders trying to establish more democratic societies.

"If we want to build democracy and better human rights in the Middle East and other places," Colaresi said, "we have to understand why groups accept aid from rival nations and help to create incentives that drive it out or at least counterincentives to build new governance."

The study is titled "With friends like these, who needs democracy? The effect of transnational support from rivals on post-conflict democratization."

<http://bit.ly/1fq430J>

New cache of fresh neurons found in human brains

Brain cell regeneration has been discovered in a new location in human brains.

18:51 20 February 2014 by Clare Wilson

The finding raises hopes that these cells could be used to help people recover after a stroke, or to treat other brain diseases.

For years it was unclear whether or not we could generate new brain cells during our lifetime, as the process – neurogenesis – had only been seen in animals. Instead, it was thought that humans, with our large and complex brains, are born with all the required neurons.

Then last year Jonas Frisén of the Karolinska Institute in Stockholm, Sweden, and his colleagues found that neurogenesis occurs in the hippocampi of the human brain. These structures are crucial for memory formation (Cell, DOI: 10.1016/j.cell.2013.05.002)

Now they have found more new brain cells in a second location – golf-ball-sized structures called the striata. These seem to be involved in many different functions, including in learning and memory. These particular aspects, related as they are to the hippocampi, lead Frisén to speculate that these new brain cells may also be involved with learning. "New neurons may convey some sort of plasticity," he says, which might help people learn and adapt to new situations.

Radioactive clue

To reveal the new brain cells, the team exploited the fact that there have been varying levels of a radioactive isotope of carbon – carbon-14 – in the atmosphere since nuclear bomb tests during the cold war. This means that the year of creation of many cells in the body can be found by measuring the ratio of carbon-14 to carbon-12 in its DNA. Analysis of 30 donated brains revealed which brain cells had been born during the lifetimes of the donors.

The finding of new brain cells in the striata solves a long-standing mystery. In rodents, neurogenesis is seen in the hippocampi, as well as another area called the lateral ventricle wall. After they are created, the cells made in this second location migrate to the part of the brain that controls the sense of smell. Hints of neurogenesis had already been seen in the lateral ventricle walls of human brains. But when Frisén looked for new brain cells in human smell centres, he couldn't find any. Now it looks like we know where they ended up.

Arnold Kriegstein at the University of California, San Francisco, agrees that the latest carbon-14 work is confirmation that in humans, the striatum is their destination. "It's nicely demonstrated," he says.

Fresh hope

It is too early to know what these new brain cells are doing in the striata, but any evidence of neurogenesis in the human brain provides fresh hope for the development of treatments for neurodegenerative brain diseases. Frisén's team also found that the donor brains of 11 people who had had Huntington's disease – a rare, degenerative brain disorder – had fewer new neurons in their striata than the donor brains of formerly healthy people. This lack of new neurons may have contributed to the characteristic problems of Huntington's disease, which include movement issues and cognitive deficits.

And immature neurons have in the past been spotted in the striata of people who had had a stroke. "It's very tempting to think that it would be possible to promote the generation of more striatal neurons," says Frisén.

Journal reference: Cell, DOI: 10.1016/j.cell.2014.01.044

http://www.eurekalert.org/pub_releases/2014-02/uok-iyt022114.php

If you think you have Alzheimer's, you just might be right, study suggests

A recent study suggests that self-reported memory complaints might predict clinical memory impairment later in life.

Lexington, Ky. - Erin Abner, Ph.D, an assistant professor at the University of Kentucky's Sanders-Brown Center on Aging, asked 3,701 men aged 60 and higher a simple question: "Have you noticed any change in your memory since you last came in?"

That question led to some interesting results. "It seems that subjective memory complaint can be predictive of clinical memory impairment," Abner said. "Other epidemiologists have seen similar results, which is encouraging, since it means we might really be on to something."

The results are meaningful because it might help identify people who are at risk of developing Alzheimer's Disease sooner. "If the memory and thinking lapses people notice themselves could be early markers of risk for Alzheimer's disease, we might eventually be able to intervene earlier in the aging process to postpone and/or reduce the effects of cognitive memory impairment."

Abner, who is also a member of the faculty in the UK Department of Epidemiology, took pains to emphasize that her work shouldn't necessarily worry everyone who's ever forgotten where they left their keys.

"I don't want to alarm people," she said. "It's important to distinguish between normal memory lapses and significant memory problems, which usually change over time and affect multiple aspects of daily life."

http://www.eurekalert.org/pub_releases/2014-02/aaon-amb021214.php

Antibody may be detectable in blood years before MS symptoms appear

Antibody found in the blood of people with multiple sclerosis (MS) may be present long before the onset of the disease and its symptoms

PHILADELPHIA – An antibody found in the blood of people with multiple sclerosis (MS) may be present long before the onset of the disease and its symptoms, according to a study released today that will be presented at the American Academy of Neurology's 66th Annual Meeting in Philadelphia, April 26 to May 3, 2014.

"If our results can be replicated in larger populations, our findings may help to detect MS earlier in a subgroup of patients," said study author Viola Biberacher, MD, with Technical University in Munich, Germany. "Finding the disease before symptoms appear means we can better prepare to treat and possibly even prevent those symptoms. This finding also demonstrates that the antibody development to the KIR4.1 protein, a protein found in some people with MS, precedes the clinical onset of disease suggesting a role of the autoantibody in how the disease develops."

For the study, 16 healthy blood donors who were later diagnosed with MS were compared to 16 healthy blood donors of the same age and sex who did not develop MS. Scientists looked for a specific antibody to KIR4.1. Samples were collected between two and nine months before the first symptoms of MS appeared.

Next, researchers looked at antibody levels in the blood at additional time points up to six years before and then after disease onset in those who had the KIR4.1 antibody in their blood.

All of the healthy controls tested negative for the KIR4.1 antibody. Of those who later developed MS, seven people tested positive for the antibodies, two showed borderline activity and seven were negative.

In the study, KIR4.1 antibodies were found in the people with pre-clinical MS several years before the first clinical attack. Concentrations of the antibody varied at different time points during pre-MS in individual people. "The next step is to confirm these findings in larger groups and determine how many years before onset of disease the antibody response develops," said Biberacher.

The study was supported by the German Ministry for Education and Research and the German Competence Network for Multiple Sclerosis.

http://www.eurekalert.org/pub_releases/2014-02/uow-obo022014.php

Oldest bit of crust firms up idea of a cool early Earth

With the help of a tiny fragment of zircon extracted from a remote rock outcrop in Australia, the picture of how our planet became habitable to life about 4.4 billion years ago is coming into sharper focus.

MADISON, Wis. – Writing today (Feb. 23, 2014) in the journal *Nature Geoscience*, an international team of researchers led by University of Wisconsin-Madison geoscience Professor John Valley reveals data that confirm the Earth's crust first formed at least 4.4 billion years ago, just 160 million years after the formation of our solar system. The work shows, Valley says, that the time when our planet was a fiery ball covered in a magma ocean came earlier.

"This confirms our view of how the Earth cooled and became habitable," says Valley, a geochemist whose studies of zircons, the oldest known terrestrial materials, have helped portray how the Earth's crust formed during the first geologic eon of the planet. "This may also help us understand how other habitable planets would form."

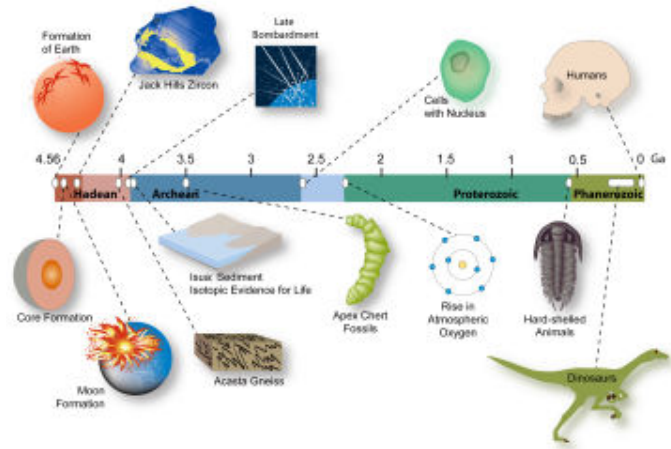
The new study confirms that zircon crystals from Western Australia's Jack Hills region crystallized 4.4 billion years ago, building on earlier studies that used lead isotopes to date the Australian zircons and identify them as the oldest bits of the Earth's crust. The microscopic zircon crystal used by Valley and his group in the current study is now confirmed to be the oldest known material of any kind formed on Earth.

The study, according to Valley, strengthens the theory of a "cool early Earth," where temperatures were low enough for liquid water, oceans and a hydrosphere not long after the planet's crust congealed from a sea of molten rock. "The study reinforces our conclusion that Earth had a hydrosphere before 4.3 billion years ago," and possibly life not long after, says Valley.

The study was conducted using a new technique called atom-probe tomography that, in conjunction with secondary ion mass spectrometry, permitted the scientists to accurately establish the age and thermal history of the zircon by determining the mass of individual atoms of lead in the sample. Instead of being randomly distributed in the sample, as predicted, lead atoms in the zircon were clumped together, like "raisins in a pudding," notes Valley.

The clusters of lead atoms formed 1 billion years after crystallization of the zircon, by which time the radioactive decay of uranium had formed the lead atoms that then diffused into clusters during reheating. "The zircon formed 4.4 billion years ago, and at 3.4 billion years, all the lead that existed at that time was concentrated in these hotspots," Valley says. "This allows us to read a new page of the thermal history recorded by these tiny zircon time capsules."

The formation, isotope ratio and size of the clumps — less than 50 atoms in diameter — become, in effect, a clock, says Valley, and verify that existing geochronology methods provide reliable and accurate estimates of the sample's age. In addition, Valley and his group measured oxygen isotope ratios, which give evidence of early homogenization and later cooling of the Earth.



A timeline of the history of our planet places the formation of the Jack Hills zircon and a "cool early Earth" at 4.4 billion years. Credit: Timeline courtesy of Andree Valley

"The Earth was assembled from a lot of heterogeneous material from the solar system," Valley explains, noting that the early Earth experienced intense bombardment by meteors, including a collision with a Mars-sized object about 4.5 billion years ago "that formed our moon, and melted and homogenized the Earth. Our samples formed after the magma oceans cooled and prove that these events were very early."

The new study was supported by grants from the National Science Foundation, Department of Energy and the NASA Astrobiology Institute.

http://www.eurekalert.org/pub_releases/2014-02/aaon-mpi021214.php

Mysterious polio-like illness found in 5 California children

Researchers have identified a polio-like syndrome in a cluster of children from California over a one-year period

PHILADELPHIA — Researchers have identified a polio-like syndrome in a cluster of children from California over a one-year period, according to a case report released today that will be presented at the American Academy of Neurology's 66th Annual Meeting in Philadelphia, April 26 to May 3, 2014.

"Although poliovirus has been eradicated from most of the globe, other viruses can also injure the spine, leading to a polio-like syndrome," said case report author Keith Van Haren, MD, with Stanford University in Palo Alto, Calif., and a member of the American Academy of Neurology. Van Haren also works with co-author Emanuelle Waubant, MD, University of California, San Francisco. "In the past decade, newly identified strains of enterovirus have been linked to polio-like outbreaks among children in Asia and Australia. These five new cases highlight the possibility of an emerging infectious polio-like syndrome in California."

Polio is a contagious disease that sometimes caused paralysis. The United States experienced a polio epidemic in the 1950s, until a vaccine was introduced.

Van Haren said he and his colleagues noticed several of these cases at their medical centers and decided to look for similar cases in California. They reviewed all polio-like cases among children who had samples referred to California's Neurologic and Surveillance Testing program from August 2012 to July 2013. Cases were included in the analysis if the children had paralysis affecting one or more limbs with abnormal MRI scans of the spinal cord that explained the paralysis. They did not include children who met criteria for Guillain-Barré syndrome and botulism, which can cause similar symptoms.

The five children experienced paralysis of one or more arms or legs that came on suddenly and reached the height of its severity within two days of onset. Three of the children had a respiratory illness before the symptoms began. All of the children had been previously vaccinated against poliovirus.

The children were treated but their symptoms did not improve and they still had poor limb function after six months. Two children tested positive for enterovirus-68, a rare virus previously associated with polio-like symptoms. No cause was identified in the remaining three children.

"Our findings have important implications for disease surveillance, testing and treatment," said Van Haren.

"We would like to stress that this syndrome appears to be very, very rare. Any time a parent sees symptoms of paralysis in a child, the child should be seen by a doctor right away."

The case report was supported by the McHugh/Sprague Award from the Lucile Packard Foundation.

http://www.eurekalert.org/pub_releases/2014-02/uob-nii022114.php

New insights into the origin of birds

The key characteristics of birds which allow them to fly -- their wings and their small size -- arose much earlier than previously thought - the first birds and their closest dinosaurian relatives which lived 160 to 120 million years ago.

Mark Puttick and colleagues investigated the rates of evolution of the two key characteristics that preceded flight: body size and forelimb length. In order to fly, hulking meat-eating dinosaurs had to shrink in size and grow much longer arms to support their feathered wings.

"We were really surprised to discover that the key size shifts happened at the same time, at the origin of Paraves," said Mr Puttick of Bristol's School of Earth Sciences. "This was at least 20 million years before the first bird, the famous Archaeopteryx, and it shows that flight in birds arose through several evolutionary steps." Being small and light is important for a flyer, and it now seems a whole group of dozens of little dinosaurs were lightweight and had wings of one sort or another. Most were gliders or parachutists, spreading their feathered wings, but not flapping them.

"Out of all these flappers and gliders, only the birds seem to have been capable of powered flight," said co-author Mike Benton, Professor of Vertebrate Palaeontology at Bristol.

"But you wouldn't have picked out Archaeopteryx as the founder of a remarkable new group."

The study applied new numerical methods that calculate the rate of evolution of different characteristics across a whole evolutionary tree, and identify where bursts of fast evolution occurred.

"Up to now you could only have guessed roughly where the major evolutionary transitions occurred," said Dr Gavin Thomas of the University of Sheffield, "but the new methods pinpoint the size changes. The small size of birds and their long wings originated long before birds themselves did."

Birds owe their success to their flight, wings and feathers. Until the 1990s, when the first feathered dinosaurs were found in China, birds were thought to have originated rapidly, marking a major transition from dinosaurs. Now, we know that Archaeopteryx was only one of a large number of small, flying dinosaurs.

"The origin of birds used to be seen as a rapid transition," said Mark Puttick, "but now we know that the key characteristics we associate with them arose much earlier."

http://www.eurekalert.org/pub_releases/2014-02/cumc-rp022014.php

Researchers pinpoint brain region essential for social memory

Potential target for treating autism, schizophrenia, and other brain disorders

NEW YORK, NY - Columbia University Medical Center (CUMC) researchers have determined that a small region of the hippocampus known as CA2 is essential for social memory, the ability of an animal to recognize another of the same species. A better grasp of the function of CA2 could prove useful in understanding and treating disorders characterized by altered social behaviors, such as autism, schizophrenia, and bipolar disorder. The findings, made in mice, were published today in the online edition of Nature.

Scientists have long understood that the hippocampus—a pair of seahorse-shaped structures in the brain's temporal lobes—plays a critical role in our ability to remember the who, what, where, and when of our daily lives. Recent studies have shown that different subregions of the hippocampus have different functions. For instance, the dentate gyrus is critical for distinguishing between similar environments, while CA3 enables us to recall a memory from partial cues (e.g., Proust's famous madeleine). The CA1 region is critical for all forms of memory.

"However, the role of CA2, a relatively small region of the hippocampus sandwiched between CA3 and CA1, has remained largely unknown," said senior author Steven A. Siegelbaum, PhD, professor of neuroscience and pharmacology, chair of the Department of Neuroscience, a member of the Mortimer B. Zuckerman Mind Brain Behavior Institute and Kavli Institute for Brain Science, and a Howard Hughes Medical Institute Investigator. A few studies have suggested that CA2 might be involved in social memory, as this region has a high level of expression of a receptor for vasopressin, a hormone linked to sexual motivation, bonding, and other social behaviors.

To learn more about this part of the hippocampus, the researchers created a transgenic mouse in which CA2 neurons could be selectively inhibited in adult animals. Once the neurons were inhibited, the mice were given a series of behavioral tests. "The mice looked quite normal until we looked at social memory," said first author Frederick L. Hitti, an MD-PhD student in Dr. Siegelbaum's laboratory, who developed the transgenic mouse. "Normally, mice are naturally curious about a mouse they've never met; they spend more time investigating an unfamiliar mouse than a familiar one. In our experiment, however, mice with an inactivated CA2 region

showed no preference for a novel mouse versus a previously encountered mouse, indicating a lack of social memory."

In two separate novel-object recognition tests, the CA2-deficient mice showed a normal preference for an object they had not previously encountered, showing that the mice did not have a global lack of interest in novelty. In another experiment, the researchers tested whether the animals' inability to form social memories might have to do with deficits in olfaction (sense of smell), which is crucial for normal social interaction. However, the mice showed no loss in ability to discriminate social or non-social odors.

In humans, the importance of the hippocampus for social memory was famously illustrated by the case of Henry Molaison, who had much of his hippocampus removed by surgeons in 1953 in an attempt to cure severe epilepsy. Molaison (often referred to as HM in the scientific literature) was subsequently unable to form new memories of people. Scientists have observed that lesions limited to the hippocampus also impair social memory in both rodents and humans.

"Because several neuropsychiatric disorders are associated with altered social behaviors, our findings raise the possibility that CA2 dysfunction may contribute to these behavioral changes," said Dr. Siegelbaum. This possibility is supported by findings of a decreased number of CA2 inhibitory neurons in individuals with schizophrenia and bipolar disorder and altered vasopressin signaling in autism. Thus, CA2 may provide a new target for therapeutic approaches to the treatment of social disorders.

The paper is titled, "The hippocampal CA2 region is essential for social memory."

The study was supported by a Ruth L. Kirschstein F30 National Research Service Award from the National Institute of Mental Health and the Howard Hughes Medical Institute. The authors declare no financial or other conflicts of interests.

<http://www.bbc.co.uk/news/science-environment-26258662>

How do we really make decisions?

With every decision you take, every judgement you make, there is a battle in your mind - a battle between intuition and logic.

By Toby Macdonald Producer, Horizon: How You Really Make Decisions

And the intuitive part of your mind is a lot more powerful than you may think.

Most of us like to think that we are capable of making rational decisions. We may at times rely on our gut instinct, but if necessary we can call on our powers of reason to arrive at a logical decision. We like to think that our beliefs, judgements and opinions are based on solid reasoning. But we may have to think again.

Prof Daniel Kahneman, from Princeton University, started a revolution in our understanding of the human mind. It's a revolution that led to him winning a Nobel Prize. His insight into the way our minds work springs from the mistakes that we make. Not random mistakes, but systematic errors that we all make, all the time, without realising.

Prof Kahneman and his late colleague Amos Tversky, who worked at the Hebrew University of Jerusalem and Stanford University, realised that we actually have two systems of thinking. There's the deliberate, logical part of your mind that is capable of analysing a problem and coming up with a rational answer.

This is the part of your mind that you are aware of. It's expert at solving problems, but it is slow, requires a great deal of energy, and is extremely lazy. Even the act of walking is enough to occupy most of your attentive mind. If you are asked to solve a tricky problem while walking, you will most likely stop because your attentive mind cannot attend to both tasks at the same time. If you want to test your own ability to pay attention, try the invisible gorilla test devised by Chris Chabris and Daniel Simon.

But then there is another system in your mind that is intuitive, fast and automatic. This fast way of thinking is incredibly powerful, but totally hidden. It is so powerful, it is actually responsible for most of the things that you say, do, think and believe. And yet you have no idea this is happening. This system is your hidden auto-pilot, and it has a mind of its own. It is sometimes known as the stranger within.

Most of the time, our fast, intuitive mind is in control, efficiently taking charge of all the thousands of decisions we make each day. The problem comes when we allow our fast, intuitive system to make decisions that we really should pass over to our slow, logical system. This is where the mistakes creep in.

Our thinking is riddled with systematic mistakes known to psychologists as cognitive biases. And they affect everything we do. They make us spend impulsively, be overly influenced by what other people think. They affect our beliefs, our opinions, and our decisions, and we have no idea it is happening.

It may seem hard to believe, but that's because your logical, slow mind is a master at inventing a cover story. Most of the beliefs or opinions you have come from an automatic response. But then your logical mind invents a reason why you think or believe something.

According to Daniel Kahneman, "if we think that we have reasons for what we believe, that is often a mistake. Our beliefs and our wishes and our hopes are not always anchored in reasons".

Since Kahneman and Tversky first investigated this radical picture of the mind, the list of identified cognitive biases has mushroomed. The "present bias" causes us to pay attention to what is happening now, but not to worry about the future. If I offer you half a box of chocolates in a year's time, or a whole box in a year and a day, you'll probably choose to wait the extra day.

But if I offer you half a box of chocolates right now, or a whole box of chocolates tomorrow, you will most likely take half a box of chocolates now. It's the same difference, but waiting an extra day in a year's time seems insignificant. Waiting a day now seems impossible when faced with the immediate promise of chocolate.

According to Prof Dan Ariely, from Duke University in North Carolina, this is one of the most important biases: "That's the bias that causes things like overeating and smoking and texting and driving and having unprotected sex," he explains.

Confirmation bias is the tendency to look for information that confirms what we already know. It's why we tend to buy a newspaper that agrees with our views. There's the hindsight bias, the halo effect, the spotlight effect, loss aversion and the negativity bias. This is the bias that means that negative events are far more easily remembered than positive ones. It means that for every argument you have in a relationship, you need to have five positive memories just to maintain an even keel.

The area of our lives where these cognitive biases cause most grief is anything to do with money. It was for his work in this area that Prof Kahneman was awarded the Nobel Prize - not for psychology (no such prize exists) but for economics. His insights led to a whole new branch of economics - behavioural economics.

Kahneman realised that we respond very differently to losses than to gains. We feel the pain of a loss much more than we feel the pleasure of a gain. He even worked out by how much. If you lose £10 today, you will feel the pain of the loss. But if you find some money tomorrow, you will have to find more than £20 to make up for the loss of £10. This is loss aversion, and its cumulative effect can be catastrophic.

One difficulty with the traditional economic view is that it tends to assume that we all make rational decisions. The reality seems to be very different. Behavioural economists are trying to form an economic system based on the reality of how we actually make decisions.

Dan Ariely argues that the implications of ignoring this research are catastrophic: "I'm quite certain if the regulators listened to behavioural economists early on we would have designed a very different financial system, and we wouldn't have had the incredible increase in the housing market and we wouldn't have this financial catastrophe," he says. These biases affect us all, whether we are choosing a cup of coffee, buying a car, running an investment bank or gathering military intelligence.

So what are we to do? Dr Laurie Santos, a psychologist at Yale University, has been investigating how deep seated these biases really are. Until we know the evolutionary origins of these two systems of thinking, we won't know if we can change them.

Dr Santos taught a troop of monkeys to use money. It's called monkeynomics, and she wanted to find out whether monkeys would make the same stupid mistakes as humans. She taught the monkeys to use tokens to buy treats, and found that monkeys also show loss aversion - making the same mistakes as humans.

Her conclusion is that these biases are so deep rooted in our evolutionary past, they may be impossible to change.

"What we learn from the monkeys is that if this bias is really that old, if we really have had this strategy for the last 35 million years, simply deciding to overcome it is just not going to work. We need other ways to make ourselves avoid some of these pitfalls," she explained.

We may not be able to change ourselves, but by being aware of our cognitive limitations, we may be able to design the environment around us in a way that allows for our likely mistakes.

Dan Ariely sums it up: "We are limited, we are not perfect, we are irrational in all kinds of ways. But we can build a world that is compatible with this that gets us to make better decisions rather than worse decisions.

That's my hope."

<http://phys.org/news/2014-02-cooking-oil-based-bioasphalt.html>

Researcher creates cooking-oil-based 'bioasphalt'

A Washington State University researcher has developed a way to use restaurant cooking oil in a type of asphalt that looks and handles just like its petroleum-based counterpart.

The road surface developed by Haifang Wen, assistant professor in Civil Engineering in the WSU Department of Civil and Environmental Engineering, may soon have Washington motorists driving the first highways in the nation paved with waste cooking oil-based asphalt.

"We are shooting for summer 2014 to construct a trial road—probably at least a quarter mile long," Wen said.

Wen recently received a 2014 Federal Highway Administration grant of \$1 million to continue his research. It follows a \$190,000 grant from the National Science Foundation.

Faced with increasing petroleum prices, new environmental regulations, and changes to the crude oil refining process, asphalt has become a scarce and costly commodity. Made from the residue left behind after production of gasoline, plastics, and other materials, lowly asphalt still commands \$700-800 per ton, or half the price of gasoline at \$1,500 per ton, Wen estimates.

"Every year in the U.S., we use about 30 million tons of asphalt binder for roads," more if you include roofing shingles," Wen said. "It's easily a multi-billion dollar business."

But, it's also a business that will need to make inroads into an industry that hasn't changed much over the years. "Only in the last decade has the green asphalt industry started coming together," Wen said. "It's slowly picking up—more slowly than I wish."

In Iowa, for example, scientists are making a corn-based bioasphalt from residue left after the production of ethanol. In North Carolina, swine manure is being incorporated as a paving substitute.

"Building roads is a big investment in taxpayer money," said Wen. "In general, a one-mile road in a rural area costs at least a million dollars to build. With the waste cooking oil technology, we can reduce the cost of asphalt binder to under \$200 per ton, making road building much cheaper."

Asphalt binder, the sticky "glue" that holds crushed stone and sand together to form pavement, only accounts for about five percent of the final hot mix asphalt (HMA) that is steamrolled into glossy new lanes and boulevards.

HMA has to be tough and reliable, able to withstand the ravages of heavy trucks as well as the extremes of Mother Nature. In Wen's lab, each component of his bioasphalt is subjected to a series of rigorous stress tests, such as intense heat, freezing temperatures, compression, and loading.

After four years working with a chemist and "adjusting the recipe," Wen is confident that his green, sustainable asphalt "is as good as the old-school petroleum asphalt."

"I am very excited to have patented a solid technology."

All of which has the undivided attention of both federal and state highway agencies. Wen has been collaborating with both and says the industry is "very interested and eagerly awaiting the roll out of (his) product."

Nationwide, it's an industry that supports more than 300,000 Americans in about 4,000 asphalt plants, one in every congressional district, according to the National Asphalt Pavement Association.

Wen's waste cooking oil asphalt study also fits with President Obama's 2012 Moving Ahead for Progress in the 21st Century Act (MAP-21)—where Congress is addressing the need for sustainability in the national infrastructure system, including surface transportation.