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Growing evidence that probiotics are good for your liver

In mice, probiotic treatment shown to protect against liver damage from acetaminophen

Increased awareness of the importance of the microbes that live in our gut has spurred a great deal of research on the microbiome and fueled a booming probiotics industry. A new study suggests probiotics can improve not only the health of our gut but liver health, as well.

"Probiotics have been studied most intensely in the context of the gastrointestinal tract," said Bejan Saeedi, a doctoral candidate at Emory University who conducted the research. "This study provides evidence that the effects of probiotics extend beyond the gastrointestinal tract. What makes this study unique is that it suggests a discreet molecular mechanism by which these effects are elicited."

Saeedi will present the research at the American Society for Investigative Pathology annual meeting during the 2018 Experimental Biology meeting, held April 21-25 in San Diego.

The vast populations of microbes that reside on and inside of our bodies have been shown to play a role in numerous functions that keep our bodies healthy. Probiotics are bacteria that are consumed or administered in an effort to boost the populations of these beneficial microbes.

Saeedi and his colleagues focused their study on the probiotic Lactobacillus rhamnosus GG (known as LGG), a species common in many over-the-counter probiotic formulations. They gave mice food laced with LGG for two weeks and then examined how they responded to a high dose of acetaminophen (the active ingredient in Tylenol®).

Taking too much acetaminophen can cause serious liver damage and even death by increasing the abundance of a form of oxygen called free radicals, a process known as oxidative stress. However, the researchers found that mice receiving the probiotic treatment suffered less liver damage when presented with an overdose of acetaminophen compared with mice that did not receive probiotics.

"Administration of the probiotic LGG to mice improves the antioxidant response of the liver, protecting it from oxidative damage produced by drugs such as acetaminophen," explained Saeedi.

The liver is a hub for removing toxins from the blood and plays an important role in the body's processes for converting food into energy. Since it is "downstream" of the gastrointestinal tract in the digestive process, it makes sense that the composition of bacteria in the gut could affect the functioning of the liver.

Previous research by Saeedi's colleagues has traced the molecular process by which LGG appears to protect against oxidative liver injury. That research points to the role of a protein called Nrf2, which regulates the expression of genes involved in fighting free radicals.

Other studies in mice have previously shown that LGG can protect against alcoholic liver disease and non-alcoholic fatty liver disease. Saeedi said studies in human volunteers would be needed to definitively test the potential clinical benefits of LGG in humans.

Bejan Saeedi will present this research on Sunday, April 22, from 2:45-3 p.m. in Room 4, San Diego Convention Center (abstract) and on Tuesday, April 24, from 5:30-7:30 p.m. in Ballroom 20BC (poster 150.4). Contact the media team for more information or to obtain a free press pass to attend the meeting.

http://bit.ly/2HwDrxw

Multiple sclerosis may be linked to sheep disease toxin

Exposure to a toxin primarily found in sheep could be linked to the development of multiple sclerosis (MS) in humans, new research suggests.

Carried out by the University of Exeter and MS Sciences Ltd., the study has found that people with MS are more likely than other people to have antibodies against the Epsilon toxin, or ETX, - suggesting they may have been exposed to the toxin at some time.

ETX, produced in the gut of livestock by the bacterium *Clostridium perfringens*, damages the animal's brain and can kill them.

While the toxin can also occur in the gut of other animals, and even in soil, it has mostly been studied as the cause of a type of blood poisoning in sheep, known as enterotoxaemia.

"Our research suggests that there is a link between epsilon toxin and MS," said Professor Rick Titball, of the University of Exeter. "The causes of MS are still not fully understood and, while it's possible that this toxin plays a role, it's too early to say for certain.

"More research is now needed to understand how the toxin might play a role in MS, and how these findings might be used to develop new tests or treatments."

Following reports that some MS patients in the US had antibodies against epsilon toxin, the Exeter researchers tested UK patients for such antibodies.

Using two different methods, 43% of MS patients were found to be positive for antibodies to epsilon toxin, in comparison to 16% of people in a control group. "There is a growing body of wider evidence that points to a hypothesis linking MS and ETX, and we are confident that these significant findings from our latest study will help people get even closer to an answer for the elusive triggers of MS," said Simon Slater, Director of MS Sciences Ltd.

"If the link between epsilon toxin and MS is proven, then this would suggest that vaccination would be an effective treatment for its prevention or in the early stages of the disease.

"Interestingly, although epsilon toxin is known to be highly potent, no human vaccine has ever been developed."

MS, most commonly diagnosed in people in their 20s and 30s, can affect the brain, causing a wide range of potential symptoms including problems with vision, arm or leg movement, sensation and balance.

It's estimated that there are more than 100,000 people diagnosed with MS in the UK.

The research was funded by MS Sciences Ltd and the National Institute for Health Research Exeter Clinical Research Facility.

Samples for the research were provided by Barts Health NHS Trust, Imperial College London and the University of Exeter Medical School.

The paper, published in the Multiple Sclerosis Journal, is entitled: "Evidence of Clostridium perfringens epsilon toxin associated with multiple sclerosis."

http://bit.ly/2Ficdc9

Researchers discover potential source of gender differences in migraines

Findings could lead to better treatments for men and women who suffer from migraines

Of the more than 38 million Americans who experience migraine headaches, 28 million are women. Compared to men, women also experience more frequent and severe migraines and don't respond as well to drug treatments.

Findings from a new study conducted in rats reveal that females may be more susceptible to migraines and less responsive to treatment because of the way fluctuations in the hormone estrogen affect cells in the brain.

Emily Galloway, an undergraduate research assistant in the laboratory of Tally Largent-Milnes in the Department of Pharmacology at the University of Arizona in Tucson, will present this research at the American Society for Biochemistry and Molecular Biology annual meeting during the 2018 Experimental Biology meeting to be held April 21-25 in San Diego.

"Conducting research on the molecular mechanisms behind migraine is the first step in creating more targeted drugs to treat this condition, for men and women," said Galloway. "Knowledge gained from this work could lead to relief for millions of those who suffer from migraines and identify individuals who may have better responses to specific therapies."

The new study is one of the first to examine the role of the sodium proton exchanger NHE1 in migraine headaches. NHE1 regulates the transport of protons and sodium ions across cell membranes, including those that make up the blood-brain barrier. When NHE1 isn't present at high enough levels or doesn't function properly, it can cause increased pain signaling that leads to a migraine. Problems with NHE1 can also directly alter the ability of migraine drugs to cross the blood-brain barrier.

Even though women are much more likely to experience migraines than men, most migraine research is conducted using male animal models. In the new study, the researchers examined both male and female rats and found NHE1 expression levels were four times higher in the brains of the male rats. In the female rats, they observed that the highest estrogen levels corresponded with the lowest levels of NHE1 expressed in the endothelial cells that form the blood vessels in the brain.

"Based on our findings, we think that women are more susceptible to migraine because the larger magnitude sex hormone fluctuations lead to changes in NHE1 expression, which may leave the brain vulnerable to ion dysregulation and pain activation," said Galloway.

The new work is part of an effort to create a molecular map of how sex hormones affect NHE1 expression. In the future, the researchers want to see if drugs that target certain players in this map would prevent dysregulation of NHE1 expression at the blood brain barrier. This could lead to new treatments for people who suffer from migraines.

Emily Galloway will present the findings during the Signal Transduction and Cellular Regulation Session from 12:15-1:00 p.m. Sunday, April 22, in Exhibit Halls A-D, San Diego Convention Center (poster B291 553.60) (abstract). Contact the media team for more information or to obtain a free press pass to attend the meeting.

http://bit.ly/2HsKqeT

A common anti-inflammatory therapy may help reduce risk of developing Parkinson's disease

Mount Sinai shows potential link between Parkinson's disease and inflammatory bowel disease, suggests anti-TNFα therapy may reduce the risk of developing Parkinson's disease

A recent study from researchers at the Icahn School of Medicine at Mount Sinai provides new insights into a link between inflammatory bowel disease (IBD) and Parkinson's disease, and may have significant implications for the treatment and prevention of Parkinson's disease.

The recent study, published in *JAMA Neurology*, shows that individuals with IBD are at a 28% higher risk of developing Parkinson's disease than those without IBD. However, if they are treated with anti-Tumor Necrosis Factor alpha (anti-TNFα) therapy, a monoclonal antibody that is commonly used to control inflammation in IBD patients, then their risk of developing Parkinson's disease goes down significantly, and becomes even lower than that in the general population.

These new insights will allow for better screening of IBD patients for Parkinson's disease, given that IBD onset usually precedes that of Parkinson's disease by decades, and they also offer evidence to support exploring anti-TNFα therapy to prevent Parkinson's disease in at-risk individuals.

While previous research had shown genetic and functional connections between IBD and Parkinson's disease, clinical evidence linking the two has been scarce. The authors of the study previously identified a number of genetic variants that contributed to either an increased risk of both Parkinson's disease and of Crohn's disease, a type of IBD, or a decreased risk of both diseases, which prompted them to further study the co-occurrence of the two diseases.

"Systemic inflammation is a major component of IBD, and it's also thought to contribute to the neuronal inflammation found in Parkinson's disease," explained Inga Peter, Professor in the Department of Genetics and Genomic Sciences at Mount Sinai and lead investigator in the study. "We wanted to determine if anti-TNFα therapy, could mitigate a patient's risk in developing Parkinson's disease."

The Mount Sinai team found a 78% reduction in the incidence of Parkinson's disease among IBD patients who were treated with anti-TNFα therapy when compared to those who were not.

It was previously thought that anti-TNFα therapies had limited effects on the central nervous system, the site where molecular mechanisms of Parkinson's disease are found, because the large molecules in the anti-TNFα compounds cannot independently pass through the blood brain barrier. The outcomes of this study suggest that it may not be necessary for the drug to pass through the blood brain barrier to treat or prevent inflammation within the central nervous system, or that the blood-brain barrier in patients with IBD may be compromised, allowing the large molecules of the compound to pass through.

Parkinson's disease ranks among the most common late-life neurodegenerative diseases, affecting approximately 1-2% of people 60 years or older. "Current therapies for Parkinson's disease focus on ameliorating symptoms," said Peter, "Our findings provide promising insights that support further investigations into how reducing systemic inflammation could help treat or prevent Parkinson's disease."

http://bit.ly/2r6R8NF

Asthma and hay fever linked to increased risk of psychiatric disorders

A new study is the first to find a significant link between common allergic diseases and a broad spectrum of psychiatric disorders

Patients with asthma and hay fever have an increased risk of developing psychiatric disorders, finds a new study published in open-access journal *Frontiers in Psychiatry*. Almost 11% of patients with common allergic diseases developed a psychiatric disorder within a 15-year period, compared to only 6.7% of those without - a 1.66-fold increased risk. While previous studies have linked allergies with certain psychiatric or emotional disorders, this is the first to find a connection between common allergies and the overall risk of developing psychiatric disorders. The findings could have implications for how doctors care for and monitor patients with allergic diseases.

Asthma, allergic rhinitis (hay fever) and atopic dermatitis (eczema), are among some of the most common allergic diseases and are nicknamed the three "A"s. Dr. Nian-Sheng Tzeng , from Tri-Service General Hospital in Taiwan and lead author of the study, noticed something unexpected about these patients.

"As a clinician, I observed that some patients with the three 'A's appeared to suffer emotionally," says Tzeng. "Therefore, I wanted to clarify whether these allergic diseases are associated with psychiatric disorders."

When Tzeng and colleagues searched the literature, they found that previous studies had reported links between allergic diseases and specific psychiatric disorders or emotional problems. For example, a study in Denmark found that children with allergic diseases had more emotional and behavioral problems.

However, not all previous research supported this positive link, with one study in Taiwan suggesting that allergic rhinitis is less common among patients with schizophrenia, for example. Clearly, more extensive research was needed for a more complete picture.

Despite the previous research, no-one had studied the link between the three "A"s and the overall risk of developing psychiatric disorders. To study this in a large sample of people, the researchers used an extensive database of health insurance claims in Taiwan, covering a 15-year period.

The researchers identified 46,647 people in the database with allergic diseases and 139,941 without. Unlike previous studies, the researchers included patients of all ages. They found that over the 15-year period, 10.8% of people with allergic diseases developed a psychiatric disorder, compared with 6.7% of those with no allergic disease. This translated to a 1.66-fold increased risk of developing psychiatric disorders for people with an allergic disease.

A closer look at the data revealed that people with atopic dermatitis had a lower risk of developing a psychiatric disorder, while those with asthma and allergic rhinitis had a higher risk. Interestingly, the team discovered that using certain asthma medications was associated with a lower risk of psychiatric disorders in asthma patients.

So, why might patients with certain allergic diseases have a higher risk of psychiatric disorders? Recent research suggests that inflammation is linked to psychiatric disorders, such as depression and anxiety disorders. As allergies also involve inflammation, it is possible that it may contribute to psychiatric disorders in the same patients. The psychological stress of a psychiatric disorder might also contribute to physical symptoms.

The current study did not examine the potential cause of this phenomenon and researchers need to complete further studies to identify the precise mechanisms involved. However, knowing that there

is a link between allergic diseases and psychiatric disorders could help doctors to care for their patients.

"We would like to let clinicians who care for patients with allergic diseases know that their risk for psychiatric diseases may be higher," says Tzeng. "Assessing their emotional condition and monitoring their mental health could help to avoid later psychiatric problems."

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http://bit.ly/2Fi2jXS

Dementia trend shows later onset with fewer years of the disease

People may be developing dementia later and living with it for less time

SAN ANTONIO, Texas -- The diagnosis is one that a family never wants to hear: Your father has Alzheimer's disease. Your mother has stroke-related dementia.

A recently released study, included in a special supplement to the *Journal of Gerontology*, indicates that dementia's impact might be compressing a bit. That is, people might be developing dementia later and living with it for a shorter period of time.

Sudha Seshadri, M.D., professor of neurology and founding director of the Glenn Biggs Institute for Alzheimer's & Neurodegenerative Diseases at UT Health San Antonio, is the senior author on the study, which draws evidence from the Framingham Heart Study.

In data from four different time periods over a period of 30 years, the mean age at dementia onset increased, while the length of time living with dementia decreased. Is it because prevention and care of stroke today is superior compared to decades ago? Stroke is a major risk factor for dementia.

"Prevention of stroke and reduced impact of stroke are great advances, but neither completely explains the trend we are seeing," Dr. Seshadri said. "We are looking at other causes, such as lower burden of multiple infections because of vaccination, and possibly lower levels of lead or other pollutants in the atmosphere. Early education and nutrition might also play a role."

Stroke risk has decreased because of greater control of blood pressure. Dr. Seshadri again cited Framingham data: "In the past, if you had a stroke you were at 90 percent greater risk to develop dementia. Today, you have a 40 percent greater risk," she said.

http://bit.ly/2vRkPHa

Six in 7 women at high risk of breast cancer shun tamoxifen as a preventative measure

Six in seven women with a family history of breast cancer opt out of taking tamoxifen as a preventative measure, according to a study funded by Cancer Research UK and published in* Breast Cancer Research and Treatment *today (Tuesday)*.

Researchers asked 258 healthy women across England who had been identified as having an increased risk of the disease whether they had agreed to take the drug to help prevent breast cancer developing, and interviewed 16 women to identify what influenced their decision to take it.

Women chose not to start taking the drug because they thought cancer was down to fate, they distrusted medication in general or they feared side effects would interfere with looking after their family.

But overall the team, based at the University of Leeds, Northwestern University, University College London and Queen Mary University of London, found women with children were more likely to take up the offer of tamoxifen.

The research, which is the first of its kind since the drug was approved to be used for prevention, also suggested that social class, educational attainment and ethnicity had no effect on uptake.

Tamoxifen is most commonly given to women who have been treated for breast cancer to lower the risk of it recurring.

But in 2013 the National Institute for Health and Care Excellence (NICE) also approved it for cancer prevention in women at increased risk of the disease due to a family history of breast or ovarian cancer,

following research which showed it could lower risk by around a third**.

Dr Samuel Smith, study author from the University of Leeds, said: "While it's reassuring a woman's background doesn't seem to be a barrier to taking tamoxifen, only one in seven of those at increased risk of breast cancer are taking up the option. Therefore it's important doctors can discuss women's concerns and provide information to help them while they are considering their options.

"Further research is needed to understand if all women eligible to take tamoxifen for prevention are getting the help and support they need."

Dr Richard Roope, Cancer Research UK's senior clinical adviser and GP expert, said: "When an established drug like tamoxifen is found to work not only as a treatment for breast cancer, but is also shown to reduce the risk of the disease, it seems we're making real progress.

"It's valuable to understand why women might reject tamoxifen, and this research highlights there are a range of complex reasons behind the decision. "It's vital more work is done to understand these barriers, improve treatments and ensure doctors are getting the support they need to help women decide whether preventative medication is right for them.

"Whatever a woman's risk of developing breast cancer, keeping a healthy weight and cutting back on alcohol are also ways of reducing it."

*Hackett J., Thorneloe R., Side L., Wolf M., Horne R., Cuzick J., Smith S.G. (2018) Uptake of breast cancer preventive therapy in the UK: results from a multicentre prospective survey and qualitative interviews. Breast Cancer Research and Treatment DOI:10.1007/s10549-018-4775-1

http://bit.ly/2vR9Zkx

Vitamin A derivative selectively kills liver cancer stem cells

Acyclic retinoid targets one class of cancer stem cells, preventing them from giving rise to new tumors

Acyclic retinoid, an artificial compound derived from vitamin A, has been found to prevent the recurrence of hepatocellular carcinoma (HCC), the most common form of liver cancer. Now, in research published in Proceedings of the National Academy of Sciences, scientists have discovered that the compound targets one class of cancer stem cells, preventing them from giving rise to new tumors.

HCC is a highly lethal cancer, which causes approximately 600,000 deaths each year around the world, making it the second deadliest cancer after non-small cell lung cancer. One of the reasons for the high lethality is that it has a high rate of recurrence--surgery and other treatments are initially effective, but the cancer often relapses. As a result, researchers have looked for ways to prevent recurrence, and acyclic retinoid was recently found to be effective in stopping recurrence of tumors. However, scientists were not sure exactly why it worked.

To find clues, a research group led by Soichi Kojima of the RIKEN Center for Integrative Medical Science looked at the transcriptome of cells that had been exposed to acyclic retinoid, and found that compared to control untreated cells, they had low expression of MYCN, a gene that is often expressed in tumors and is correlated with poor prognosis. Further experiments, which involved deliberately repressing the expression of the gene in cancer cells, showed that the reduction in MYCN expression led functionally to slower cell-cycle progression, proliferation, and colony formation, and to greater cell death, implying that the action of the acyclic retinoid on MYCN was slowing the cancer growth.

The group then focused on the role of "cancer stem cells"--special cells that are able to survive the onslaught of chemotherapy or other treatments and to then differentiate into new cancer cells, leading to recurrence. They found, indeed, that high expression of MYCN was correlated with the expression of a number of markers that are associated with cancer stem cells.

"The most interesting part of our finding," says Kojima, "is when we then looked at different subpopulations of heterogeneous cancer cells. We found one specific group of EpCAM-positive cancer stem cells,

where MYCN was elevated. We wondered if perhaps the key to acyclic retinoid's effect was its ability to target these hepatic cancer stem cells."
Indeed, experiments revealed that when exposed to acyclic retinoid, in a dose dependent manner, the EpCAM-positive cells were selectively depleted. To test whether this had clinical significance, they took liver biopsies of patients who had been given acyclic retinoid following liver cancer surgery, and found that in four of the six who had received a higher dosage of 600 mg/d but rather than 300 mg/d, there were decreased levels of MYCN expression, suggesting that MYCN expression in response to acyclic retinoid could be an important part of the difference in recurrence seen in trials. Finally, they looked at data from the Cancer Genome Atlas, and found that elevated expression of MYCN correlated with dramatically poorer prognosis.
According to Kojima, "It is remarkable that the acyclic retinoid clearly targets a certain category of cancer stem cells, and this provides us with important hints for decreasing cancer recurrence and truly curing patients. We are waiting to see what clinical data will show us."
A phase 3 clinical trial of acyclic retinoid (also called Peretinoin), is currently underway in Korea, Taiwan and Singapore to test the drug's ability to prevent HCC recurrence.

https://bbc.in/2Ki0Btt

Prostate cancer diagnosis breakthrough hailed

A new ultrasound process offering more successful diagnosis and management of prostate cancer has been identified by Dundee University researchers.

The university said non-invasive shear wave elastography (SWE) offers "much greater accuracy and reliability" than current testing and is less expensive.
Prostate cancer is the most common cancer in men in the UK.
Former Dundee University rector Stephen Fry, who underwent surgery for prostate cancer, called the research "exciting".
Over 47,000 new cases of prostate cancer are diagnosed in the UK every year.
The most common tests for the disease include the PSA blood test, a digital rectal examination (DRE), MRI scans and a biopsy.
The university said each of these carried "significant problems".

"Unnecessary treatments"

The new method targets the prostate with ultrasound. The Dundee University study involved about 200 patients.
Cancerous tissue is stiffer than normal tissue, so the shear waves are slowed as they pass through it.
The technology was able to detect 89 per cent of prostate cancers and could identify more aggressive cancers and those beginning to spread outside the prostate.
Ghulam Nabi, professor of surgical uro-oncology at the university, said, "Prostate cancer is one of the most difficult to pinpoint. "We are still in a position where our diagnosis of prostate cancer is extremely inefficient, leading to unnecessary treatments for many patients."
Prof Nabi said the new treatment was "like someone has turned the lights on in a darkened room." He said: "We have had cases where the SWE technique has picked up cancers which MRI did not reveal.
"We can now see with much greater accuracy what tissue is cancerous, where it is and what level of treatment it needs."
Stephen Fry underwent surgery for prostate cancer in January.
He said it was "doubly, triply exciting" to hear of the new techniques.
He said: "Anyone who has been in my position will know that when it comes to this pernicious disease early screening and diagnosis is the absolute key to a successful outcome.
"The news of this breakthrough comes at a time when prostate cancer is being pushed to the forefront of our consciousness in the UK, not least because of the disturbing upward trend in its prevalence.
"So hurrah for Dundee University and Medical School and a huge thank you to Professor Nabi and his team for their work in developing this new weapon in the war against a deadly killer."
The project was funded by Prostate Cancer UK with support from the Movember Foundation.

https://wb.md/2I2BQR8

When Ancient Treatments Meet Western Medicine

Giving up insulin is easy, but is quitting all of the pills a good idea?

Seema Yasmin, MD

On a trip to India in 2012, my uncle made an appointment with a sugar doctor. *The sugar doctors here are so good*, our relatives in the village told him. *They're so good that you can stop swallowing your Western medicine. They will make your diabetes fly away*.

A popular Ayurvedic dispensary in Gujarat.

My uncle had been diagnosed with diabetes in 1984 by his general practitioner (GP) in England. Nearly 30 years after that diagnosis was made in a National Health Service (NHS) clinic, he gripped the handrail of a rickshaw and trundled along the road towards Navsari, a city in the Indian state of Gujarat.

Back in England, his GP had followed the guidelines, starting him on metformin and then insulin when pills alone couldn't control his sugar. Still, my uncle's blood sugar levels peaked and crashed weekly; and sitting in the rickshaw, he felt hopeful that traditional healers could fix him.

There were two sugar doctors in Navsari who were especially revered. Visitors came from Canada, the United States, and England to sit at their feet, absorb the ancient wisdom, and replace insulin injections with ground-up herbs and roots.

My uncle knew that his GP wouldn't be impressed, but the sugar doctor was convincing. He spoke of a 3000-year-old medical system that originated in India before there was an NHS in England. The sugar doctor took note of my uncle's medical history and the fact that sugar ran in his blood and in our family.

He counted the pills my uncle took to treat hypertension, arthritis, and hypercholesterolemia. He shook his head.

He asked about my uncle's doshas, or constitution, an Ayurvedic practice that takes into consideration a patient's diet and environment. *Western medicines are for Westerners*, some sugar doctors said. *You must make medicine from the things that grow in the country of your birth.*

When the consultation was over, the sugar doctor handed my uncle plastic bags and boxes filled with tablets and a bill for 37,000 rupees (close to $600). This was a large sum by my uncle's standards, given that his NHS medicines cost around $10 each. But the sugar doctor promised him glycemic control unlike anything Western medicine could achieve—if he stopped taking his English medicines.

My uncle followed orders. Giving up the insulin was easy, but he wondered if quitting all of his pills was a good idea. Then he remembered how many people in our community, both in the village in India and in England, used traditional medicine. Consulting hakeems—wise men who offer medical and life advice—was as common as making an appointment for an annual flu shot.

Ground Ayurvedic herbs and spices.

On a trip to India in 2017, I visited a popular Ayurvedic dispensary in Gujarat. I had grown up hearing stories about Hakeem ChiChi, an especially popular Ayurvedic dispensary whose tonics rattled in the door of our English fridge next to pasteurized milk and orange juice. Hakeem ChiChi's pharmacy sits above a more conventional-looking pharmacy on the first floor of dusty building in Surat. As you ascend the narrow stairway to the second floor, a hazy cloud of ground spices infiltrates your nose and burns the lining of your mucous membranes. Glass jars line the walls of Hakeem ChiChi's dispensary, and in the

center of the room, little boys weep and rub their stinging eyes, while grown men sneeze into handkerchiefs.

Behind the counters, men prepare herbs, weigh powders, and fill orders for the two dozen people waiting in the small space. There is a collective belief in the power of these tonics to heal and fix every ailment that has eluded Western medicine.

Back in England, those who can't travel to India place orders over the phone and await shipments. They stuff the pills into their weekly dispensers along with the day's beta blockers and aspirin. Others eschew Western medicines altogether in favor of pills made from vegetables, roots, and herbs.

When my uncle returned to England, the skies were gray and his forehead clammy. He shivered beneath a blanket even with the central heating cranked up. Some mornings the room spun, and he felt too light-headed to get out of bed. One day, at the urging of my aunt, he went looking for professional help—not from his GP but from his pharmacist. He walked the hundred yards to the local chemist and confessed his Indian adventure. The pharmacist was a safer bet than the doctor, he thought. What if the GP refused to treat complications caused by non-NHS medicines? What if he got in trouble for using Ayurvedic medicine?

The pharmacist had heard the story before. More than half of Brits surveyed in a 2015 government poll said they believed that herbal medicines were "genuinely effective at treating illnesses," and nearly a quarter said that herbal medicines should be offered free on the NHS. Forty percent believed that Chinese medicines were effective, and 39% said the same about homeopathy.

In the United States, almost 1 in 5 adults uses complementary or alternative treatment, although these official data from the National Center on Health Statistics lump together treatments including homeopathy, yoga, and massage. In 2012, Americans spent more than $30 billion on complementary treatments, an average of $500 per person.

The pharmacist was not surprised by my uncle's confession. Up and down the street, his customers came back from India sporting new treatments and strange symptoms. The pharmacist shook his head. "You shouldn't have done that," he said. "You should never stop taking the medicines your doctor has prescribed. Go and see your GP straight away."

My uncle mustered the courage to face his doctor, who promptly restarted his medications and warned him against the dangers of swallowing unlicensed and often untested drugs.

Ayurvedic medicines have started to be evaluated in placebo-controlled clinical trials. In a 2011 study by the US National Center for Complementary and Integrative Health, Ayurvedic medicines were found to be as effective as methotrexate for the treatment of rheumatoid arthritis. One study found that a compound in frankincense offered better pain relief to osteoarthritis sufferers compared with placebo.

But too often Ayurvedic medicines contain dangerous levels of lead, arsenic, mercury, and other toxins that have caused outbreaks of poisoning. Users of Ayurvedic medicines are also prone to stopping their usual medicines and keeping their Ayurvedic treatments a secret from their doctor.

You might think that the Indian episode was my uncle's first and final foray into complementary medicines, but there was a second incident in England involving samosas and a white van.

In our community, sweetmeats and savory delicacies are sold out of vans that travel down English streets and stop outside the houses of brown people. One van sold spicy samosas alongside a powder touted as a natural treatment for diabetes, arthritis, and other ailments. "*Desi dawa*," said the young man, meaning, "native medicine," as he spooned the powder into small plastic bags and pressed it into the hands of elders. "It's all natural."

The elders were pleased with the treatment. Their aching joints were soothed, and even their fluctuating blood sugars seemed to settle. But when authorities got hold of the powder and analyzed it, they found it

wasn't roots and herbs but a mixture of crushed acetaminophen and metformin.

After that, my uncle grudgingly stuck to his English medicines and vowed to be more skeptical about alternative treatments. But when I visit my community in England and in India, people speak in confident and excited tones about the power of Ayurvedic medicines. They tell stories about the man whose vision returned; the child whose kidney function was restored; and, of course, the many who have been supposedly cured of diabetes. *Desi dawa*, they say.

https://bbc.in/2FrVrYd

The foods that might help with dementia

A man has told of how he "got his mum back" after a diagnosis of Alzheimer's disease, in part, by getting her to follow a diet high in berries and leafy green vegetables.

But how realistic is it that dementia can be tackled through diet?

The bulk of the research had been on the preventative side rather than treating Alzheimer's.

Mark Hatzer's mum Sylvia was diagnosed with Alzheimer's in December 2016 and it progressed fast, so that at its worst she forgot who he was. Mark said after a change in her diet and daily activities, her condition improved. "I slowly got my mum back. Her memory is improving all the time. She is more alert and engaged. She is basically her old self again," he wrote in a blog.

So what did Sylvia's diet entail?

- ***Berries***
- ***Leafy green vegetables***
- ***Sweet potatoes***
- ***Few processed/fatty foods***

Blueberries 'boost memory'

Sylvia ate a diet rich in blueberries, blackberries and strawberries.

Berries are part of the flavonoid nutrient family which is known for its antioxidant and anti-inflammatory abilities.

Investigators have claimed that blueberries may activate part of the brain which controls learning and memory, but more studies are needed.

Sylvia's diet was also rich in leafy green vegetables, such as spinach and kale. Like berries, green leaves and vegetables contain high levels of antioxidants. The Alzheimer's Society says that high levels of antioxidants may help to protect against some of the damage to brain cells associated with the disease.

Inflammation - in the form of a chemical change in the brain - is associated with Alzheimer's disease and the charity says there are suggestions that a diet high in antioxidants reduces the signs of this inflammation.

Also on Sylvia's diet plan were sweet potatoes, carrots and swede.

These orange-coloured vegetables are rich in another antioxidant, called beta-carotene, which some scientists say may benefit the brain and memory. Sylvia excluded refined sugar and sugary drinks, fried foods and fast food and pastries, cakes and sweets from her diet - foods that experts agree should be kept to a minimum for a healthy diet.

What do experts think?

Sue Clarke from Alzheimer's Society said: "It's fantastic that Sylvia and her son Mark have taken action to create a personal plan that works well for her dementia diagnosis. There currently no cure or way of preventing the progression of the condition, but taking regular gentle exercise, eating a healthy diet and doing cognitive exercises can help someone with dementia manage their symptoms more effectively."

Adopting a healthy lifestyle can help people with dementia to manage their symptoms, but there is no strong evidence that these steps will slow or stop the underlying diseases that cause dementia.

What Sylvia is following in her diet is very much like the Mediterranean diet, with few processed and fatty foods and lots of fresh fruit and veg.

Alzheimer's Research UK said the latest research presented at the Alzheimer's Association International Conference 2017 found four studies highlighting the potential benefits of certain diets, including the

Mediterranean diet, and how they can support healthy brain ageing and help to reduce dementia risk.

Dr David Reynolds, chief scientific officer at Alzheimer's Research UK, said the studies built on "growing evidence" suggesting that following a Mediterranean style diet may hold valuable health benefits as we enter our later years.

"Observational studies like these can be useful for highlighting factors linked to healthy ageing, but this type of research can't definitively answer whether specific diets can prevent dementia," he said.

Dr Doug Brown, chief policy and research officer at the Alzheimer's Society, says they are still waiting for proof from big scientific trials to show whether changing your diet can reduce the risk of dementia, and by how much. "But eating a healthy, balanced diet can reduce the risk of heart disease, cancer and stroke, so it's likely eating healthily is a good way to look after the health of your brain too."

The Alzheimer's Society points out that while there are multiple studies into diet and the disease that are very promising, there have also been large studies that have not shown similar trends. There are scientific limits too as studies have not shown whether diet can help with anyone with a genetic predisposition to getting Alzheimer's.

Apart from food, an extra element in Sylvia's plan was regular walking, a good night's sleep, and an increase in socialising. She also did memory games and puzzles. The Alzheimer's Society says research has found all of these things have been found to reduce your risk of dementia.

Dr Brown said that as dementia is set to be the 21st Century's biggest killer, with no way yet to cure the condition, "prevention is key".

http://bit.ly/2ji1t4Y

Leading genetics study method may need reconsideration, significant distortions discovered

Study of Mendelian randomization results detects factor called horizontal pleiotropy in close to 50 percent of significant causal relationships, a finding of great importance for detecting biomarkers for drug development and disease management

Many conclusions drawn from a common approach to the study of human genetics could be distorted because of a previously overlooked phenomenon, according to researchers at the Department of Genetics and Genomics Sciences at the Icahn School of Medicine at Mount Sinai and collaborators from Massachusetts General Hospital and the Broad Institute. Their conclusions and a unique method they developed to help correct for this distortion were recently published in Nature Genetics.

The common approach, called Mendelian randomization (MR), is a method that uses genetic variation to assess how risk factors such as obesity and lipid levels affect the likelihood of disease and mortality. The researchers found that a phenomenon called horizontal pleiotropy - in which genetic variants influence disease through pathways different from the risk factors being tested - was present in 48 percent of the MR studies they analyzed. The results were distorted, on average, by -131 to 201 percent, meaning certain exposures analyzed in these studies may have appeared to have more or less influence on disease than they actually do. They also found that widespread horizontal pleiotropy induced false positive causal relationships in up to 10 percent of results in certain tests.

As technology in genomic analysis has evolved rapidly in the past decade, researchers have developed multiple MR methods to study health and disease. A study of the validity of MR methods and innovation to correct for factors such as horizontal pleiotropy comes at a crucial time.

"Mendelian randomization has significant implications for drug discovery and validation," said Ron Do, PhD, Assistant Professor in the Department of Genetics and Genomic Sciences at the Icahn School of Medicine. "It can be used to determine whether biomarkers are causal for disease, which can determine what types of drug therapeutics may be worth exploring in clinical trials, and can potentially predict accurate dosing for drug effectiveness."

In light of these findings, the study authors stress the importance of assessing all MR studies for the occurrence of horizontal pleiotropy,

and have developed open-source software to detect and correct for it, MR-PRESSO, which is available on GitHub at https://github.com/rondolab/MR-PRESSO

http://bit.ly/2JBaRvA

Drinking baking soda could be an inexpensive, safe way to combat autoimmune disease

A daily dose of baking soda may help reduce the destructive inflammation of autoimmune diseases like rheumatoid arthritis, scientists say.

AUGUSTA, Ga. - A daily dose of baking soda may help reduce the destructive inflammation of autoimmune diseases like rheumatoid arthritis, scientists say.

They have some of the first evidence of how the cheap, over-the-counter antacid can encourage our spleen to promote instead an anti-inflammatory environment that could be therapeutic in the face of inflammatory disease, Medical College of Georgia scientists report in the *Journal of Immunology*.

They have shown that when rats or healthy people drink a solution of baking soda, or sodium bicarbonate, it becomes a trigger for the stomach to make more acid to digest the next meal and for little-studied mesothelial cells sitting on the spleen to tell the fist-sized organ that there's no need to mount a protective immune response.

"It's most likely a hamburger not a bacterial infection," is basically the message, says Dr. Paul O'Connor, renal physiologist in the MCG Department of Physiology at Augusta University and the study's corresponding author.

Mesothelial cells line body cavities, like the one that contains our digestive tract, and they also cover the exterior of our organs to quite literally keep them from rubbing together. About a decade ago, it was found that these cells also provide another level of protection. They have little fingers, called microvilli, that sense the environment, and warn the organs they cover that there is an invader and an immune response is needed.

Drinking baking soda, the MCG scientists think, tells the spleen - which is part of the immune system, acts like a big blood filter and is where some white blood cells, like macrophages, are stored - to go easy on the immune response. "Certainly drinking bicarbonate affects the spleen and we think it's through the mesothelial cells," O'Connor says.

The conversation, which occurs with the help of the chemical messenger acetylcholine, appears to promote a landscape that shifts against inflammation, they report.

In the spleen, as well as the blood and kidneys, they found after drinking water with baking soda for two weeks, the population of immune cells called macrophages, shifted from primarily those that promote inflammation, called M1, to those that reduce it, called M2. Macrophages, perhaps best known for their ability to consume garbage in the body like debris from injured or dead cells, are early arrivers to a call for an immune response.

In the case of the lab animals, the problems were hypertension and chronic kidney disease, problems which got O'Connor's lab thinking about baking soda.

One of the many functions of the kidneys is balancing important compounds like acid, potassium and sodium. With kidney disease, there is impaired kidney function and one of the resulting problems can be that the blood becomes too acidic, O'Connor says. Significant consequences can include increased risk of cardiovascular disease and osteoporosis.

"It sets the whole system up to fail basically," O'Connor says. Clinical trials have shown that a daily dose of baking soda can not only reduce acidity but actually slow progression of the kidney disease, and it's now a therapy offered to patients.

"We started thinking, how does baking soda slow progression of kidney disease?" O'Connor says.

That's when the anti-inflammatory impact began to unfold as they saw reduced numbers of M1s and increased M2s in their kidney disease model after consuming the common compound.

When they looked at a rat model without actual kidney damage, they saw the same response. So the basic scientists worked with the investigators at MCG's Georgia Prevention Institute to bring in healthy medical students who drank baking soda in a bottle of water and also had a similar response.

"The shift from inflammatory to an anti-inflammatory profile is happening everywhere," O'Connor says. "We saw it in the kidneys, we saw it in the spleen, now we see it in the peripheral blood."

The shifting landscape, he says, is likely due to increased conversion of some of the proinflammatory cells to anti-inflammatory ones coupled with actual production of more anti-inflammatory macrophages. The scientists also saw a shift in other immune cell types, like more regulatory T cells, which generally drive down the immune response and help keep the immune system from attacking our own tissues. That anti-inflammatory shift was sustained for at least four hours in humans and three days in rats.

The shift ties back to the mesothelial cells and their conversations with our spleen with the help of acetylcholine. Part of the new information about mesothelial cells is that they are neuron-like, but not neurons O'Connor is quick to clarify.

"We think the cholinergic (acetylcholine) signals that we know mediate this anti-inflammatory response aren't coming directly from the vagal nerve innervating the spleen, but from the mesothelial cells that form these connections to the spleen," O'Connor says.

In fact, when they cut the vagal nerve, a big cranial nerve that starts in the brain and reaches into the heart, lungs and gut to help control things like a constant heart rate and food digestion, it did not impact the mesothelial cells' neuron-like behavior.

The affect, it appears, was more local because just touching the spleen did have an effect.

When they removed or even just moved the spleen, it broke the fragile mesothelial connections and the anti-inflammatory response was lost, O'Connor says. In fact, when they only slightly moved the spleen as might occur in surgery, the previously smooth covering of mesothelial cells became lumpier and changed colors.

"We think this helps explain the cholinergic (acetylcholine) anti-inflammatory response that people have been studying for a long time," O'Connor says.

Studies are currently underway at other institutions that, much like vagal nerve stimulation for seizures, electrically stimulate the vagal nerve to tamp down the immune response in people with rheumatoid arthritis.

While there is no known direct connection between the vagal nerve and the spleen - and O'Connor and his team looked again for one - the treatment also attenuates inflammation and disease severity in rheumatoid arthritis, researchers at the Feinstein Institute for Medical Research reported in 2016 in the journal Proceedings of the National Academy of Sciences.

O'Connor hopes drinking baking soda can one day produce similar results for people with autoimmune disease.

"You are not really turning anything off or on, you are just pushing it toward one side by giving an anti-inflammatory stimulus," he says, in this case, away from harmful inflammation. "It's potentially a really safe way to treat inflammatory disease."

The spleen also got bigger with consuming baking soda, the scientists think because of the anti-inflammatory stimulus it produces. Infection also can increase spleen size and physicians often palpate the spleen when concerned about a big infection.

Other cells besides neurons are known to use the chemical communicator acetylcholine. Baking soda also interact with acidic ingredients like buttermilk and cocoa in cakes and other baked goods to help the batter expand and, along with heat from the oven, to rise. It can also help raise the pH in pools, is found in antacids and can help clean your teeth and tub.

The research was funded by the National Institutes of Health.

http://bit.ly/2HFZnKU

Fetal immune system rejects the mother in preterm labor

Discovery upends conventional thinking about immune development

Preterm labor, a common pregnancy complication, has long been a mystery to scientists. But a new study from UC San Francisco shows it may sometimes happen when the fetal immune system "wakes up" too early and begins to reject the mother, causing the uterus to start contracting.

The researchers think the fetal immune system becomes triggered in a case of mistaken identity. An initial infection in the mother can result in inflammation and arouse the fetal immune system. The fetal immune cells confuse the mother's cells for an invader and mount an attack, in the form of inflammatory chemicals. These chemicals then trigger contractions, leading to preterm labor, the leading cause of infant mortality.

"The dogma has always been that the fetus has a very immature immune system, and as a result, people haven't really considered its possible role in pregnancy complications," said senior author Tippi MacKenzie, MD, associate professor in the UCSF Division of Pediatric Surgery and the Fetal Treatment Center. "We showed that in patients who have preterm labor as a result of some kind of infection or inflammation--the most common cause of preterm labor--the fetal immune system awakens prematurely and may trigger labor."

In the new study, published Wednesday, April 25, 2018, in *Science Translational Medicine*, the researchers tested umbilical cord blood, which contains fetal cells, along with blood taken from 89 women who had healthy pregnancies and 70 who went into early labor. But the scientists saw no signs of an immune response in the mother's blood. Instead, they detected activation in two types of immune cells in the cord blood of preterm infants. The researchers also found greater numbers of the mother's cells circulating in the cord blood of preterm infants.

During pregnancy, cells from the mother and the fetus travel back and forth across the placenta. Just as in an organ transplant, the immune systems of the mother and the fetus have to tolerate one another, so the fetus is not rejected. This tolerance is governed by immune cells known as regulatory T cells, which dampen the immune system by keeping the other types of T cells in check.

However, during preterm labor the infant's immune system was found to be activated specifically to attack the mother's cells. The researchers detected higher levels of both dendritic cells and effector T cells in the cord blood of preterm infants; dendritic cells present foreign substances to the T cells to signify that they are a potential threat, and T cells--the primary fighter cells of the immune system--then mount an attack by releasing inflammatory chemicals.

T cells from preterm infants made significantly higher levels of these inflammatory chemicals, TNF alpha and interferon gamma than those from full-term infants, and in a laboratory model of uterine contraction, the researchers discovered that these chemicals induced contraction of uterine cells.

"If you're a fetus and your immune system is developing in a healthy environment, it's in your best interest to keep things quiet so that you can develop and be born at a normal time. But if you encounter trouble in the form of an infection or inflammation, then that can trigger your dendritic cells and T cells to wake up," said first author Michela Frascoli, PhD, a former postdoctoral researcher in MacKenzie's lab, now an adjunct assistant professor at the University of Massachusetts Medical School. "Ultimately, it could be a defense mechanism to exit a hostile uterine environment."

MacKenzie, a member of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF, has long studied the fetal immune system in the context of fetal stem cell transplants. She became interested in preterm labor during her own pregnancy, when she experienced a long period of bed rest because she was at risk of delivering her baby early.

"The medicines we use to treat preterm labor right now are just aimed at stopping the uterus from contracting. But at that point, the horse is out of the barn," MacKenzie said. "What we really have to do is diagnose and treat fetal immune activation, which is probably starting weeks before the patient comes in with the uterine contractions."

Her lab is now pursuing biomarkers in the mother's blood that can identify whether the fetal immune system is activated and increasing risk for preterm labor.

Other authors on the study were Lacy Coniglio, Russell Witt, Cerine Jeanty, Shannon Fleck, Dana Henry, and Qizhi Tang of UCSF; Tzong-Hae Lee, Sheila Keating, Michael Busch, and Philip Norris of the Blood Systems Research Institute; Giovanna Cruz and Lisa Barcellos of UC Berkeley; and Nardhy Gomez-Lopez and Roberto Romero of Wayne State University.

The research was supported in part by funding from the Swiss National Science Foundation, the March of Dimes, the California Institute of Regenerative Medicine, the National Institute of Allergy and Infectious Diseases (R01 AI116880), the UCSF Center for Maternal-Fetal Precision Medicine, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

http://bit.ly/2w0cPni

Belief in fake causes of cancer is rife

***Mistaken belief in mythical causes of cancer is rife according to new research jointly funded by Cancer Research UK and published today (Thursday) in the* European Journal of Cancer*.**

Researchers at University College London (UCL) and the University of Leeds surveyed 1,330 people in England and found that more than 40% wrongly thought that stress (43%) and food additives (42%) caused cancer.

A third incorrectly believed that electromagnetic frequencies (35%) and eating GM food (34%) were risk factors, while 19% thought microwave ovens and 15% said drinking from plastic bottles caused cancer despite a lack of good scientific evidence.

Among the proven causes of cancer, 88% of people correctly selected smoking, 80% picked passive smoking and 60% said sunburn.

Belief in mythical causes of cancer did not mean a person was more likely to have risky lifestyle habits.

But those who had better knowledge of proven causes were more likely not to smoke.

Dr Samuel Smith from the University of Leeds said: "It's worrying to see so many people endorse risk factors for which there is no convincing evidence.

"Compared to past research it appears the number of people believing in unproven causes of cancer has increased since the start of the century which could be a result of changes to how we access news and information through the internet and social media.

"It's vital to improve public education about the causes of cancer if we want to help people make informed decisions about their lives and ensure they aren't worrying unnecessarily."

Dr Lion Shahab from UCL said: "People's beliefs are so important because they have an impact on the lifestyle choices they make. Those with better awareness of proven causes of cancer were more likely not to smoke and to eat more fruit and vegetables."

Clare Hyde from Cancer Research UK said: "Around four in 10 cancer cases could be prevented through lifestyle changes** so it's crucial we have the right information to help us separate the wheat from the chaff.

"Smoking, being overweight and overexposure to UV radiation from the sun and sunbeds are the biggest preventable causes of cancer.

"There is no guarantee against getting cancer but by knowing the biggest risk factors we can stack the odds in our favour to help reduce our individual risk of the disease, rather than wasting time worrying about fake news."

**Lion Shahab, Jennifer A. McGowan, Jo Waller and Samuel G. Smith. Prevalence of beliefs about actual and mythical causes of cancer and their association with socio-demographic and health-related characteristics: findings from a national cross-sectional survey.* European Journal of Cancer

Embargoed weblink: https://doi.org/10.1016/j.ejca.2018.03.029

This work was supported by a Cancer Research UK/Bupa Foundation Innovation Award

*** Brown et al. The fraction of cancer attributable to known risk factors in England, Wales, Scotland, Northern Ireland, and the UK overall in 2015.* British Journal of Cancer. *DOI: 10.1038/s41416-018-0029-6*

http://bit.ly/2r8PWZR

Noninvasive spinal stimulation method enables paralyzed people to regain use of hands

Nonsurgical technique allows them to turn doorknobs, open water bottles for the first time in years

The ability to perform simple daily tasks can make a big difference in people's lives, especially for those with spinal cord injuries. A UCLA-led team of scientists reports that six people with severe spinal cord injuries -- three of them completely paralyzed -- have regained use of their hands and fingers for the first time in years after undergoing a nonsurgical, noninvasive spinal stimulation procedure the researchers developed.

At the beginning of the study, three of the participants could not move their fingers at all, and none could turn a doorknob with one hand or twist a cap off a plastic water bottle. Each of them also had great difficulty using a cellphone. After only eight researcher-led training sessions with the spinal stimulation, all six individuals showed substantial improvements. The study participants had chronic and severe paralysis for more than one year, and some for more than 10 years.

From before the first session to the end of the last session, the participants improved their grip strength.

"About midway through the sessions, I could open my bedroom door with my left hand for the first time since my injury and could open new water bottles, when previously someone else had to do this for me," said Cecilia Villarruel, one of the participants, whose injury resulted from a car accident 13 years earlier. "Most people with a spinal cord injury say they just want to go to the bathroom like a normal person again," she said. "Small accomplishments like opening jars, bottles and doors enable a level of independence and self-reliance that is quite satisfying, and have a profound effect on people's lives."

In addition to regaining use of their fingers, the research subjects also gained other health benefits, including improved blood pressure, bladder function, cardiovascular function and the ability to sit upright without support.

"Within two or three sessions, everyone started showing significant improvements, and kept improving from there," said the study's lead author, UCLA research scientist Parag Gad.

"After just eight sessions, they could do things they haven't been able to do for years," said V. Reggie Edgerton, senior author of the research and a UCLA distinguished professor of integrative biology and physiology, neurobiology and neurosurgery.

This is the largest reported recovery of the use of hands that has been reported in patients with such severe spinal cord injuries, Edgerton said.

The researchers placed electrodes on the skin to stimulate the circuitry of the spinal cord. They call their method "transcutaneous enabling motor control," or tEmc. In the stimulation, electrical current is applied at varying frequencies and intensities to specific locations on the spinal cord.

In the training sessions, the participants squeezed a small gripping device 36 times (18 times with each hand) and held their grip for three seconds; the researchers measured the amount of force they used. The training consisted of two sessions a week over four weeks; the eight sessions each lasted about 90 minutes.

"The combination of spinal stimulation plus training with the hands allows them to regain the lost function," Gad said. They were less dependent on their caregivers, and could feed and dress themselves, he added.

Two of the six returned to Edgerton's laboratory 60 days after the training ended and maintained their grip strength; they could turn a doorknob with one hand, twist off a bottle cap and use a fork with one hand. (The four others did not return to the laboratory. The research subjects live in New York, Minnesota and elsewhere.) The research is published online this month in the *Journal of Neurotrauma*.

More than 1.2 million Americans are living with paralysis from spinal cord injuries, according to the Christopher and Dana Reeve Foundation.

Hundreds of thousands of people in the United States have lost control of vital body functions due to such injuries, including use of their hands and fingers.

"Improved hand function can mean the difference between needing around-the-clock care and living more independently," said Peter Wilderotter, president and CEO of the Reeve Foundation. "These findings bring great hope to those who were told recovery following paralysis would be impossible. As new discoveries and breakthroughs are uncovered, it is clear the word 'impossible' no longer applies to spinal cord injury."

Edgerton's research team has worked with more than two dozen people with severe spinal cord injuries, the vast majority of whom have shown substantial improvements.

"Nearly everyone thought the only people who would benefit from treatment were those who had been injured for less than a year; that was the dogma. Now we know the dogma is dead," said Edgerton, who is also affiliated with the University of Technology Sydney's Centre for Neuroscience and Regenerative Medicine in Australia. "All of our subjects have been paralyzed for more than a year. We know that in a high percentage of subjects who are severely injured, we can improve their quality of life."

Edgerton is seeking FDA approval for the motor control device so that it can be used by rehabilitation clinics and others. He is able to accept only a small number of people into his research program.

The spinal stimulation approach is inexpensive, does not require surgery and can be used in poor communities and countries without advanced medical facilities -- "and the effects are in some ways, we think, better than surgery," Edgerton said.

"I get criticized a lot for giving 'false hope' but we follow where the science tells us to go and just give the research results," Edgerton said. "Everything is telling us the nervous system is much more adaptable than we've given it credit for, and can relearn and recover from severe injury."

Co-authors are Sujin Lee, a physician with the Veterans Affair Healthcare System Spinal Cord Injury and Disorders Center in Long Beach; Nicholas Terrafranca, CEO of NeuroRecovery Technologies, a medical technology company Edgerton co-founded that helps restore movement in patients with paralysis; Hui Zhong, a research scientist in Edgerton's laboratory; Amanda Turner, Edgerton's former administrative assistant, who helped to recruit and select the research subjects; and Yury Gerasimenko, director of the laboratory of movement physiology at Russia's Pavlov Institute and a researcher in the UCLA department of integrative biology and physiology.

The research was funded by the Christopher and Dana Reeve Foundation; the National Institutes of Health's National Institute of Biomedical Imaging and Bioengineering; the Dana and Albert R. Broccoli Foundation; and the Walkabout Foundation.

http://bit.ly/2I7W8uO

New breath and urine tests detect early breast cancer more accurately

Researchers detected breast cancer with more than 95 percent average accuracy using an inexpensive commercial electronic nose

New York - A new method for early and accurate breast cancer screening has been developed by researchers at Ben-Gurion University of the Negev and Soroka University Medical Center, using commercially available technology.

The researchers were able to isolate relevant data to more accurately identify breast cancer biomarkers using two different electronic nose gas sensors for breath, along with gas-chromatography mass spectrometry (GC-MS) to quantify substances found in urine.

In their study published in Computers in Biology and Medicine, researchers detected breast cancer with more than 95 percent average accuracy using an inexpensive commercial electronic nose (e-nose) that identifies unique breath patterns in women with breast cancer. In addition, their revamped statistical analyses of urine samples submitted both by healthy patients and those diagnosed with breast cancer yielded 85 percent average accuracy.

"Breast cancer survival is strongly tied to the sensitivity of tumor detection; accurate methods for detecting smaller, earlier tumors remains a priority," says Prof. Yehuda Zeiri, a member of Ben-Gurion University's Department of Biomedical Engineering. "Our new approach utilizing urine and exhaled breath samples, analyzed with

inexpensive, commercially available processes, is non-invasive, accessible and may be easily implemented in a variety of settings."

The study reports breast cancer is the most commonly diagnosed malignancy among females and the leading cause of death around the world. In 2016, breast cancer accounted for 29 percent of all new cancers identified in the United States and was responsible for 14 percent of all cancer-related deaths.

Mammography screenings, which are proven to significantly reduce breast cancer mortality, are not always able to detect small tumors in dense breast tissue. In fact, typical mammography sensitivity, which is 75 to 85 percent accurate, decreases to 30 to 50 percent in dense tissue. Current diagnostic imaging detection for smaller tumors has significant drawbacks: dual-energy digital mammography, while effective, increases radiation exposure, and magnetic resonance imaging (MRI) is expensive. Biopsies and serum biomarker identification processes are invasive, equipment-intensive and require significant expertise.

"We've now shown that inexpensive, commercial electronic noses are sufficient for classifying cancer patients at early stages," says Prof. Zeiri. "With further study, it may also be possible to analyze exhaled breath and urine samples to identify other cancer types, as well."

Study contributors include: Ben-Gurion University biomedical engineering researchers Prof. Yehuda Zeiri, Or Herman-Saffar, Zvi Boger, and Raphael Gonen; Dr. Shai Libson, a surgeon in the Breast Health Center at Soroka; and Dr. David Lieberman, an associate professor in Ben-Gurion University's Joyce and Irving Goldman Medical School, Faculty of Health Sciences.

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

Chinese physician released after 3 months in jail for criticizing a traditional medicine

Lawyers and physicians fear the case could silence scientific debate on traditional remedies.

David Cyranoski

A Chinese doctor who was arrested after he criticized a best-selling traditional Chinese remedy has been released, after more than three months in detention. Tan Qindong had been held at the Liangcheng county detention centre since January, when police said a post Tan had made on social media damaged the reputation of the traditional medicine and the company that makes it.

On 17 April, a provincial court found the police evidence for the case insufficient. Tan, a former anaesthesiologist who has founded several biomedical companies, was released on bail on that day. Tan, who lives in Guangzhou in southern China, is now awaiting trial. Lawyers familiar with Chinese criminal law told *Nature* that police have a year to collect more evidence or the case will be dismissed. They say the trial is unlikely to go ahead.

The episode highlights the sensitivities over traditional Chinese medicines (TCMs) in China. Although most of these therapies have not been tested for efficacy in randomized clinical trials — and serious side effects have been reported in some[1] — TCM has support from the highest levels of government. Criticism of remedies is often blocked on the Internet in China. Some lawyers and physicians worry that Tan's arrest will make people even more hesitant to criticize traditional therapies.

Liquor allegations

Tan's post about a medicine called Hongmao liquor was published on the Chinese social-media app Meipian on 19 December. It has since been removed, but according to the police report it alleged that Hongmao liquor, which purports to treat dozens of conditions, is a "poison". The post also contained health advice for ageing patients.

Three days later, the liquor's maker, Hongmao Pharmaceuticals in Liangcheng county of Inner Mongolia autonomous region, told local police that Tan had defamed the company. Liangcheng police hired an accountant who estimated that the damage to the company's reputation was 1.4 million Chinese yuan (US$220,000), according to official state media, the *Beijing Youth Daily*.

In January, Liangcheng police travelled to Guangzhou to arrest Tan and escort him back to Liangcheng, according to a police statement.

Xia Nan, a criminal lawyer at Beijing Huayi law firm, says that the statute under which the police arrested Tan, Criminal Law Article 221, calls for punishment of those who spread "falsified information". "Tan is a specialist with a doctor's credentials, who commented from a scientific perspective," says Xia. "His comments clearly were not illegal." The Liangcheng police department did not pick up the phone when *Nature* called.

Upon his release, Tan told an online Chinese news outlet *The Paper* that he did not deserve to be arrested. Tan said he considers his stint in detention a form of "life training" and does "not regret writing the post, which is something I am supposed to do as a doctor". *Nature's* attempts to contact Tan were unsuccessful.

Popular therapy

Sales of Hongmao liquor reached 1.63 billion yuan in 2016, making it the second best-selling TCM in China that year. It was approved to be sold by licensed TCM shops and physicians in 1992 and approved for sale over the counter in 2003. Hongmao Pharmaceuticals says that the liquor can treat dozens of different disorders, including problems with the spleen, stomach and kidney, as well as backaches.

But Tan's arrest has also drawn significant media attention on the company. More than two dozen provincial or city health authorities have reprimanded Hongmao Pharmaceuticals over the past decade for misleading advertisements about the therapy's health benefits. This led to temporary suspension of sales in several cities until the advertisements were removed.

On 16 April, China's drug regulator issued a statement calling on the company to explain punishments it has received for false advertisements in the past five years, to report all adverse effects recorded in that period and to provide further explanation of the liquor's safety and efficacy to address public concerns.

The drug regulator also requested that the Inner Mongolian drug agency, which is tasked with enforcing the regulator's rules, take a closer look at Hongmao Pharmaceuticals to ensure its products are safe. The agency has threatened to revoke the company's license to make drugs if the company is found to have violated any regulations.

Company response

Hongmao Pharmaceuticals did not respond to *Nature*'s request for an interview. However, Wang Shengwang, general manager of the production center of Hongmao Liquor, and Han Jun, assistant to the general manager, gave an interview to *The Paper* on 16 April. The pair said the company did not need not publicize clinical trial data because Hongmao liquor is a "protected TCM composition". Wang denied allegations in Chinese media that the company pressured the police to pursue Tan or that it dispatched staff to accompany the police.

Han said that only 137 cases of people experiencing adverse side effects from the liquor have been reported in the past 13 years, and most of those were mild. Wang also said that local distributors of Hongmao liquor — not the company — were responsible for many of the advertisements that led to temporary suspensions of liquor sales.

Li Qingchen, a paediatric surgeon at the Harbin Children's Hospital and a prominent critic of TCMs, says that the Tan case might make Chinese people more sceptical about the safety and effectiveness of Chinese medicine. "But most will probably think this is just a problem with Hongmao liquor, and still think Chinese medicine is reliable," he says.

Xia is worried that the case could further silence public criticism of TCMs, environmental degredation, and other fields where comment from experts is crucial. The Tan arrest "could cause fear among scientists" and dissuade them from posting scientific comments, he says.

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http://bit.ly/2HB5zUl

Want to remember your dreams? Try taking vitamin B6

New research from the University of Adelaide has found that taking vitamin B6 could help people to recall their dreams.

The study published online ahead of print in *Perceptual and Motor Skills*, included 100 participants from around Australia taking high-

dose vitamin B6 supplements before going to bed for five consecutive days.

"Our results show that taking vitamin B6 improved people's ability to recall dreams compared to a placebo," says research author Dr Denholm Aspy, from the University's School of Psychology.

"Vitamin B6 did not affect the vividness, bizarreness or colour of their dreams, and did not affect other aspects of their sleep patterns.

"This is the first time that such a study into the effects of vitamin B6 and other B vitamins on dreams has been carried out on a large and diverse group of people," Dr Aspy says.

The randomised, double-blind, placebo-controlled study saw participants taking 240mg of vitamin B6 immediately before bed.

Prior to taking the supplements, many of the participants rarely remembered their dreams, but they reported improvements by the end of the study.

"It seems as time went on my dreams were clearer and clearer and easier to remember. I also did not lose fragments as the day went on," said one of the participants after completing the study.

According to another participant of the study, "My dreams were more real, I couldn't wait to go to bed and dream!"

Dr Aspy says: "The average person spends around six years of their lives dreaming. If we are able to become lucid and control our dreams, we can then use our dreaming time more productively.

"Lucid dreaming, where you know that you are dreaming while the dream is still happening, has many potential benefits. For example, it may be possible to use lucid dreaming for overcoming nightmares, treating phobias, creative problem solving, refining motor skills and even helping with rehabilitation from physical trauma.

"In order to have lucid dreams it is very important to first be able to recall dreams on a regular basis. This study suggests that vitamin B6 may be one way to help people have lucid dreams."

Vitamin B6 occurs naturally in various foods, including whole grain cereals, legumes, fruits (such as banana and avocado), vegetables (such as spinach and potato), milk, cheese, eggs, red meat, liver, and fish.

"Further research is needed to investigate whether the effects of vitamin B6 vary according to how much is obtained from the diet. If vitamin B6 is only effective for people with low dietary intake, its effects on dreaming may diminish with prolonged supplementation," says Dr Aspy.

http://bit.ly/2KpK2vl

Zika virus eliminates advanced human tumor in central nervous system of rodents

A group of Brazilian researchers confirmed for the 1st time in vivo the efficiency of Zika virus in infecting CNS tumor cells - tests even showed that the resulting viral particles were less harmful than the ones created from infection of healthy cells

A Brazilian study published April 26 in the journal *Cancer Research* shows for the first time in vivo that Zika virus can be used as a tool to treat aggressive human central nervous system (CNS) tumors.

After injecting small amounts of the pathogen into the brains of mice with an advanced stage of the disease, the scientists observed a significant reduction in tumor mass and an increase in survival. In some cases, the tumor was completely eliminated, even where the disease had metastasized to the spinal cord.

"We're excited about the possibility of testing the treatment in human patients, and we're already discussing this with oncologists. We've also applied for a patent for the therapeutic protocol used in rodents," said Mayana Zatz, a professor in the University of São Paulo's Bioscience Institute (IB-USP) in Brazil and director of the Human Genome & Stem Cell Research Center (HUG-CELL), one of the Research, Innovation and Dissemination Centers (RIDCs http://cepid.fapesp.br/home) supported by the Sao Paulo Research Foundation - FAPESP.

Zatz led the study alongside Oswaldo Keith Okamoto, also a professor at IB-USP and a member of HUG-CELL. The research team included

scientists at Butantan Institute, Brazil's National Bioscience Laboratory (LNBio) and the Federal University of de São Paulo (UNIFESP).

"Our results suggest Zika has an even greater affinity with central nervous system tumor cells than with healthy neural stem cells [the virus's main targets in the brains of fetuses exposed during pregnancy]. When it infects tumor cells, it swiftly destroys them," Okamoto said.

In his laboratory at IB-USP, Okamoto has devoted the last few years to studying a group of genes which, when expressed in malignant tumors, endow tumor cells with properties similar to those of stem cells, making them more aggressive and treatment-resistant.

According to Okamoto, these tumor cells with stem cell-like characteristics have been observed in various kinds of solid tumor including those that affect the central nervous system. Data in the scientific literature suggests they help cancer spread through the organism and restore tumor growth after chemotherapy and radiation therapy have all but eliminated the disease.

"Our research and studies by other groups have shown that Zika virus causes microcephaly because it infects and destroys neural stem cells in the fetus, preventing the formation of new neurons. So we had the idea of investigating whether the virus also attacked tumor stem cells in the central nervous system," he said.

Methodology

The study just published focused on what are known as embryonal CNS tumors. The experiments were performed with three human tumor cell lines: two derived from medulloblastoma and the third from atypical teratoid/rhabdoid tumor (AT/RT).

As Okamoto explained, both kinds of cancer are caused by genetic or epigenetic aberrations in stem cells and neural progenitors during embryonic development, when the nervous system is under construction.

"The neural stem cells that undergo these alterations give rise to tumor cells at a later stage. They form aggressive, fast-growing tumors that can manifest shortly after birth or until adolescence," Okamoto said.

In the first stage of their research, the group tested in vitro whether Zika was capable of infecting these three CNS tumor cell lines, as well as cells from other frequent types of tumor, such as breast, prostate and colorectal cancer.

The researchers performed a dose escalation study, adding steadily larger amounts of Zika virus to cultured tumor cells until they found the quantity that promoted infection. Using immunofluorescence microscopy they confirmed that the virus had in fact invaded the tumor cells and begun to replicate inside them.

"We observed that small amounts of Zika were sufficient to infect CNS tumor cells," Okamoto said. "They also infected the prostate cancer cells, but far fewer. On the other hand, even a large viral dose failed to cause infection in breast and colorectal cancer cells."

The second experiment consisted of comparing Zika's capacity to infect healthy neural stem cells obtained from induced pluripotent stem cells (adult cells reprogrammed in the laboratory to behave like stem cells) with its infection of CNS tumor stem cells.

"We infected both cell types in vitro and found tumor stem cells to be even more susceptible to destruction by Zika than healthy neural stem cells," Okamoto said. "In this same experiment, we exposed mature neurons differentiated from human neural stem cells to Zika and found that they weren't infected or destroyed by the virus." "This is very good news, since our specific goal is to destroy tumor cells," Zatz noted.

The neural stem cells used in the experiment, she explained, were obtained during a previous study conducted by the group with pairs of discordant twins - cases in which only one twin was affected by the virus although both had been equally exposed during pregnancy.

According to Okamoto, the AT/RT cell line was the most sensitive to infection.

"We analyzed the genetic and molecular profile of these cell lines very thoroughly. This analysis included whole exome sequencing [to look for disease-causing variants in exons, the pieces of genes that code for proteins], global gene expression and chromosome alterations," he said.

"We concluded that this tumor cell line was not only more sensitive to the virus than the others but also more closely resembled the molecular characteristics of healthy neural stem cells."

The group's preliminary results suggest Zika can also infect and destroy other kinds of CNS tumor such as glioblastoma and ependymoma.

In vivo assays

In the third and last part of the project the researchers conducted in vivo assays with immunosuppressed mice, injecting human tumor cells from medulloblastoma and AT/RT into different groups.

In this study model, the tumor is induced in the lateral ventricles of the brain, spreads to other regions of the central nervous system and then descends the spinal cord, mimicking advanced human cancer.

After inducing the tumor, the researchers injected a small dose of Zika into the lateral ventricles of some mice. "Tumor volume was significantly reduced in the treated group. In some cases both the tumor and spinal metastases were completely eliminated," Okamoto said.

The largest increase in survival time was observed in the animals with AT/RT. While the untreated group survived up to 30 days, those injected with Zika in this group survived up to 80 days.

"Even when the tumor was completely eliminated the animals eventually died from complications of advanced-stage cancer," Okamoto said. "It's possible survival rates could become even longer if patients are treated at an earlier stage. This is something we need to investigate."

The researchers also injected the virus into a group of immunosuppressed mice that did not have induced cancer. In this case, the virus circulated for longer in the organism and the animals died from the viral infection after only two weeks.

"Immunosuppressed mice are highly sensitive to any pathogen, but we had to use this model because it's the only one in which human tumor cells are capable of proliferating," Okamoto explained.

When they sought to find out why the virus was more lethal in the animals without cancer than in the sick animals, the researchers discovered that the viral particles created when Zika infected the tumor cells were less virulent, meaning they were less able to infect new cells than particles created in healthy cells.

"All these results taken together suggest that various kinds of aggressive CNS tumors can be treated with some kind of approach involving Zika in future," Okamoto said. "First of all, however, we need to investigate more profoundly which tumor types respond to this oncolytic effect, what are the benefits of this treatment, and what are the side-effects of exposure to the virus."

In parallel with development of the theoretical research in the laboratory, Zatz added, the group plan to move on to clinical trials in humans. "Today there are few options for treatment of these tumors," she said. "The idea is to start with two or three patients who don't respond to conventional treatment, and then embark on a larger trial with more patients."

According to Zatz, the fact that thousands of Brazilians were infected by Zika during the 2015 epidemic suggests the procedure is sufficiently safe. "Some 80% of the people infected have never displayed symptoms. Most of the other 20% have displayed mild symptoms far less aggressive than those of dengue or the adverse effects of chemotherapy," she explained.

Zatz stressed the importance of FAPESP's RIDC program in making this kind of research feasible. "It enables researchers with different kinds of expertise to collaborate and get results very quickly, which can make all the difference," she said.

http://bit.ly/2Kq94uH

Too liberal use of oxygen increases risk of death in acutely ill adult patients

McMaster University researchers have found there is such a thing as too much oxygen for acutely ill adults.

Hamilton, ON - Extensive data analyses in a study from the university show that supplemental oxygen, when given liberally to these patients, increases the risk of death without improving other health outcomes.

The results were published today in *The Lancet*.

"Supplemental oxygen is administered to millions of acutely unwell patients around the world every day," said Waleed Alhazzani, senior author of the paper, assistant professor of medicine at McMaster and an intensive care and general internal medicine staff member at St. Joseph's Healthcare Hamilton.

"Despite this, there is a striking lack of definitive, high-quality evidence related to this common intervention."

The McMaster-led team of researchers searched electronic academic databases from their inception through to October 2017 for randomized controlled trials done worldwide which compared liberal versus conservative oxygen therapy and death rates, as well as impacts on such aspects as disability, infections and hospital length of stay.

The 25 randomized controlled trials encompassed more than 16,000 adult patients with sepsis, stoke, trauma, emergency surgery, heart attack or cardiac arrest.

Data analysis demonstrated that, compared to the conservative strategy, liberal administration of oxygen resulted in increased in-hospital death by 21 per cent. Additional analyses suggested that the more supplemental oxygen patients were given, the higher their risk was for death. However, the incidence of other conditions, such as infections or length of hospital stay, were similar between the two groups.

The researchers estimated one additional death for every 71 patients treated with a liberal oxygen strategy.

"Our findings are distinct from the pervasive view that liberal oxygen therapy for acute illnesses is at worst, harmless," said Alhazzani.

The results of the study, called Improving Oxygen Therapy in Acute-illness (IOTA), have immediate and important implications for health-care providers, policymakers and researchers, say the authors.

"Prior practice guidelines and medical directives on oxygen therapy for acute illnesses have been inconsistent," said Derek Chu, first author of the paper and a McMaster clinical fellow.

"Our results provide much-needed clarification by showing, with high-quality evidence, that administering too much supplemental oxygen increases mortality among a broad range of acute illnesses.

"Currently, patients are frequently given supplemental oxygen and at excessive levels. A simple change to current practice - being more moderate and cautious with how much oxygen is administered to acutely unwell patients - could save lives."

There was no external funding for this study.

There is also an accompanying commentary by John W. McEvoy, John Hopkins University, Baltimore, MD.

http://bit.ly/2w1I8hw

Meningococcal meningitis: Stomach pain should be seen as a warning sign

Patients with meningococcal infection generally develop symptoms including a high temperature, vomiting and a stiff neck... but they might also just have a bad stomach ache.

This can be so severe that they are sometimes wrongly operated for appendicitis. Teams from the Institut Pasteur and the Department of Pediatrics at Bicêtre Hospital (AP-HP) decided to investigate the question. And the results speak for themselves: 10% of patients infected by the meningococcal strain that is on the rise in Europe suffer from abdominal pain. This atypical form of the disease is becoming increasingly common and needs to be brought to the attention of physicians. The findings are published in Clinical Infectious Diseases.

Within the first 24 hours of meningococcal infection - which can give rise to meningitis and septicemia as well as arthritis, peritonitis, etc. -, patients generally suffer from headaches, vomiting and a stiff neck. Over the past few years, however, abdominal pain has been observed as another early clinical sign - but physicians tend not to think of invasive meningococcal disease. "When doctors see patients suffering from stomach pain, invasive meningococcal disease doesn't immediately spring to mind. They tend to think of gastroenteritis or possibly appendicitis," explains Muhamed-Kheir Taha, lead author of the study and Head of the National Reference Center for Meningococci

(CNRM) at the Institut Pasteur. "But delays in diagnosis and appropriate treatment for those affected can be deadly. Invasive meningococcal disease is fatal in virtually all cases if antibiotics are not administered rapidly." The team led by Muhamed-Kheir Taha, in collaboration with a team from the Department of Pediatrics at Bicêtre Hospital (AP-HP), decided to take a closer look at these abdominal forms to assess their frequency and raise awareness among physicians of this new face of the disease.

Since meningococcal disease is a notifiable condition, the CNRM has received all the bacterial strains responsible for meningococcal infections in France since the 1980s. So the scientists were able to analyze some 12,000 meningococcal strains kept at the CNRM between 1991 and 2016 and examine the clinical presentations of the patients infected. They isolated 105 cases associated with abdominal pain, gastroenteritis or diarrhea. "That number represents just 1% of patients, which is not very many, even if the real figure is probably higher since it is hard to know whether babies are suffering from stomach pains," says Muhamed-Kheir Taha. "But if we focus on the past two or three years and the group W bacterial strain, which arrived in Europe in 2013-2014 and has grown rapidly ever since, the figure rises to 10% of cases." In other words, the emergence of these new W isolates changed clinical presentations and people with meningococcal infection today are more likely to suffer from abdominal pains. So it is urgently necessary to take this symptom into consideration in medical diagnosis. Abdominal pains, together with other signs such as leg pain, headaches and poor blood supply to the nails, should raise alarm bells for meningococcal meningitis.

To investigate their findings further, the team sequenced all the genomes of the bacteria in their collection to identify what sets them apart from other strains and what might explain the resulting abdominal pains. Here again, the scientists' findings were relatively clear. The group W bacterial strain that is currently spreading across Europe and the world has around a hundred specific genes, some of which are involved in the inflammatory response. "We should remember that the bacteria infect the vessels which supply blood to the abdomen and the digestive system," emphasizes Muhamed-Kheir Taha. "If these bacteria are likely to induce a stronger inflammatory response in tissues, that could explain the abdominal pains." The scientists will continue their research by looking more closely at these genes to try to understand the mechanism of action of this strain, paving the way for more rapid diagnosis of a disease which still claims some 135,000 lives worldwide every year.

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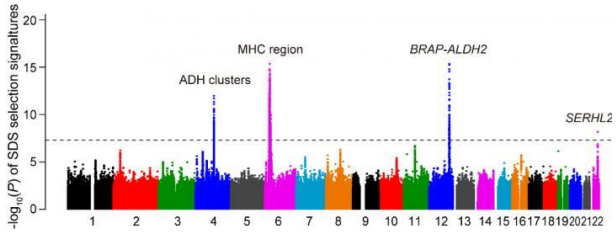
Study sheds light on recently evolved traits among Japanese descendants

Researchers centered at Osaka University identify genetic traits that evolved very recently in human history among Japanese populations

Osaka - Evolution enables beneficial traits to dominate a population. Given enough time, groups exposed to different environments will eventually evolve unique adaptive traits. Knowing how environmental pressures shape human evolution can lead to a better understanding of why certain populations or ethnic groups today are predisposed to certain characteristics.

In a new study published in *Nature Communications*, researchers centered at Osaka University conducted a large-scale genomic analysis to explore recent evolutionary events among individuals of Japanese descent.



Genetic loci with strong recent selection pressure in the Japanese population.
Osaka University

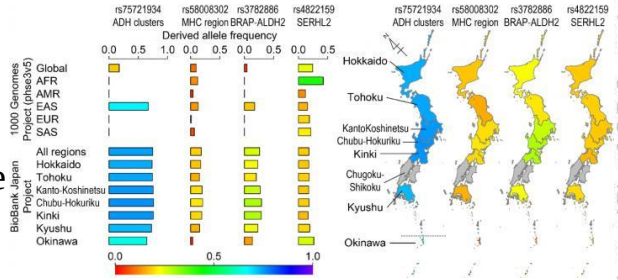
The team performed whole-genome sequencing using 2,234 Japanese participants. As its name suggest, the technique attempts to read the entirety of a genome--all three billion letters of it.

Comparing the genomes of many individuals at once makes it possible to find regions that have changed more rapidly than others--in other words, places where evolution has caused a particular genetic trait to predominate.

Not all genome sequencing studies are created equal; however, with some doing a better job of reading genomes than others.

"Whole-genome sequencing is a common technique, but our analysis achieved exceptionally 'deep' sequencing," lead author Yukinori Okada explains.

"This means that we collected significantly more information from each person's genome compared with similar studies. This allowed us to identify evolutionary changes that occurred over much more recent periods of time, on the scale of the last 2,000 to 3,000 years."

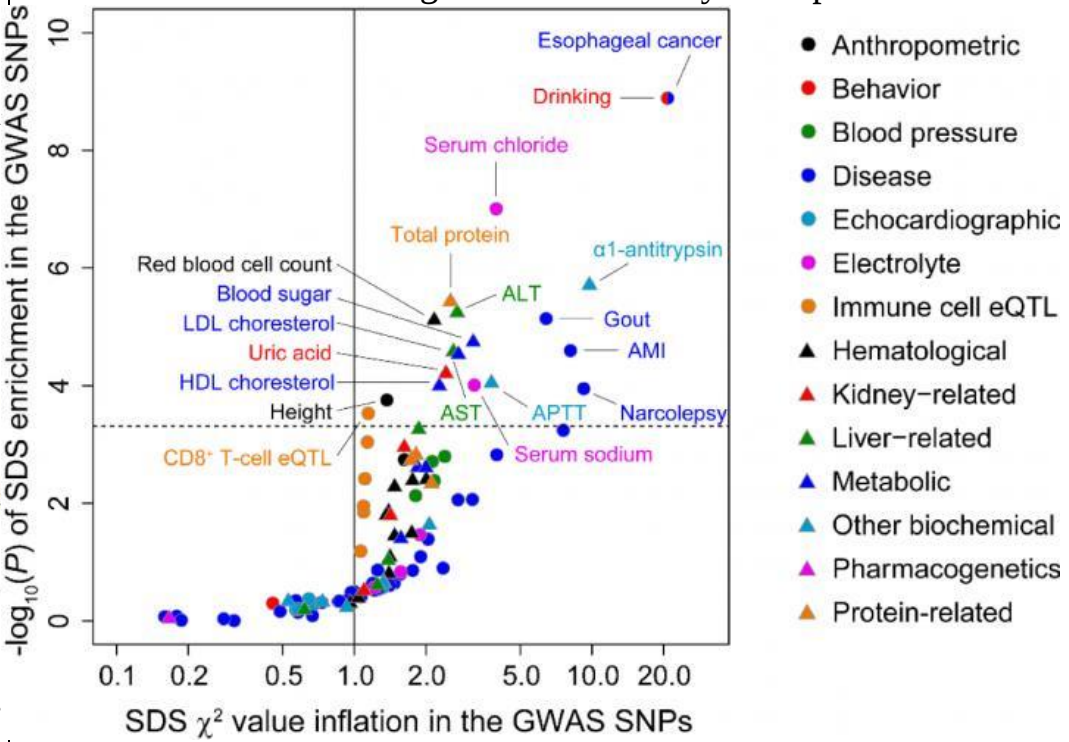


Genetic variants with selection pressure showed regional heterogeneity in allele frequency spectra, especially at the Okinawa region. **Osaka University**

Previous studies looking at similar time scales have focused exclusively on European ancestry. In those studies, it was found that Europeans mostly experienced adaptations related to height, obesity, and the immune system.

The current study supplements these findings by focusing on Japanese individuals--from an area where evolutionary pressures have had a distinct impact on adaptive traits.

"Our study is the largest high-depth sequencing study conducted to date on a non-European population," contributing author Saori Sakaue adds. "We found that very different evolutionary traits have evolved in Japanese populations over the last few thousand years, particularly traits involved in the metabolism of alcohol, glucose, and lipids. Given the clear evolutionary differences between European and Japanese populations, we expect our findings to shed light on how different ancestries can evolve divergent traits over very short periods of time."



Overlap of the human complex traits with selection pressure in the Japanese population. **Osaka University**

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Obesity inhibits key cancer defense mechanism

Obesity could enhance cancer development while aspirin might prevent it -- a new insight into potential targets for cancer prevention

Obesity is a known risk factor for certain types of cancer, including colon, pancreatic and breast cancer. Studies have shown its role in promoting tumor growth and malignant progression. But its role in cancer initiation has been uncertain.

"Epithelial" cells lining the surfaces of organs have the intrinsic ability to remove potentially malignant cells from their midst. This is called the "epithelial defense against cancer" mechanism. Normally, the cells

sense harmful cells and push them out by the process called cell competition.

To study how obesity affects this defense mechanism, researchers from Hokkaido University and their collaborators bred mice that were designed to express a known cancer-inducing mutant protein called Ras. Epithelial cells usually remove the potentially malignant Ras-transformed cells.

Feeding the Ras mice high-fat diets, which resulted in severe obesity, suppressed the defense mechanism and therefore increased the number of Ras-transformed cells remaining in the tissue. This suppression was seen in the intestine and pancreas, but not in the lungs. Furthermore, a month later the Ras-transformed cells developed a tumor in the pancreas of mice with the high-fat diet. The result supports previous correlations made between intestinal and pancreatic cancer and obesity, but not lung cancer.

Following experiments using the mice model and cultured cells revealed that fatty acids and chronic inflammation cause the suppression of the defense mechanism.

When mice fed a high-fat diet were treated with aspirin, known for its anti-inflammatory properties, the defense mechanism was substantially enhanced. This implies that reinforcing the epithelial defense mechanism with anti-inflammatory drugs could be utilized for cancer prevention.

"This is the first report to show that obesity and chronic inflammation can influence competitive interaction between normal cells and transformed cells. It implies other factors such as infection, smoking, sleeping patterns and aging may also affect cell competition," says Yasuyuki Fujita of Hokkaido University who led the study.

https://nyti.ms/2Fsp8s5

‘Desperation Oncology’: When Patients Are Dying, Some Cancer Doctors Turn to Immunotherapy

Dr. Oliver Sartor has a provocative question for patients who are running out of time.

By GINA KOLATA APRIL 26, 2018

Most are dying of prostate cancer. They have tried every standard treatment, to no avail. New immunotherapy drugs, which can work miracles against a few types of cancer, are not known to work for this kind.

Still, Dr. Sartor, assistant dean for oncology at Tulane Medical School, asks a diplomatic version of this: Do you want to try an immunotherapy drug before you die?

The chance such a drug will help is vanishingly small — but not zero. “Under rules of desperation oncology, you engage in a different kind of oncology than the rational guideline thought,” Dr. Sartor said.

The promise of immunotherapy has drawn cancer specialists into a conundrum. When the drugs work, a cancer may seem to melt away overnight. But little is known about which patients might benefit, and from which drugs.

Some oncologists choose not to mention immunotherapy to dying patients, arguing that scientists first must gather rigorous evidence about the benefits and pitfalls, and that treating patients experimentally outside a clinical trial is perilous business.

But others, like Dr. Sartor, are offering the drugs to some terminal patients as a roll of the dice. If the patient is dying and there’s a remote chance the drug will help, then why not?

“Immunotherapy is a particularly nuanced problem,” said Dr. Paul Helft, an ethicist and oncologist at Indiana University School of Medicine.

Cancer doctors are well aware of the pitfalls of treating patients before all the evidence is in.

Many still shudder at the fiasco that unfolded in the 1980s and 1990s, when doctors started giving women with breast cancer extremely high doses of chemotherapy and radiation on the theory that more must be better. The doctors did not systematically collect data; instead, they reported patient anecdotes claiming success.

Then a clinical trial found that this treatment was much worse than the conventional one — the cancers remained just as deadly when treated with high doses, and the regimen itself killed or maimed women.

But immunotherapy is like no cancer treatment ever seen. It can work no matter what kind of tumor a person has. All that matters is that the immune system be trained to see the tumor as a foreign invader.

Tumors have mutations that stud them with bizarre proteins. The white blood cells of the immune system try to attack but are repelled by a molecular shield created by the tumors. The new drugs allow white blood cells to pierce that shield and destroy the tumors.

Last week brought a yet another example of the surprising power of this approach. Lung cancer patients who normally would receive only chemotherapy lived longer when immunotherapy was added, researchers reported in a clinical trial.

But the drugs are exorbitantly expensive. One that Dr. Sartor often uses costs $9,000 per dose if used once every three weeks, and $7,000 if used once every two weeks. Often, he and other doctors persuade a patient's insurer to pay. If that fails, sometimes the maker will provide the drug free of charge.

Immunotherapy drugs can have severe side effects that can even lead to death. Once the immune system is activated, it may attack normal tissues as well as tumors. The result can be holes in the intestines, liver failure, nerve damage that can cause paralysis, serious rashes and eye problems, and problems with the pituitary, adrenal or thyroid glands. Side effects can arise during treatment or after the treatment is finished.

For most patients, though, there are no side effects or only minor ones. That makes giving an immunotherapy drug to a dying patient different from trying a harsh experimental chemotherapy or a treatment like intense radiation.

The problem is deciding ahead of time if an immunotherapy drug will help. Doctors check biomarkers, chemical signals like proteins that arise when the immune system is trying to attack. But they are not very reliable.

"A positive biomarker does not guarantee that a patient will benefit, and a negative biomarker does not mean a patient will not benefit," said Dr. Richard Schilsky, senior vice president and chief medical officer of the American Society of Clinical Oncology. "You don't have a solid biology to go on."

It was this problem, described at a medical conference a couple of years ago, that led Dr. Sartor to begin offering immunotherapy to dying patients.

"I was thinking, 'My God, these tests that are used to drive clinical decision making are not worth a damn,'" he said. "These are peoples' lives here. We are playing with the highest of stakes."

"For certain people it is like, bingo, you give the drug to them and they have a long-lasting and positive benefit," he added. "When our knowledge is not sufficient to inform our decisions, then we have an ethical conundrum."

Out of curiosity, Dr. Sartor emailed eight prominent prostate cancer specialists asking if they, too, offered immunotherapy drugs to patients on the off-chance the treatments would help.

Five said they offer it, with a variety of provisos, offering comments like, "If I was a patient, I want my doc to do everything."

Dr. Daniel George, at Duke University, said he does not offer immunotherapy to every man who is dying of prostate cancer. But, he said, "for those patients who want to do everything they possibly can, that's the group where we try checkpoint inhibitors," a type of immunotherapy.

To the others — the majority of his patients with metastatic prostate cancer — he does not mention immunotherapy.

"We have to balance between hope and reality," he said. "The most difficult conversation we have with patients is when we have to tell them that more treatment is actually hurting them more than the cancer."

Dr. Daniel Petrylak, a prostate cancer specialist at Yale, said his inclination was to offer immunotherapy only to those rare patients whose tumors have a genetic marker indicating the immune system is

trying to attack — already an approved indication for prostate cancer, he noted. But this strategy gives him a rationale for trying the drugs on patients with other cancers.

With the possibility of a dramatic and prolonged response, he said in an interview, "how can you ethically deny this to patients?"

At the Dana-Farber Cancer Institute in Boston, Dr. Christopher Sweeney said he petitions an insurance company to get an immunotherapy drug when the patient has a genetic marker predicting a possible response — an indicator the drug might work even if there is as yet no clinical trial evidence that it will — and is strong enough to tolerate the treatment.

But if those conditions do not apply, as is usually the case, Dr. Sweeney only gives the drugs to patients if he can do so as part of a clinical trial, where something can be learned from their experience.

And if there is no clinical trial for the patient? "I basically say I don't have any approved therapies," Dr. Sweeney said. "Here's the truth — most patients don't benefit from these drugs."

He tells patients that just because he has no more drugs to give does not mean he has abandoned them. Supportive care can make patients more comfortable, even prolong their lives.

Dr. Sartor disagreed with the approach. "I would love for every patient to be on a clinical trial," he said. "But does that mean I shouldn't try because I don't have a trial?"

One of the first patients Dr. Sartor treated with immunotherapy was George Villere, a retired investment adviser who lived in New Orleans. Mr. Villere had bladder cancer and had tried chemotherapy. It didn't work, so Dr. Sartor told Mr. Villere that he had run out of conventional options and asked if he wanted to try immunotherapy. At the time, the drugs had not been approved for bladder cancer.

Mr. Villere and his wife, Fran Villere, thought it over, asking themselves whether they would regret it if they did not try. "I thought we would," Mrs. Villere recalled in an interview.

Their insurance agreed to pay, and Mr. Villere took the drug for several months. Nonetheless, he died on November 15, 2016, at age 72.

"He had no side effects," Mrs. Villere said. "But the drug didn't do a damn thing."

Then there is Clark Gordin, 67, who lives in Ocean Springs, Miss. He had metastatic prostate cancer, "a bad deck of cards," he said in an interview.

Dr. Sartor tried conventional treatments, but they didn't work for Mr. Gordin. Finally, the doctor suggested immunotherapy.

Mr. Gordin's insurer refused. But then the lab that had analyzed his tumor discovered it had made a mistake.

There was a chance Mr. Gordin might respond to immunotherapy, because he had a rare mutation. So his insurer agreed to pay.

Immediately after taking the drugs, Mr. Gordin's PSA level — an indicator of the cancer's presence — went down to nearly zero.

"Makes my heart nearly stop every time I think about it," Dr. Sartor said. "Life sometimes hangs on a thin thread."

http://bit.ly/2rq78qn

Human Brain Gain: Computer Models Hint at Why We Bested Neandertals

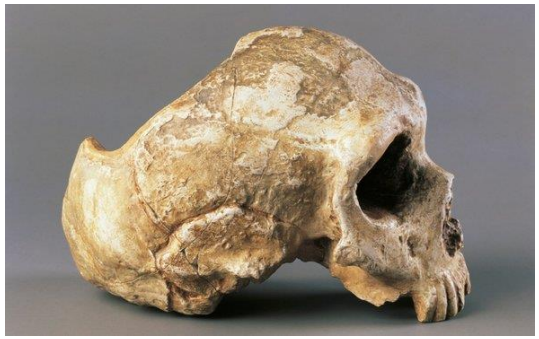
Differences in the structure of the brain's cerebellum may help explain our superior cognitive abilities

By Simon Makin on April 26, 2018

The parallel existence of an intelligent species closely related to us has long fascinated scientists and the public alike. The most debated issue is why Neandertals ultimately disappeared. Potential explanations include violent conflict with *Homo sapiens*, disease, difficulty adapting to rapid environmental and climate change, interbreeding with modern humans and differences between the two species in technical, social and cognitive abilities.

Now new research from a group led by paleoanthropologist Takeru Akazawa of Kochi University of Technology in Japan has shed light on the question using computational techniques to reconstruct the

Neandertal brain and estimate differences in the size of specific regions between species. The results add weight to the idea that cognitive differences contributed to the Neandertals being out-competed and ultimately replaced by our ancestors.



Male Neanderthal skull (*Homo sapiens Neanderthalensis*) from Gibraltar. G. Cigolini *Getty Images*

The study, published April 5 in *Scientific Reports*, used fossils of four Neandertals and four early human skulls to estimate the shapes and structures of their brains. "Previous studies studied shape differences of braincases but there are no studies of reconstruction of the brain itself," says biomechanical engineer and co-lead author Naomichi Ogihara of Keio University in Japan. "Our method allows estimation of the shape and volume of each brain region, which is quite impossible just by analyzing the endocranial surfaces."

The team achieved this feat by averaging brain scans from 1,185 living humans to generate a model of the average human brain. "[The authors] deform a statistical model of the human brain onto Neandertals' braincases, proposing a new method to delineate the brain in fossil species," says paleoneurologist Emiliano Bruner of the National Research Center for Human Evolution in Spain who was not involved in the study. This allowed them to estimate what the brains of the two species may have looked like and how specific regions may have differed between them.

The results show that although there was no difference in the overall size of Neandertals' brains, significant differences may have characterized the dimensions of specific regions, particularly the cerebellum. "This was surprising since the cerebellum is traditionally considered important for motor-related functions, Ogihara says. "We initially expected that the frontal lobe would be different between the two species because it has been considered to be related to higher cognitive functions, but it was not the case."

The researchers, however, went further by analyzing correlations between brain scans and behavioral data in an existing database (from the Human Connectome Project). They found greater cerebellum volume is associated with abilities such as cognitive flexibility, attention, language processing and memory. "The paper gives the impression the cerebellum is intimately involved in a large number of higher cognitive functions, says evolutionary psychologist Robin Dunbar of the University of Oxford in England who was not involved in the work. "This isn't strictly true—its function seems to be rather one of coordination between different brain units and cognitive processings—in effect, making sure computations are done in the right order. That role is almost certainly crucial to higher cognitive functions and allows us to do what we do," he says. One reason for the importance of cerebellum volume, the authors suggest, is that unlike other regions it consists of a large array of identical processing units, so larger volumes logically equate to higher processing capacity.

One caveat, Bruner says, is the methods used in the study would be blind to any brain changes that occurred after Neandertals split from humans on the evolutionary tree. "Deforming a modern brain into a Neandertal one may obscure changes specific to the two lineages," he says. "After their separation, the Neandertal and modern lineages could have undergone some specific changes that cannot be detected by this method." The authors reason, however, that since chimpanzee and bonobo brains can be morphed into each other, and they diverged around two million years ago, the approach is a reasonable one, because Neandertals more recently diverged from humans some 700,000 years ago.

The findings do not conclusively prove what caused the Neandertals' extinction but they do suggest brain differences probably contributed to their disappearance. "What we can say based on the present study is

that innate differences in brain structure actually existed between the two species, possibly leading to differences in cognitive and social abilities," Ogihara says. "Although the difference could be subtle, such a difference may become significant in terms of natural selection."

Dunbar has previously shown a relationship between brain size and social group size in primates, including human social networks. Those findings involved parts of the cortex, but similar effects may be at work here. "If [the cerebellum's function was reduced in Neandertals, it confirms that their cognitive abilities weren't quite as advanced as those of modern humans," he says. "That of course doesn't make them any less human, or shambling ape-men, but it does mean their social and cultural capacities—the traits that survival really hinges on, especially in tough times—wouldn't have been quite as effective as those of modern humans, which may well explain why they went extinct and our lineage didn't."

Ogihara says they would next like to develop their new methods by exchanging ideas with researchers working on human brain evolution. "We are also interested in applying our methodology to brain reconstruction of other hominins," he says.

http://bit.ly/2HZBRHY

Researchers map the potential spread of yellow fever virus to cities around the world

New analysis shows potential risk for yellow fever virus to spread to urban centres where it previously has not been seen

TORONTO - The deadly yellow fever virus has the potential to spread into cities around the world where it previously hasn't been seen, according to a new study led by St. Michael's Hospital.

Researchers led by Dr. Kamran Khan of St. Michael's have mapped the worldwide pathways through which yellow fever virus could spread by analyzing global patterns of airline travellers, the environmental conditions needed to enable transmission of the virus within a city, and countries' requirements for travellers to provide proof of yellow fever vaccination upon entry.

Published in the *Bulletin of the World Health Organization*, the research does not model a particular outbreak, but rather examines the potential spread for yellow fever virus to spread between the world's cities.

"Imagine a yellow fever outbreak as a fire," said Dr. Khan, who is a scientist at the Li Ka Shing Knowledge Institute of St. Michael's Hospital. "Embers can fly off in different directions, and if they land in the right place, they can create another fire. We studied the global conduits through which yellow fever virus can spread, and the potential for new yellow fever outbreaks to occur in the world's urban areas."

The team of researchers took a global panoramic view of yellow fever virus. They separated the world into three types of places: endemic areas, places where yellow fever virus is established; areas that appear suitable for yellow fever virus transmission but where it has not yet been seen; and non-endemic areas where there is no yellow fever virus and the environment appears unsuitable for it to spread. Yellow fever is spread through the bite of an Aedes aegypti mosquito, which can also transmit viruses such as dengue, chikungunya and Zika.

According to the U.S. Centers for Disease Control and Prevention (CDC), about 15 per cent of people who get yellow fever develop serious illness that can be fatal.

"Yellow fever vaccine is the best protection against yellow fever disease," says Dr. Martin Cetron, head of CDC's Division of Global Migration and Quarantine. "CDC urges anyone traveling to a country where yellow fever is circulating to be vaccinated against yellow fever. Yellow fever vaccine is available at a limited number of clinics in the U.S., and people with some medical conditions shouldn't be vaccinated, so travellers should plan ahead."

Some countries have set up policies requiring international travellers to provide proof of yellow fever vaccination upon entry. Dr. Khan and his team took into account which countries require proof and which currently don't. They then analyzed the travel patterns of 1.4 billion people flying through commercial airports around the world.

"There are different levels of risk depending on where the person is travelling to and where they are coming from," Dr. Khan said. "In today's increasingly connected world, one of the key concerns is that yellow fever virus could be carried by a traveller into a densely populated city that has the environmental conditions necessary to support its transmission, but where the virus has never been seen before. In this setting, the urban population would have essentially have no preexisting immunity to the virus."

Through their analysis, Dr. Khan's team found that:

- ***89 per cent of travellers departing from yellow fever-endemic areas to other yellow fever-endemic areas were required to provide proof of vaccination upon entry***
- ***Less than 35 per cent of travellers departing yellow fever-endemic areas for cities that appear suitable for yellow fever virus transmission were required to provide proof of vaccination upon entry***
- ***Less than 25 per cent of travellers who departed from areas of the world where there is no yellow fever virus for areas that are endemic with yellow fever virus were required to provide proof of vaccination upon entry***
- ***Brazil, China, India, Mexico, Peru and the United States had the highest volumes of travellers arriving from yellow-fever endemic areas and the largest populations living in cities that appear suitable for yellow fever virus transmission***

"Now that we have a global view of how yellow fever virus can travel between the world's cities, countries can reexamine their policies to prevent the importation of yellow fever virus, protect travellers from getting infected with the virus, and in turn prevent its exportation to other parts of the world," Dr. Khan said. "We can't assume that if a yellow fever outbreak has never occurred before in a specific urban area of the world that it will never occur in the future."

In the meantime, Dr. Khan recommends that travellers maintain awareness of the current requirements for yellow fever vaccination and that they have a thoughtful discussion with their physician about whether or not they should receive the yellow fever vaccine before they travel.

The full paper is available online here:

- *In draft form until 1 May: http://www.who.int/bulletin/online_first/BLT.17.205658.pdf*
- *As of 1 May: http://dx.doi.org/10.2471/BLT.17.205658*

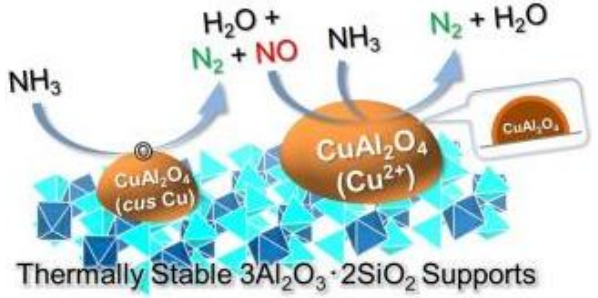
http://bit.ly/2KpHVaY

New catalyst turns ammonia into an innovative clean fuel

NH_3 has been drawing attention recently as a carbon-free alternative fuel

日本のニュース

Taking measures against climate change and converting into societies that use significant amounts of renewable energy for power are two of the most important issues common to developed countries today. One promising technology in those efforts uses hydrogen (H_2) as a renewable energy source. Although it is a primary candidate for clean secondary energy, large amounts of H_2 must be converted into liquid form, which is a difficult process, for easier storage and transportation. Among the possible forms of liquid H_2, ammonia (NH_3) is a promising carrier because it has high H_2 density, is easily liquefied, and can be produced on a large-scale.



CuOx/3A2S selectively produces N_2 and H_2O from NH_3 through a two-step reaction. **Dr. Satoshi Hinokuma**

Additionally, NH_3 has been drawing attention recently as a carbon-free alternative fuel. NH_3 is a combustible gas that can be widely used in thermal power generation and industrial furnaces as an alternative to gasoline and light oil. However, it is difficult to burn (high ignition temperature) and generates harmful nitrogen oxides (NOx) during combustion.

Researchers at the International Research Organization for Advanced Science and Technology (IROAST) in Kumamoto University, Japan focused on a "catalytic combustion method" to solve the NH_3 fuel problems. This method adds substances that promote or suppress

chemical reactions during fuel combustion. Recently, they succeeded in developing a new catalyst which improves NH_3 combustibility and suppresses the generation of NOx. The novel catalyst (CuOx/3A2S) is a mullite-type crystal structure $3Al_2O_3{\cdot}2SiO_2$ (3A2S) carrying copper oxide (CuOx). When NH_3 was burned with this catalyst, researchers found that it stayed highly active in the selective production of N_2, meaning that it suppressed NOx formation, and the catalyst itself did not change even at high temperatures. Additionally, they succeeded with *in situ* (*Operando*) observations during the CuOx/3A2S reaction, and clarified the NH_3 catalytic combustion reaction mechanism.

Since 3A2S is a commercially available material and CuOx can be produced by a method widely used in industry (wet impregnation method), this new catalyst can be manufactured easily and at low cost. Its use allows for the decomposition of NH_3 into H_2 with the heat from (low ignition temperature) NH_3 fuel combustion, and the purification of NH_3 through oxidation.

"Our catalyst appears to be a step in the right direction to fight anthropogenic climate change since it does not emit greenhouse gasses like CO_2 and should improve the sophistication of renewable energy within our society," said study leader Dr. Satoshi Hinokuma of IROAST. "We are planning to conduct further research and development under more practical conditions in the future."

This research was posted online in the *Journal of Catalysis* on 26 March 2018.

Hinokuma, S., Kiritoshi, S., Kawabata, Y., Araki, K., Matsuki, S., Sato, T., & Machida, M. (2018). Catalytic ammonia combustion properties and operando characterization of copper oxides supported on aluminum silicates and silicon oxides. Journal of Catalysis, 361, 267-277. doi:10.1016/j.jcat.2018.03.008

http://bit.ly/2jfXFkB

New development in contact lenses for red-green color blindness using simple dye

Hope that contact lens with low-cost dye will help people with color blindness

Researchers at the University of Birmingham have developed a contact lens that may help people with colour blindness simply by using a low cost dye, according to research published today (26 April 2018) in the journal *Advanced Healthcare Materials*.

Colour blindness – or colour vision deficiency (CVD) – is an inherited genetic ocular disorder where some people have difficulty distinguishing certain colours. While no cure for this disorder exists, several methods have been used to increase the colour perception of those affected. However, current products on the market such as colour filtering glasses are expensive, bulky and incompatible with other vision corrective glasses.

University of Birmingham

Normal colour vision is trichromatic – this means any colour can be created by combining the colours blue, red and green, which are perceived by a cluster of cones at the back of the eye. These cones are divided into three groups, responsible for short wavelengths – blue – medium wavelengths – green – and long wavelengths – red. In normal vision all three are present. When any of these cones are missing, the brain receives incorrect information leading to limited ability to identify certain colours in some people.

Several companies are already selling glasses and custom made lenses for colour blindness correction which can be expensive for many users, however, in this research an inexpensive soft commercial contact lens was dyed with a non-toxic rhodamine derivative dye. This particular derivative of rhodamine was chosen as it is known for its ability to absorb certain wavelengths of light in the optical spectrum. Researchers found that the dye blocked the band that lies between the red and green wavelengths, which is perceived by two sets of corresponding optical cones simultaneously. The removal of this band through the dyed lens inhibited the simultaneous triggering of the cones designated for green

and red wavelength bands, enabling better differentiation between red and green colours.

The dyed lens was tested on people with red-green colour vision deficiency (the most common form of CVD). The dyed contact lens was applied to a glass slide. The participants were asked to look at several numbers through the dyed lens, and to note whether there were any improvements to the colours or the clarity of the number. They were also asked to observe their surroundings and note whether they saw any improvements in their colour perception.

The results verified that dye tinted lenses can be used to enhance the colour perception of people affected by colour vision deficiency. Further patient studies are now underway.

Dr. Haider Butt, lead researcher from the University of Birmingham's Department of Mechanical Engineering and the Institute of Healthcare Technologies., said: "Contact lenses are of interest for colour blindness correction because it is easier to correct the entire field of view. The dye processing we carried out does not need any complex preparation, it is not toxic to the human eye, and our method could be easily used in both glasses and contact lenses at low cost."

He continued: "We are now looking into using a similar process to correct purple-blue colour blindness, and also to bring together a number of dyes to make lenses perform for both red-green and purple-blue colour blindness simultaneously. We are about to commence human clinical trials shortly."

More information: *Abdel-Rahman Badawy et al. Contact Lenses for Color Blindness, Advanced Healthcare Materials (2018). DOI: 10.1002/adhm.201800152*