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Study finds onion and garlic consumption may reduce breast cancer risk

Onions and garlic may also be a recipe for reducing the risk of breast cancer

BUFFALO, N.Y. -- Onions and garlic are key ingredients in sofrito, a condiment that's a staple of Puerto Rican cuisine. They may also be a recipe for reducing the risk of breast cancer.

That's according to the findings of a study led by University at Buffalo and University of Puerto Rico researchers. It's the first population-based study to examine the association between onion and garlic consumption and breast cancer in Puerto Rico. The results were published in the journal Nutrition and Cancer.

"We found that among Puerto Rican women, the combined intake of onion and garlic, as well as sofrito, was associated with a reduced risk of breast cancer," said Gauri Desai, the study's lead author, who is an epidemiology PhD student in UB's School of Public Health and Health Professions.

In fact, those who consumed sofrito more than once per day had a 67% decrease in risk compared to women who never ate it. The idea for the study stemmed from previous scientific evidence showing that eating onions and garlic may have a protective effect against cancer.

"Studying Puerto Rican women who consume a lot of onions and garlic as sofrito was unique," Desai said, adding that it was total intake of onions and garlic, not sofrito alone, that was associated with breast cancer risk.

Puerto Rico was a perfect place to study, because women there consume larger amounts of onions and garlic than in Europe and the U.S., due largely to the popularity of sofrito, Desai noted. Onions and garlic also are eaten regularly in "guisos" (stews), as well as in bean- and rice-based dishes in Puerto Rican cuisine.

In addition, "Puerto Rico has lower breast cancer rates compared to the mainland U.S., which makes it an important population to study," Desai said.

"There is very little research on breast cancer in Puerto Rico. This study was a collaboration between my colleagues here at UB and at the University of Puerto Rico to help us understand why rates there are lower than in the rest of the U.S., and why rates there are continuing to increase while they are decreasing in the rest of the United States," said study co-author Jo Freudenheim, PhD, chair of epidemiology and environmental health at UB.

So, why the focus on these two ingredients? "Onions and garlic are rich in flavonols and organosulfar compounds," Desai said.

In particular, garlic contains compounds such as S-allylcysteine, diallyl sulfide and diallyl disulfide, while onions contain alk(en)yl cysteine sulphoxides. "These compounds show anticarcinogenic properties in humans, as well as in experimental animal studies," said Lina Mu, the study's senior author, who is an associate professor of epidemiology and environmental health at UB.

Study participants were enrolled in the Atabey Study of Breast Cancer, a case-control study named after the Puerto Rican goddess of fertility. The study was conducted between 2008 and 2014 and included 314 women with breast cancer and 346 control subjects.

Desai's co-authors are, from UB's Department of Epidemiology and Environmental Health: Jing Nie, research assistant professor, and Ajay Myneni, research scientist; from the University of Puerto Rico: Michelle Schelske-Santos, Cruz Nazario, Rosa Rosario-Rosado, Imar Mansilla-Rivera and Farah Ramirez-Marrero; and from the University of California at Los Angeles: Zuo-Feng Zhang.

http://bit.ly/2mgYPkZ

Mummy study: Heart disease was bigger issue for human ancestors than initially thought

Mummies' arteries were more clogged than originally thought

A new imaging study of the mummified arteries of people who lived thousands of years ago revealed that their arteries were more

clogged than originally thought, according to a proof-of-concept study led by a researcher with The University of Texas Health Science Center at Houston (UTHealth). It is in the October print edition of the American Heart Journal.

"I wanted to see if heart disease is a modern-day problem. It appears to have been a problem for a very long time," said Mohammad Madjid, MD, MS, the study's lead author and an assistant professor of cardiovascular medicine with McGovern Medical School at UTHealth.

In the past when researchers analyzed the hearts and arteries of mummies, they used an imaging technique called computed tomography (CT scan) that creates meticulous images of blood vessels, organs, and bones. However, these scans detect only accumulated calcium in the arteries, not buildup of cholesterol.

Madjid said his team is the first to examine mummified arterial remains from different parts of the world with an imaging technique that detects cholesterol. It is called near-infrared spectroscopy.

"A catheter is placed on the sample and it sends out signals. The signals bounce off the tissue and come back. You can tell the difference between various tissue components because each has a unique molecular signature like a fingerprint," Madjid said.

Madjid's samples included mummified arterial tissue from three men and two women ranging in age from 18 to 55-60. Three died presumably of pneumonia and one of renal failure. The cause of death for the fifth person is unknown. Four lived in South America and one in the Middle East. They lived from the late Chinchorro era, 2000 B.C., to Cabuza, 350 to 1000 A.D.

The type of arterial disease detected is the result of cholesterol plaque buildup in arteries and is formally called atherosclerosis. It limits the flow of oxygen-rich blood to various parts of the body, and it can lead to a heart attack.

Cholesterol buildup is a hallmark of atherosclerosis from the very early stages, while calcium accumulation is a sign of late stages of the disease. Therefore, relying only on calcium by CT scan underestimates the true prevalence of the disease, Madjid said.

Madjid, who is affiliated with UT Physicians and the Memorial Hermann Heart & Vascular Institute -Texas Medical Center, said factors such as exposure to smoke from fire pits, viral infections, bacterial infections, and bad genes might have contributed to the plaque buildup in people living centuries ago. The buildup was also present in people at a relatively young age, he said.

The study offers new insight into the earlier pathological stages of atherosclerosis, showing a prevalence of cholesterol-rich plaques even in ancient times, the authors reported.

Madjid plans to examine additional mummified remains to see how widespread the arterial problems were.

The authors concluded, "Noninvasive near-infrared spectroscopy is a promising technique for studying ancient mummies of various cultures to gain insight into the origins of atherosclerosis."

Madjid's coauthors are Payam Safavi-Naeini, MD, of the Texas Heart Institute and Robert A. Lodder, PhD, of the University of Kentucky.

http://bit.ly/2ne94qa

Green tea could hold the key to reducing antibiotic resistance

Scientists at the University of Surrey have discovered that a natural antioxidant commonly found in green tea can help eliminate antibiotic resistant bacteria.

The study, published in the *Journal of Medical Microbiology*, found that epigallocatechin (EGCG) can restore the activity of aztreonam, an antibiotic commonly used to treat infections caused by the bacterial pathogen *Pseudomonas aeruginosa*.

P. aeruginosa is associated with serious respiratory tract and bloodstream infections and in recent years has become resistant to

many major classes of antibiotics. Currently a combination of antibiotics is used to fight *P. aeruginosa*.

However, these infections are becoming increasingly difficult to treat, as resistance to last line antibiotics is being observed.

To assess the synergy of EGCG and aztreonam, researchers conducted in vitro tests to analyse how they interacted with the *P. aeruginosa*, individually and in combination. The Surrey team found that the combination of aztreonam and EGCG was significantly more effective at reducing *P. aeruginosa* numbers than either agent alone.

This synergistic activity was also confirmed in vivo using Galleria mellonella (Greater Wax Moth larvae), with survival rates being significantly higher in those treated with the combination than those treated with EGCG or aztreonam alone. Furthermore, minimal to no toxicity was observed in human skin cells and in Galleria mellonella larvae.

Researchers believe that in *P. aeruginosa*, EGCG may facilitate increased uptake of aztreonam by increasing permeability in the bacteria. Another potential mechanism is EGCG's interference with a biochemical pathway linked to antibiotic susceptibility.

Lead author Dr Jonathan Betts, Senior Research Fellow in the School of Veterinary Medicine at the University of Surrey, said:

"Antimicrobial resistance (AMR) is a serious threat to global public health. Without effective antibiotics, the success of medical treatments will be compromised. We urgently need to develop novel antibiotics in the fight against AMR. Natural products such as EGCG, used in combination with currently licenced antibiotics, may be a way of improving their effectiveness and clinically useful lifespan."

Professor Roberto La Ragione, Head of the Department of Pathology and Infectious Diseases in the School of Veterinary Medicine at the University of Surrey, said:

"The World Health Organisation has listed antibiotic resistant *Pseudomonas aeruginosa* as a critical threat to human health. We have shown that we can successfully eliminate such threats with the use of natural products, in combination with antibiotics already in use. Further development of these alternatives to antibiotics may allow them to be used in clinical settings in the future."

This research was carried out in partnership with Public Health England, the German Centre for Infection Research and the University of Cologne.

https://bbc.in/2nq0K6Y

Medical cannabis product approved for epilepsy

The EU has approved for the first time the use of a medicinal cannabis product aimed at patients with two rare, but severe, forms of childhood epilepsy.

Doctors can prescribe Epidyolex - an oral solution of cannabidiol, which comes from the cannabis plant - if they think it will help sufferers.

It has been approved for use in the UK and other European countries, but the NHS does not currently recommend it.

But some parents want alternatives that contain a component not in this drug.

Last month, the UK's National Institute for Health and Care Excellence made an initial decision not to recommend prescribing Epidyolex, due to lack of evidence of long-term effectiveness.

Final guidance is due later this year.

What is Epidyolex?

The drug does not contain any of the psycho-active component of cannabis, a compound called tetrahydrocannabinol (THC).

Some parents, who have travelled to the Netherlands to buy cannabis medicines, feel the treatment will not help many children because it does not contain THC, which they argue has helped their children.

Epidyolex has been approved as a treatment option for children as young as two with Lennox-Gastaut syndrome or Dravet syndrome - difficult-to-treat conditions that can cause multiple seizures a day.

The medication, developed by GW Pharmaceuticals, will be used in combination with another epilepsy medication called clobazam.

What about other medical cannabis products?

There are many different medical cannabis products. The use of ones containing THC was legalised across the UK in November 2018.

These treatments can be prescribed only by specialist doctors in a limited number of circumstances where other medicines have failed.

Few of these unlicensed prescriptions have been made on the NHS.

There are some other cannabis-based medicines that are licensed in the UK.

Nabilone is a medicine, taken as a capsule, that has been developed to act in a similar way to THC.

Doctors can give it to people having chemotherapy to help with nausea.

Sativex is a cannabis-based medicine that contains THC and CBD and is licensed in the UK for people with multiple sclerosis.

Recreational use of cannabis remains illegal.

What do experts say?

Ley Sander, Medical Director at the Epilepsy Society and Professor of Neurology at University College London, said: "This new drug will bring hope for some families and EU approval feels like a positive step. Medicinal cannabis, however, still remains a medical minefield and there are many hurdles ahead.

"CBD was not recommended by NICE for prescription on the NHS. It is important that the pharmaceutical industry continues to work with the medical advisory body to ensure that drugs are cost effective and that its long-term effects are clear."

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Strip steak: Bacterial enzyme removes inflammation-causing meat carbohydrates

Gut bacteria employ enzymes to strip our cells of their Neu5Gc content so they can feast on underlying sugars

Most mammals naturally produce a carbohydrate known as Neu5Gc—humans do not. However, when we eat red meat, animal Neu5Gc is incorporated in our tissues. As the carbohydrate builds up, our immune systems treat Neu5Gc as a foreign invader, generating antibodies against it. That's why red meat-rich diets are associated with chronic inflammation and related diseases, such as colon cancer and atherosclerosis.

Researchers at University of California San Diego School of Medicine recently discovered how gut bacteria employ enzymes to strip our cells of their Neu5Gc content so they can feast on underlying sugars, and in doing so, release the carbohydrate into the bloodstream.

The study, published September 23, 2019 in *Nature Microbiology*, introduces the possibility of using these bacterial enzymes, called sialidases, to clear Neu5Gc from our tissues and potentially remove the carbohydrate from red meat before it's consumed.

"It's our hope that this approach could be used as a sort of probiotic or prebiotic to help reduce inflammation and the risk of inflammatory diseases—without giving up steak," said senior author Karsten Zengler, Ph.D., professor of pediatrics and bioengineering at UC San Diego.

Scientists have known for decades that colon cancer and atherosclerosis are more common in people who eat a lot of red meat, but not in non-human carnivores. Neu5Gc was implicated as the link between red meat consumption and these human diseases in previous studies by study co-author Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular Medicine at UC

San Diego School of Medicine, and colleagues. They showed that dietary Neu5Gc promotes inflammation, tumors and atherosclerosis in Neu5Gc-deficient (humanized) mice.

In their latest study, Zengler's team used similar humanized mice (mouse models that have been genetically modified to reflect human biology in some way) to determine how diet influences the makeup of the microbiomes—communities of microbes, particularly bacteria—living in the gut. The mice were fed either an Neu5Gc-rich red meat diet or one of two control diets that lacked the carbohydrate.

Overall, the red meat-like diet was associated with less bacterial diversity in the mouse gut microbiomes. Yet there were several bacteria types that were more abundant in the guts of the Neu5Gc-fed mice than the mice that didn't consume the meat-related carbohydrate. One of these was *Bacteroides*, a type of bacteria known for surviving on carbohydrates. More specifically, a *Bacteroides* enzyme was especially plentiful in the Neu5Gc-fed mice—a new type of sialidase that cleaves Neu5Gc off of cells.

To determine how the mouse results might translate to humans, Zengler originally hoped to conduct a study in which people would eat a vegetarian diet for two months, then switch to meat consumption for two months, all while the team tracked how their gut microbiomes and sialidases changed. Instead of launching such a study, which would have been costly, Zengler found a naturally occurring experiment in the lifestyle of the Hadza, an indigenous hunter-gatherer group that lives in a remote region of Tanzania, in East Africa. In the dry season, the Hadza hunt and eat meat. In the wet season, they can't hunt and rely instead on a diet primarily of berries and honey.

Other research groups have previously studied the Hadza and their microbiomes. Examining publicly available genomic data from Hadza gut bacteria over time, Zengler's team noticed that *Bacteroides* containing the sialidase gene were at least twice more abundant during the dry (meat-eating) season, compared to the wet season.

But just because sialidase genes are present doesn't necessarily mean they're also active. So researchers synthesized the Hadza bacterial sialidase gene and produced the enzyme in the lab. The resulting sialidase was active and preferred non-human Neu5Gc over similar human carbohydrates.

Zengler then took the study a step further: to the grocery store. His team bought steak and pork sausage from a local store and brought it back to the lab. They rubbed their lab-made sialidase on the meat and, sure enough, most of the Neu5Gc came right off.

"The approach isn't perfect yet—the sialidase enzyme prefers to cleave Neu5Gc, but it still cleaves a bit of a similar human carbohydrate," said Zengler, who is also a faculty member in the Center for Microbiome Innovation at UC San Diego.

He and his team are now working to optimize the enzyme to increase its specificity. The team also wants to explore methods to mass produce the enzyme and further explore its potential for preventing inflammation and inflammatory diseases.

More information: *Gut bacteria responding to dietary change encode sialidases that exhibit preference for red meat-associated carbohydrates, Nature Microbiology (2019). DOI: 10.1038/s41564-019-0564-9 , https://nature.com/articles/s41564-019-0564-9*

https://wb.md/2nwY33n

Plain Water Better Than Hand Sanitizer for Influenza A

Simple handwashing — even without soap — is more effective than many hand disinfectants for killing influenza A virus (IAV) in typical clinical situations, new data show.

Troy Brown, RN

The researchers say the key factor that determines the effectiveness of ethanol-based disinfectants (EBDs) is whether there is wet

mucus surrounding the virus. Wet mucus prevents the disinfectant from reaching the virus, which means the virus remained active after 120 seconds of EBD exposure. By contrast, washing hands under plain water for 30 seconds inactivated the virus, regardless of whether it was initially surrounded by wet or dry mucus.

"The physical properties of mucus protect the virus from inactivation," lead researcher Ryohei Hirose, PhD, MD, a physician and molecular gastroenterologist at Kyoto Prefectural University of Medicine in Japan, said in a news release. "Until the mucus has completely dried, infectious IAV can remain on the hands and fingers, even after appropriate antiseptic hand rubbing." Hirose and colleagues published their findings online September 18 in *mSphere*.

For the study, they first looked at the physical properties of mucus and found that ethanol travels more slowly through the thick, sticky substance than it does through saline, which has similar properties as plain water.

Next, the researchers attempted to simulate clinical situations in which healthcare professionals might transmit the virus: they collected sputum for IAV-infected patients and applied it to human fingers. After being exposed to an EBD for 2 minutes, the IAV was still active in the mucus on participants' fingertips. The virus was deactivated by 4 minutes. If, however, the researchers allowed the mucus to fully dry on participants' hands before they used EBD, the hand sanitizer quickly inactivated the virus.

The Centers for Disease Control and Prevention and the World Health Organization recommend using disinfectants such as EBDs for 15 to 30 seconds. "However, our results suggest that this disinfection time is insufficient for the disinfection of infectious mucus of IAV-infected patients adhered to the fingers/hands and that current contact infection prevention and [antiseptic hand rubbing] regimens using EBDs are not sufficient to prevent IAV outbreaks," the researchers write.

The findings challenge those of previous studies, most of which have tested EBDs on dry mucus. Given their results, the authors recommend actually washing hands and not simply rubbing them with hand disinfectant.

http://bit.ly/2mrj1km

The Lancet Digital Health: First systematic review and meta-analysis suggests artificial intelligence may be as effective as health professionals at diagnosing disease

But with only a small number of high quality studies to draw on, the true power of AI remains uncertain, and researchers call for higher standards of research and reporting to improve future evaluations

Artificial intelligence (AI) appears to detect diseases from medical imaging with similar levels of accuracy as health-care professionals, according to the first systematic review and meta-analysis, synthesising all the available evidence from the scientific literature published in The Lancet Digital Health journal.

Nevertheless, only a few studies were of sufficient quality to be included in the analysis, and the authors caution that the true diagnostic power of the AI technique known as deep learning--the use of algorithms, big data, and computing power to emulate human learning and intelligence--remains uncertain because of the lack of studies that directly compare the performance of humans and machines, or that validate AI's performance in real clinical environments.

"We reviewed over 20,500 articles, but less than 1% of these were sufficiently robust in their design and reporting that independent reviewers had high confidence in their claims. What's more, only 25 studies validated the AI models externally (using medical images from a different population), and just 14 studies actually compared the performance of AI and health professionals using the same test

sample," explains Professor Alastair Denniston from University Hospitals Birmingham NHS Foundation Trust, UK, who led the research. [1]

"Within those handful of high-quality studies, we found that deep learning could indeed detect diseases ranging from cancers to eye diseases as accurately as health professionals. But it's important to note that AI did not substantially out-perform human diagnosis." [1]

With deep learning, computers can examine thousands of medical images to identify patterns of disease. This offers enormous potential for improving the accuracy and speed of diagnosis. Reports of deep learning models outperforming humans in diagnostic testing has generated much excitement and debate, and more than 30 AI algorithms for healthcare have already been approved by the US Food and Drug Administration.

Despite strong public interest and market forces driving the rapid development of these technologies, concerns have been raised about whether study designs are biased in favour of machine learning, and the degree to which the findings are applicable to real-world clinical practice.

To provide more evidence, researchers conducted a systematic review and meta-analysis of all studies comparing the performance of deep learning models and health professionals in detecting diseases from medical imaging published between January 2012 and June 2019. They also evaluated study design, reporting, and clinical value.

In total, 82 articles were included in the systematic review. Data were analysed for 69 articles which contained enough data to calculate test performance accurately. Pooled estimates from 25 articles that validated the results in an independent subset of images were included in the meta-analysis.

Analysis of data from 14 studies comparing the performance of deep learning with humans in the same sample found that at best, deep learning algorithms can correctly detect disease in 87% of cases, compared to 86% achieved by health-care professionals.

The ability to accurately exclude patients who don't have disease was also similar for deep learning algorithms (93% specificity) compared to health-care professionals (91%).

Importantly, the authors note several limitations in the methodology and reporting of AI-diagnostic studies included in the analysis. Deep learning was frequently assessed in isolation in a way that does not reflect clinical practice. For example, only four studies provided health professionals with additional clinical information that they would normally use to make a diagnosis in clinical practice. Additionally, few prospective studies were done in real clinical environments, and the authors say that to determine diagnostic accuracy requires high-quality comparisons in patients, not just datasets. Poor reporting was also common, with most studies not reporting missing data, which limits the conclusions that can be drawn.

"There is an inherent tension between the desire to use new, potentially life-saving diagnostics and the imperative to develop high-quality evidence in a way that can benefit patients and health systems in clinical practice," says Dr Xiaoxuan Liu from the University of Birmingham, UK. "A key lesson from our work is that in AI--as with any other part of healthcare--good study design matters. Without it, you can easily introduce bias which skews your results. These biases can lead to exaggerated claims of good performance for AI tools which do not translate into the real world. Good design and reporting of these studies is a key part of ensuring that the AI interventions that come through to patients are safe and effective." [1]

"Evidence on how AI algorithms will change patient outcomes needs to come from comparisons with alternative diagnostic tests in randomised controlled trials," adds Dr Livia Faes from Moorfields

Eye Hospital, London. "So far, there are hardly any such trials where diagnostic decisions made by an AI algorithm are acted upon to see what then happens to outcomes which really matter to patients, like timely treatment, time to discharge from hospital, or even survival rates." [1]

Writing in a linked Comment, Dr Tessa Cook from the University of Pennsylvania, USA, discusses whether AI can be effectively compared to the human physician working in the real world, where data are "messy, elusive, and imperfect". She writes: "Perhaps the better conclusion is that, the narrow public body of work comparing AI to human physicians, AI is no worse than humans, but the data are sparse and it may be too soon to tell."

NOTES TO EDITORS

This study received no funding. It was conducted by researchers from University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; University of Birmingham, Birmingham, UK; Moorfields Eye Hospital NHS Foundation Trust, London, UK; Cantonal Hospital of Lucerne, Lucerne, Switzerland; NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK; Ludwig Maximilian University of Munich, Munich, Germany; DeepMind, London, UK; Scripps Research Translational Institute, La Jolla, California; and Medignition, Zurich, Switzerland.

[1] Quote direct from author and cannot be found in the text of the Article.

http://bit.ly/2o7xIcK

Vitamin D and fish oil show promise in prevention of cancer death and heart attacks

Upcoming presentation to provide updates on VITAL clinical trial showing mixed results of how vitamin D and Omega-3 fatty acids help protect against cancer mortality and myocardial infarction

CLEVELAND, Ohio - The VITamin D and OmegA-3 Trial (VITAL) is the largest and most recent to test whether vitamin D or fish oil can effectively prevent cancer or cardiovascular disease. Results to date have been mixed but show promise for some outcomes, now confirmed by updated pooled (meta) analyses. The latest results from VITAL will be presented during The North American Menopause Society (NAMS) Annual Meeting in Chicago, September 25-28, 2019.

Nearly 26,000 U.S. men and women participated in the nationwide VITAL clinical trial. After more than five years of study and treatment, the results show promising signals for certain outcomes. For example, while Omega-3 fatty acids (fish oil) showed only a small, but nonsignificant, reduction in the primary cardiovascular endpoint of major CVD events, they were associated with significant reductions in heart attacks. The greatest treatment benefit was seen in people with dietary fish intake below the cohort median of 1.5 servings per week but not in those whose intake was above that level. In addition, African-Americans appeared to experience the greatest risk reductions. The heart health benefits are now confirmed by recent meta-analyses of omega-3 randomized trials.

Similarly, vitamin D supplementation did not reduce major CVD events or total cancer incidence but was associated with a statistically significant reduction in total cancer mortality among those in the trial at least two years. The effect of vitamin D in reducing cancer death is also confirmed by updated meta-analyses of vitamin D trials to date.

"The pattern of findings suggests a complex balance of benefits and risks for each intervention and points to the need for additional research to determine which individuals may be most likely to derive a net benefit from these supplements," says Dr. JoAnn Manson, lead author of the study from Brigham and Women's Hospital, an affiliate of Harvard Medical School.

"With heart disease and cancer representing the most significant health threats to women, it is imperative that we continue to study the viability of options that prevent these diseases and help women survive them," says Dr. Stephanie Faubion, NAMS medical director.

Drs. Manson and Faubion are available for interviews before the presentation at the Annual Meeting.

http://bit.ly/2lT1W2p

Impostor syndrome is more common than you think; Study finds best way to cope with it

A certain type of social support is a major asset when facing impostorism

The impostor syndrome, a phenomenon that manifests when people feel like frauds even if they are actually capable and well-qualified, affects people both in the workplace and in the classroom. A new study reveals that perceptions of impostorism are quite common and uncovers one of the best -- and worst -- ways to cope with such feelings.

Findings of the study, co-authored by Brigham Young University professors Jeff Bednar, Bryan Stewart, and James Oldroyd, revealed that 20 percent of the college students in their sample suffered from very strong feelings of impostorism. The researchers conducted interviews with students in an elite academic program to understand the various coping mechanisms students used to escape these feelings, but one particular method stood out above the rest: seeking social support from those outside their academic program.

The findings of their interview study suggest that if students "reached in" to other students within their major, they felt worse more often than they felt better. However, if the student "reached out" to family, friends outside their major, or even professors, perceptions of impostorism were reduced.

"Those outside the social group seem to be able to help students see the big picture and recalibrate their reference groups," said Bednar, a BYU management professor and co-author on the study. "After reaching outside their social group for support, students are able to understand themselves more holistically rather than being so focused on what they felt they lacked in just one area."

Along with seeking social support, the study also uncovered negative ways students coped with impostorism. Some students tried to get their mind off schoolwork through escapes such as video games but ended up spending more time gaming than studying. Other students tried to hide how they really felt around their classmates, pretending they were confident and excited about their performance when deep down they questioned if they actually belonged.

In a second study, the researchers surveyed 213 students to confirm what was revealed in their interview study about seeking social support: reaching out to individuals outside the major proved to be more effective than reaching in to individuals within the major.

Surprisingly, the study also reveals that perceptions of impostorism lack a significant relationship with performance. This means that individuals who suffer with the impostor syndrome are still capable of doing their jobs well, they just don't believe in themselves. Researchers also explain that social-related factors impact impostorism more than an individual's actual ability or competence.

"The root of impostorism is thinking that people don't see you as you really are," said Stewart, an accounting professor at BYU and co-author on the study. "We think people like us for something that isn't real and that they won't like us if they find out who we really are."

Outside the classroom, researchers believe that implications from this study can and should be applied in the workplace as well. "It's important to create cultures where people talk about failure and mistakes," Bednar said. "When we create those cultures, someone who is feeling strong feelings of impostorism will be more likely to get the help they need within the organization."

The study, published in the Journal of Vocational Behavior, *also features two BYU graduates, Richard Gardner, a professor at UNLV, and Joseph Moore, who is beginning a PhD program at Stanford.*

https://wb.md/2lUWn3k

Flu Vaccine Recommendations for the 2019-2020 Season

Annual influenza vaccination offers important protection against influenza illness and its potential serious complications

Lisa Grohskopf, MD, MPH

Although influenza seasons vary in severity, influenza can cause millions of illnesses, hundreds of thousands of hospitalizations, and tens of thousands of deaths worldwide each season. While not 100% effective, annual influenza vaccination offers important protection against influenza illness and its potential serious complications.

Hi. I'm Dr Lisa Grohskopf, a medical officer in the Influenza Division at the Centers for Disease Control and Prevention (CDC). For the 2019-2020 influenza season, CDC and the Advisory Committee on Immunization Practices (ACIP) continue to recommend routine annual influenza vaccination for all persons 6 months of age and older who do not have contraindications to vaccination. The full recommendations are available on the CDC website. Here are some of the key changes for the 2019-2020 season.

Vaccine Composition

This season, all US-licensed influenza vaccines will have changes in the influenza A(H1N1)pdm09 and influenza A(H3N2) vaccine virus components as compared with the 2018-2019 season. US-licensed trivalent influenza vaccines will contain hemagglutinin derived from A/H1N1, A/H3N2, and B/Victoria viruses. Quadrivalent influenza vaccines will contain hemagglutinin derived from these three vaccine viruses and from a B/Yamagata virus.

Trivalent Influenza Vaccine Composition:

- ***an A/Brisbane/02/2018 (H1N1)pdm09–like virus,***
- ***an A/Kansas/14/2017 (H3N2)–like virus, and***
- ***a B/Colorado/06/2017–like virus (Victoria lineage)***

Quadrivalent Influenza Vaccine Composition:

- ***The three recommended viruses above, plus B/Phuket/3073/2013-like (Yamagata lineage) virus***

Recent Influenza Vaccine Labeling Changes

In the past year, the US Food and Drug Administration (FDA) has approved labeling changes for two influenza vaccines, Afluria Quadrivalent and Fluzone Quadrivalent.

In October 2018, the FDA approved an expanded age indication for Afluria Quadrivalent, a quadrivalent inactivated influenza vaccine. Afluria Quadrivalent is now licensed for children 6 months of age and older. Children 6 through 35 months of age should receive 0.25 mL for each dose. All persons 36 months (or 3 years) of age and older should receive 0.5 mL for each dose.

In January 2019, FDA approved a change in dose volume for Fluzone Quadrivalent, another quadrivalent inactivated influenza vaccine. The change in dose volume affects children 6 through 35 months of age. Previously, children in this age group were recommended to receive 0.25 mL of this vaccine per dose. Children 6 through 35 months of age may now receive either 0.25 mL or 0.5 mL per dose. There is no preference for one or the other dose volume for this age group. All persons 36 months (or 3 years) of age and older should receive 0.5 mL per dose.

One important thing to consider is that for children who are 6 through 35 months of age, there are now four different inactivated influenza vaccines that may be used, but the dose volumes for this age group differ depending on the specific vaccine. Care should be taken to administer an appropriate dose of an appropriate vaccine for the recipient's age. More information is in the table below:

Inactivated Influenza Vaccine Dosing for Children 6 Through 35 Months of Age

- ***Afluria Quadrivalent: 0.25 mL per dose (containing 7.5 µg of hemagglutinin per vaccine virus)***
- ***Fluarix Quadrivalent: 0.5 mL per dose (containing 15 µg of hemagglutinin per vaccine virus)***
- ***FluLaval Quadrivalent: 0.5 mL per dose (containing 15 µg of hemagglutinin per vaccine virus)***
- ***Fluzone Quadrivalent:*** **Either** ***0.25 mL per dose (containing 7.5 µg of hemagglutinin per vaccine virus)*** **Or** ***0.5 mL per dose (containing 15 µg of hemagglutinin per vaccine virus)***

Alternatively, healthy children 2 years of age and older may receive live attenuated influenza vaccine (LAIV4), 0.2 mL intranasally (0.1 mL in each nostril). LAIV4 is not licensed for children under 2 years of age.

Number of Influenza Vaccine Doses Needed for Children 6 Months Through 8 Years of Age

As in previous seasons, some children 6 months through 8 years of age will need two doses of influenza vaccine this season. Children in this age group who have not previously received two or more total doses of any trivalent or quadrivalent influenza vaccine (including LAIV) before July 1, 2019, or whose vaccination history is not known, need two doses of 2019-2020 influenza vaccine administered at least 4 weeks apart. For 8-year-olds who are determined to need two doses, the second dose is recommended even if the child turns 9 years of age between receipt of dose 1 and dose 2. Children in this age group who have received two or more total doses of trivalent or quadrivalent influenza vaccine before July 1, 2019, need only one dose for this season.

Timing of Vaccination

Because the timing of the onset, peak, and end of influenza seasons varies from year to year and cannot be predicted, it is difficult to know the best time to be vaccinated each season. Balancing this consideration with concerns for potential waning of vaccine-induced immunity during the influenza season, CDC and ACIP recommend that vaccination be offered by the end of October. Children 6 months through 8 years of age who need two doses should receive their first dose as soon as possible after the vaccine becomes available to allow the second dose (which must be administered at least 4 weeks later) to be received by the end of October. For people who need only one dose for the season, vaccinating early—for example, in July or August—may lead to reduced protection against influenza later in the season, particularly among older adults. While vaccination should optimally occur before the onset of influenza activity in the community, providers should continue to offer and encourage vaccination as long as influenza viruses are circulating and unexpired vaccine is available. To avoid missed opportunities for vaccination, vaccination can be offered during routine healthcare visits and hospitalizations.

Available Vaccines

Providers can administer any licensed influenza vaccine that is appropriate for the recipient's age and health status. Choices include inactivated, recombinant, or live attenuated influenza vaccines. Additionally, people 65 years of age and older may receive the trivalent influenza vaccine with adjuvant or the trivalent high-dose vaccine. No preferential recommendation is made for one influenza vaccine type over another, but efforts to assess effectiveness of different influenza vaccines for different populations continue.

Groups Recommended for Vaccination

For the 2019-2020 influenza season, the CDC and ACIP continue to recommend routine annual influenza vaccination for all persons 6 months of age and older who do not have contraindications to vaccination.

Vaccination to prevent influenza is particularly important for persons who are at increased risk for severe illness and complications from influenza. When vaccine supply is limited,

vaccination efforts should focus on delivering vaccination to those groups most at risk for serious illness, such as young children, older adults, and people with chronic health problems. People who live with or care for those at higher risk for influenza-related complications should also be a focus for vaccination when vaccine supply is limited. You can find a full list of high-priority vaccination groups in the table below:

Priority Groups for Vaccination

- ***Children under 5 years of age (especially those under 2 years of age)***
- ***Adults 65 years of age and older***
- ***Adults and children who have chronic medical conditions such as chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)***
- ***People who are immunocompromised (including, but not limited to, immunosuppression caused by medications or HIV infection)***
- ***Pregnant and postpartum women***
- ***Children and adolescents (aged 6 months through 18 years) who are receiving aspirin- or salicylate-containing medications***
- ***Residents of nursing homes and other long-term care facilities***
- ***American Indians/Alaska Natives***
- ***People who are extremely obese (body mass index of 40 or greater for adults)***
- ***Healthcare personnel***
- ***Household contacts and caregivers of children under 5 years of age and adults 50 years of age and older***
- ***Household contacts and caregivers of persons with medical conditions that put them at increased risk for severe illness and complications from influenza***

I will close by reminding you about the importance of your role in protecting the public against influenza each season. Your recommendation to your patients that they receive the influenza vaccine is critical and more effective in increasing acceptance of vaccination than any other influencing factor. Healthcare providers should also lead by example and be sure that they themselves are vaccinated each and every season.

For more information, be sure to review the tables above and visit CDC's website.

Thank you for your attention.

http://bit.ly/2mLVBWK

Depression: it's a word we use a lot, but what exactly is it?

An expanded set of concepts for describing depression

Samuel Clack * **Tony Ward** **

Depression is a serious disorder marked by disturbances in mood, cognition, physiology and social functioning.

People can experience deep sadness and feelings of hopelessness, sorrow, emptiness and despair. These core features of depression have expanded to include an inability to experience pleasure, sluggish movements, changes in sleep and eating behaviour, difficulty concentrating and suicidal thoughts.

The first diagnostic criteria were introduced in the 1980s. Now we have an expanded set of concepts for describing depression, from mild to severe, major depressive disorder, chronic depression and seasonal affective disorder.

Over the past 50 years, our understanding of depression has advanced significantly. But despite the wealth of research, there is no clear consensus on how this mental disorder should be explained. We propose a new route through the thicket.

Classifying mental disorders

How we describe and classify mental disorders is a fundamental step towards explaining and treating them. When carrying out research on people with depression, diagnostic categories such as major depressive disorder (MDD) shape our explanations. But if the

descriptions are wrong, our explanations will suffer as a consequence.

The problem is that classification and explanation are not completely independent tasks. How we classify disorders directly impacts how we explain them, and these explanations in turn impact our classifications. In this way, psychiatry is stuck in a circular trap.

The danger – for depression and for other mental disorders – is that we tailor our explanations to fit the classifications available and that the classifications are inadequate.

Traditionally, research has focused on understanding mental disorders as classified in manuals such as the Diagnostic and Statistical Manual of Mental Disorders. Most of these disorders are what we call "psychiatric syndromes" – clusters of symptoms that hang together in some meaningful way and are assumed to share a common cause.

But many of these syndromes are poorly defined because disorders can manifest in different ways in different people. This is known as "disorder heterogeneity". For example, there are 227 different symptom combinations that meet the criteria for major depressive disorder.

Improving how we classify disorders

The other problem is that diagnostic criteria often overlap across multiple disorders. Symptoms of restlessness, fatigue, difficulty concentrating, irritability and sleep disturbance can be common for people experiencing generalised anxiety disorder or major depressive disorder.

This makes studying disorders like depression difficult. While we may think we are all explaining the same thing, we are actually trying to explain completely different variations of the disorder, or in some cases a completely different disorder.

A significant challenge is how to advance classification systems without abandoning their descriptive value and the decades of research they have produced. So what are our options?

A categorical approach, which sees disorders as discrete categories, has been the most prominent model of classification. But many researchers argue disorders such as depression are better seen as dimensional. For example, people who suffer from severe depression are just further along a spectrum of "depressed mood", rather than being qualitatively different from the normal population.

Novel classification approaches such as the hierarchical taxonomy of psychopathology and research domain criteria have been put forward. While these better accommodate the dimensional nature of disorders and are less complex to use, they are conceptually limited. The former relies on current diagnostic categories and all the problems that come with that. The latter relies on neuro-centrism, which means mental disorders are viewed as disorders of the brain and biological explanations are used in preference to social and cultural explanations.

A new approach called the symptom network model offers a departure from the emphasis on psychiatric syndromes. It sees mental disorders not as diseases but as the result of interactions between symptoms.

In depression, an adverse life event such as loss of a partner may activate a depressed mood. This in turn may cause neighbouring symptoms, such as insomnia and fatigue. But this model is only descriptive and offers no explanation of the processes that cause the symptoms themselves.

A simple way forward

We suggest that one way of advancing understanding of mental disorders is to move our focus from psychiatric syndromes to clinical phenomena.

Phenomena are stable and general features. Examples in clinical psychology include low self-esteem, aggression, low mood and ruminative thoughts. The difference between symptom and phenomena is that the latter are inferred from multiple information sources such as behavioural observation, self-report and psychological test scores.

For example, understanding the central processes that underpin the clinical phenomenon of the inability to experience pleasure (anhedonia) will provide greater insight for cases that are dominated by this symptom. In this way we can begin to tailor our explanations for individual cases rather than using general explanations of the broad syndrome “major depressive disorder”.

The other advantage is that the central processes that make up these phenomena are also more likely to form reliable clusters or categories. Of course, achieving this understanding will require greater specification of clinical phenomena we want to explain. It is not enough to conclude that a research finding (such as low levels of dopamine) is associated with the syndrome depression, as the features of depression may vary significantly between individuals.

We need to be more specific about exactly what people with depression in our research are experiencing.

Building descriptions of clinical phenomena will help us to better understand links between signs, symptoms and causes of mental disorder. It will put us in a better position to identify and treat depression.

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http://bit.ly/2ofyVPg

Shoe-mounted laser to 'unfreeze' people with Parkinson's scoops €1 million prize

Helps people with Parkinson's disease 'unfreeze'

by Joanna Roberts

A shoe-mounted laser beam that helps people with Parkinson's disease 'unfreeze' by shining a green line in front of their feet has been awarded the EU's €1 million Horizon Prize for Social Innovation.

Having an external visual cue such as a line has been shown to reduce the number of freezing episodes in Parkinson's patients. **Credit: Walk With Path**

The Path Finder device was invented in 2014 by Danish entrepreneur Lise Pape, whose father suffers from Parkinson's disease.

It aims to help people overcome a particular symptom of the disease—freezing of gait—in which people stop walking and are unable to restart.

'People describe it as this feeling of being glued to the floor and being unable to step forward with their feet, despite having the intention to do so,' said Pape. 'In fact, 70% of all falls in Parkinson's are thought to be due to this symptom.'

One peculiarity of gait freezing is that it is relatively easy for people to overcome—if they have an external visual cue to help them keep going.

'What researchers found is that people mostly struggle on flat floors, whereas on staircases people are generally fine (because) they have this rhythm for every step,' said Pape.

The Path Finder builds on this principle by using a small laser that clips on to someone's shoe and projects a green line in front of their foot, replicating the idea of having a stair to climb.

'Our device … is in a way converting the staircase into a wearable product that you can have with you so you don't have to change your environment,' said Pape, who explains that it works by helping people to focus their attention on walking.

Studies have shown that the laser shoes significantly reduce the number of freezing episodes as well as the amount of time someone is frozen.

In 2017, Pape's company Walk With Path, took its product to market as a medical device, selling it to both individuals and health care systems mostly in Norway, Denmark and the UK. With the prize money, she wants to better promote her device in Europe and launch in the US market.

The Horizon Prize for Social Innovation, which is awarded for the best solutions to improve the mobility of older people, was presented to Pape by Carlos Moedas, the EU's Commissioner for Research, Science and Innovation, on 24 September in Brussels, Belgium.

The idea behind social innovation is to find solutions to societal problems and this year's prize focuses on one of Europe's major challenges over the next century, an ageing society. According to the European Commission's own statistics, the proportion of Europeans aged over 65 will grow from 17.5% in 2010 to nearly 30% by 2060.

Wearable

Wearable technology was a recurring theme among the shortlisted projects, with Switzerland-based MyoSwiss awarded one of two €250,000 runner-up prizes for its Myosuit—robotic trousers designed to strengthen muscles.

The Myosuit, which is designed to help people walk and keep active by providing assistance at the hip and knee joints, acts like an 'wearable muscle', according to co-founder and CEO Jaime Duarte.

'From a mechanical point of view, it works very similarly to how muscles work,' he said, explaining that having muscles attached to bones by tendons enables the muscles to be located away from the joints they control, reducing bulk.

'In our fingers we actually have the motors, or the muscles, quite far away from where our fingers are. The motors themselves are in the forearm. We do something similar in our system.'

The 5kg suit, which is marketed at health professionals such as physiotherapists, consists of a backpack, containing a motor, joined by cables to mechanical supports at the hip and knee.

It works on the same principle as an electric bike—the user does a certain proportion of the work themselves and is aided by the technology where necessary.

It's aimed at people with conditions such as muscular dystrophy or multiple sclerosis, those recovering from injuries or strokes and people who are experiencing muscle weakness with age. What makes their product innovative, says Duarte, is that it enables people to keep moving and preserve, or even improve, their muscle function.

'When people have weakness of their legs, one of the most-used solutions today is wheelchairs,' he said. 'But once you start using technology like a wheelchair then your legs become even weaker.'

Keeping people moving is not just about physical help, however.

A third prize of €250,000 was awarded to the Municipality of Toulouse, France, who developed the Montoulouse senior card in order to increase the participation of seniors in municipal activities. The card gives people over 60 free access to museums, cultural events, libraries and sports facilities, as well as discounts at restaurants, social events.

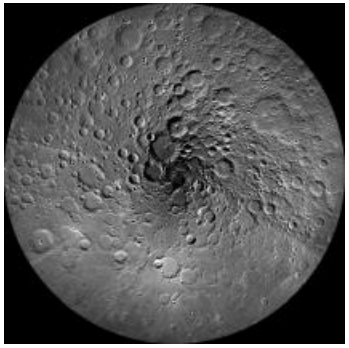
When people reach 65, or 62 for retirees, they also receive discounts on city bikes, metro, trams and buses.

http://bit.ly/2mAhR6b

The Moon as a Fishing Net for Extraterrestrial Life

Its surface could, in principle, preserve the remains of organisms or even technology from beyond our solar system

By Abraham Loeb



Credit: NASA, GSFC and Arizona State University

NASA recently announced the Artemis lunar exploration program, consolidating its plans plans to land humans on the moon by 2024 and establish a sustainable base there by 2028. This ambitious initiative revives an old question: Will the unique qualities of the lunar surface enable new frontiers in astronomy?

A few decades ago, astronomers had already begun to contemplate different ways their observations could benefit from the absence of an atmosphere on the moon. First, energetic particles such as gamma rays, x-rays, ultraviolet photons or cosmic rays would not be blocked by an atmospheric blanket as they are on earth, and hence they would reach telescopes with large collecting areas mounted to the lunar surface. Second, observatories sensitive to optical, infrared, millimeter or radio waves could reach their diffraction limit without the blurring or absorption associated with passage through turbulent air. Arrays of detectors could therefore constitute giant interferometers with unprecedented angular resolution.

Third, the lack of an ionosphere would allow radio observatories to receive signals at very low frequencies, below the terrestrial cutoff of 10 kilohertz. This would open a new spectral window into the universe, allowing to map the three-dimensional distribution of hydrogen atoms from their first appearance 0.4 million year after the big bang and through the cosmic dawn, using the highly redshifted 21-centimeter line. Although exciting and path breaking in their own right, these visions were all formulated well before the emergence of the frontier of astrobiology associated with the search for extraterrestrial life.

Can the moon provide clues for extraterrestrial life? A new paper I wrote with Manasvi Lingam answers this question in the affirmative. The idea is to consider the moon's surface as a fishing net for interstellar objects collected over time and potentially deliver building blocks of life from the habitable environments around other stars.

The lack of a lunar atmosphere guarantees that these messengers would reach the lunar surface without burning up. In addition, the geological inactivity of the moon implies that the record deposited on its surface will be preserved and not mixed with the deep lunar interior. Serving as a natural mailbox, the lunar surface collected all impacting objects during the past few billions of years. Most of this "mail" comes from within the solar system.

But the solar system also intercepts objects from interstellar space, ranging from dust particles to free-floating planets and stars. A detection of the first interstellar object, 'Oumuamua, with a size on the order of 100 meters was reported in 2017. This year, 'Oumuamua's cousin was tentatively discovered in the form of a meter-size meteor from outside the solar system that burned up in Earth's atmosphere in 2014. And most recently, yet another interstellar visitor may have been identified.

Given the search volume and duration of the surveys that made these detections, it is now possible, for the first time, to calibrate the flux of interstellar objects (assuming they enter the solar system on random trajectories). With this calibration at hand, one can calculate the amount of interstellar material that has collected on the moon's surface over its history. The buildup of interstellar matter can also be observed in real time; another new paper with

my undergraduate student, Amir Siraj, showed that a two-meter telescope on a satellite in orbit around the moon can observe interstellar impactors as they crash.

In case some interstellar impactors carry the building blocks of extraterrestrial life, one could extract these biomarkers by analyzing lunar surface samples. Moon rocks delivered to Earth by the Apollo mission were likely contaminated by terrestrial life and are not a viable alternative to a dedicated experimental base on the moon.

Identifying biomarkers from debris of material that originated in the habitable zone around other stars would inform us about the nature of extraterrestrial life. The fundamental question is whether distant life resembles the biochemical structures we find on Earth. Similarities might imply that there exists a unique chemical path for life everywhere or that life was transferred between systems. Either way, a lunar study shortcuts the need to send spacecraft on extremely long missions to visit other star systems.

Getting similar information from a trip to the nearest star system—Alpha Centauri A, B or C—would take nearly nine years round-trip, even if the spacecraft were to travel at the maximum speed allowed in nature, the speed of light; the first half of this period is required for reaching the target and the second half for the information to get back to us. With chemical rockets, this journey would take about 100,000 years, on the order of the time that elapsed since the first modern humans began migrating out of Africa. Excavating the lunar surface for physical evidence of extraterrestrial life is dramatically faster.

Based on the newly calibrated flux of interstellar objects, their debris should constitute up to 30 parts per million of lunar surface material. Extrasolar organics might amount to a fraction of an order of ***a= few parts per 10 million***. Amino acids, which serve as the building blocks of "life as we know it," could amount to a few parts per hundred billion. Standard spectroscopic techniques can be employed to examine individual grains within the lunar regolith and search for signatures that would flag them as extrasolar before unraveling the building blocks of extraterrestrial life within them.

How can extrasolar origin be identified? The simplest flag would be a deviation from the unique solar ratio for isotopes of oxygen, carbon or nitrogen. Laboratories have already demonstrated the feasibility of this method at the required sensitivity levels.

But there is also the exciting opportunity for detecting biosignatures of extinct extraterrestrial life. On Earth, the oldest microfossils, with unambiguous evidence for cells that lived about 3.4 billion years ago, were discovered in the Strelley Pool Formation in Western Australia. It would be tantalizing to find microfossils of extraterrestrial forms of life on the moon. Even more exciting would be to find traces of technological equipment that crashed on the lunar surface a billion years ago, amounting to a letter from an alien civilization saying, "We exist." Without checking our mailbox, we would never know that such a message arrived.

The opportunity to discover signs of extraterrestrial life provides a new scientific incentive for a sustainable base on the lunar surface. The moon is well known for its romantic appeal, but astrobiology offers a twist on this notion. Here's hoping that the moon will inform our civilization that we are not alone and that someone else is waiting for us out there.

http://bit.ly/2ogwjk8

Monkeys like alcohol at low concentrations, but probably not due to the calories

No support to the idea that human alcoholism originated from a predilection of primates for alcohol-containing overripe fruit

Fruit-eating monkeys show a preference for concentrations of alcohol found in fermenting fruit, but do not seem to use alcohol as a source of supplementary calories, according to a study by researchers from Linköping University, Sweden, and the

Universidad Veracruzana, Mexico. The findings do not support the idea that human alcoholism originated from a predilection of primates for alcohol-containing overripe fruit.

When overripe fruit is fermented by microbes, alcohol is produced. Some research has suggested that fruit-eating monkeys use this dietary ethanol as a source of supplementary calories. The researchers behind the new study, which is published in *Chemical Senses*, set out to test this idea.

In a first experiment performed at a field station in Mexico, the researchers presented eight spider monkeys with varying concentrations of ethanol naturally found in fermenting fruit (0.5–3 percent) and tap water as the alternative. They found that the animals were able to detect ethanol at concentrations as low as 0.5 percent. In comparison, the detection threshold of humans for this alcohol is 1.34 percent. The monkeys preferred all ethanol concentrations up to 3 percent over water.

"These results demonstrate that fruit-eating spider monkeys are extraordinarily sensitive to the taste of ethanol. We also found that they prefer this alcohol when presented at naturally occurring concentrations found in fermenting fruit," says Professor Matthias Laska at the Department of Physics, Chemistry and Biology (IFM) at Linköping University.

In a second experiment, the spider monkeys were given the choice between a sugar solution spiked with ethanol and an equally concentrated sugar solution without ethanol. Here, the animals clearly preferred the ethanol-spiked sugar solution. However, when presented with an ethanol-spiked sugar solution and a higher-concentration sugar solution without ethanol, the animals clearly preferred the pure sugar alternative, even when the sugar-ethanol mixture contained three times more calories.

A similar experiment was performed in which the spider monkeys were given the choice between puréed fruit spiked with ethanol and puréed fruit without ethanol. The tests with sugar solutions and with puréed fruit that were either spiked with ethanol or not, suggest that sweetness, and thus carbohydrate content, may be more important for the preferences displayed by the spider monkeys than the calories provided by ethanol.

"The findings, therefore, do not support the idea that dietary ethanol is used by fruit-eating primates as a source of supplementary calories. Similarly, the findings do not support the idea that a predilection of non-human primates for alcohol-containing overripe fruits reflects the evolutionary origin of human alcoholism," says Matthias Laska.

More information: *Taste responsiveness of spider monkeys to dietary ethanol, Chemical Senses, 11 August 2019, DOI: 10.1093/chemse/bjz049*

https://bbc.in/2mQbrj8

Male infertility linked to prostate cancer risk

Men who have fertility treatment have a higher risk of prostate cancer in later life, a study has suggested.

The research - in the British Medical Journal - looked at 1.2 million pregnancies in Sweden over 20 years. Men who had ICSI - a treatment specifically for male infertility - had an increased prostate cancer risk. But Prostate Cancer UK said researchers must look at a much broader age range before concluding men who have fertility treatment are at higher risk.

Researchers from Lund University in Sweden used data from national birth and cancer registers. They looked at more than a million births between 1994 and 2014, and at cancer cases.

Most babies - 97% - were conceived naturally, and 20,618 (1.7%) were conceived using IVF, although the data does not show if fertility issues lay with the man or the woman. Some 14,882 (1.3%) births resulted from ICSI, where a single, good-quality sperm is selected and injected directly into an egg. ICSI was first used in Sweden in 1992, with every case recorded by the register.

'Offer the test'

Among the natural conception group, 3,244 (0.28%) were diagnosed with prostate cancer, compared with 77 (0.37%) in the IVF group and 63 (0.42%) among those who had ICSI.

Men in the ICSI group also had a higher risk of developing early onset prostate cancer, before the age of 55.

Prof Yvonne Lundberg Giwercman, who led the study, told the BBC: "The prostate cancer numbers are quite small, but these men are very young. "They are a small, high-risk group, and we should be following them more closely." She said she hoped there would be further studies to investigate why the link existed.

Allan Pacey, professor of andrology at the University of Sheffield, said: "It has been proposed that male infertility might serve as a "canary in the coal mine" for men's health, which both men and their doctors should be better attuned to."

He added: "It is important to be clear that this is not because the techniques of assisted reproduction go on to cause prostate cancer, but probably because the two have a common cause in some way.

"Perhaps all men who are diagnosed with a fertility problem in their 20s and 30s should be given a leaflet explaining what this might mean for them in their 50s and 60s, so that they can be aware of possible future problems, and be encouraged to visit their GP a bit quicker than they often do."

'Little evidence'

But Simon Grieveson, from Prostate Cancer UK, said it was important not to "leap to any conclusions" on the basis of this study.

"Prostate cancer is more common in men over the age of 50. The men involved in this study were younger on average, and therefore already have a very low risk of prostate cancer.

"This study would need to look at a much broader age range to fully understand whether men who undergo fertility treatment actually have a higher risk overall.

"If this can be proven, more research would then need to be done to determine the underlying cause. Until then, there is little evidence that there would be any benefit in monitoring these men more closely."

He added: "We believe it's important that all men are aware of the risks of prostate cancer, and men concerned about the disease should speak to their GP. However, couples considering fertility treatment should not be put off by these results."

http://bit.ly/2nAMmsM

World's first three-organoid system opens doors for medical research and diagnosis

Scientists at Cincinnati Children's use stem cells to grow connected, functioning set of miniature human liver, pancreas, biliary ducts

Imagine trying to paint a forest when all the artist has is a leaf and a piece of bark versus having a living, growing tree as a model. Seeing how the parts fit together can make all the difference.

That's the level of advancement in organoid science that researchers at Cincinnati Children's have achieved with findings published today in the prestigious journal *Nature*. Instead of growing mini human organs independently in separate lab dishes, a team led by Takanori Takebe, MD, succeeded at growing a connected set of three organs: the liver, pancreas and biliary ducts.

Organoids, grown from stem cells, are tiny 3D formations of human tissue that actually perform the functions of multiple cells types found in full-sized organs. Organoid experts at Cincinnati Children's have already grown intestines that feature nutrient-absorbing villi, stomach organoids that produce digestive acids, and more.

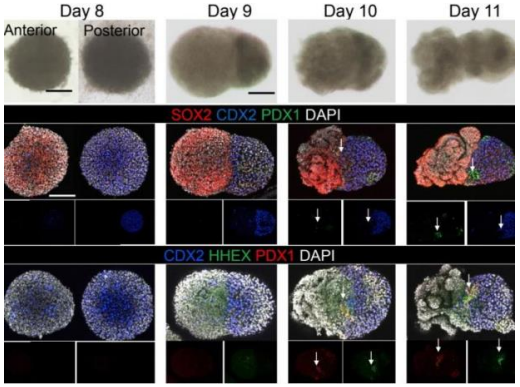
By themselves, human organoids already provide a sophisticated tool for research. But this advance allows scientists to study how human tissues work in concert.

This major step forward could begin reducing the need for animal-based medication studies, sharply accelerate the concept of precision medicine, and someday lead to transplantable tissues grown in labs.

"The connectivity is the most important part of this," Takebe says. "What we have done is design a method for producing pre-organ formation stage tissues so that they can develop naturally. We are maximizing our capacity to make multiple organs much like or body does."

A 5-year quest achieves key goal

Takebe, age 32, joined Cincinnati Children's in 2016 and holds a dual appointment at Tokyo Medical and Dental University (TMDU) in Japan. He graduated from medical school in 2011 with plans to become a liver transplant surgeon. But as he learned about the yawning gap between the supply and demand for donor organs, Takebe shifted gears to focus on organ supply.



These confocal microscope images depict the key moments that gut organoids begin to take shape, transitioning from two 'spheroids' of mixed cell types to a merged proto-gut that shows the early stages of formation for a liver, pancreas and connecting biliary ducts. Details about the project, led by Takanori Takebe, MD, were posted online Sept. 25, 2019, in the journal Nature. **Cincinnati Children's**

In previous research, Takebe has demonstrated a method to produce large supplies of liver "buds," an early-stage form of a liver organoid. He also has grown liver organoids that reflect disease states, including steatohepatitis, a dangerous form of liver scarring and inflammation that occurs in some people with obesity.

His work to date has been hailed by the Imperial Prince of Japan, who presented Takebe with an honor in 2018 from the Japan Society for the Promotion of Science. *Discover magazine* also listed Takebe's organoid work as No. 5 in its list of the top 100 science achievements of 2013.

But Takebe says this project is his highest-impact work yet. "We noted this point in organ differentiation some time ago. But it took five years to tune up the culture system to allow this development to occur," Takebe says.

How three proto-organs grow in concert

The hardest parts of the process were the earliest steps. Takebe worked for many hours with colleagues at Cincinnati Children's including first author Hiroyuki Koike, PhD, now at Nippon Medical School in Japan, to perfect the process. They started with human skin cells, converting them back into primitive stem cells, then guiding and prodding those stem cells to form two very early-stage "spheroids" of cells loosely termed the foregut and the midgut.

These balls of cells form very early in embryonic development. In humans, they form late in the first month of gestation. In mice, they form in just 8.5 days. Over time, these spheres merge and morph into the organs that eventually become the digestive tract.

Growing these spheroids in the lab was a complex process that required using the right ingredients at the right time. Once they were mature enough--a timing step that required much work to pinpoint--then came the easier part.

The team simply placed the spheroids next to each other in a special lab dish. The cells were suspended in a gel that's commonly used to support organoid growth, then placed on top of a thin membrane that covered a carefully mixed batch of growth medium.

"From this point, the cells knew what to do," Takebe says. (see video for illustration of this)

The lab team simply watched as cells from each spheroid began to transform upon meeting each other at the boundary between the two. They converted themselves, and each other, into more specialized cells that could be seen changing colors thanks to chemical tags the lab team had attached to the cells.

Soon, the merging, changing spheres sprouted into branches leading to new groups of cells that belonged to specific organs. Over a period of 70 days, these cells continued to multiply into more refined and distinct cell types.

Ultimately, the mini organoids began processing bile acids as if they were digesting and filtering food.

"This was completely unexpected. We thought we would need to add ingredients or other factors to push this process," Koike says. "Not trying to control this biological process led us to this success."

What does this advance mean?

Aaron Zorn, PhD, Director of the Center for Stem Cell and Organoid Medicine (CuSTOM) at Cincinnati Children's says this advance will be useful in multiple ways.

"The real breakthrough here was to be able to make an integrated organ system," Zorn says. "From a research perspective this is an unprecedented opportunity to study normal human development."

However, Takebe and colleagues were able to grow these organoids only so far.

For the long-term hope of growing organ tissues large enough to be useful in human transplantation, Takebe says more work is needed. He and his colleagues already have started working on ways to add in immune cells along with cell lines needed to form blood vessels, connective tissues, and more.

But for research and diagnostic purposes, this discovery may have more immediate implications.

In precision medicine, doctors are starting to use genomic data and other information to determine exactly which treatments would work best for patients with serious disease, at what dose, and with the least amount of possible side effects.

A living "gut" of multiple organs would provide scientists with a powerful tool for studying exactly how gene variations and other factors affect organ development during pregnancy, and to develop better targeted drugs to treat conditions after babies are born.

A connected system of "generic" human organoids would offer much more information than having three organoids in disconnected dishes. Growing a set of gut organoids for a specific patient could allow even more precise diagnosis and customized treatment.

"Current liver regenerative medicine approaches suffer from the absence of bile duct connectivity," Takebe says. "While much work remains before we can begin human clinical trials, our multi-organoid transplant system is poised to solve this issue and may someday provide a life-long cure for patients with liver diseases."

Someday may not be so far away

While much more work remains ahead, Takebe and colleagues already report one step toward a practical application.

The team already has grown a set of gut organoids that lack the gene HES1.

This is one of several known genes that play a major role in triggering biliary atresia, a condition that destroys the biliary duct system, which leads to liver failure and death unless a transplant can be provided. This condition is the leading cause of liver transplants for children.

The new study demonstrates how the gut organoids are harmed by the lack of HES1.

If scientists can find a way to compensate for that genetic variation, they may be able to find a medication or cell transplant that would preserve biliary function in newborns and possibly avoid the need for hard-to-obtain liver transplants.

https://wb.md/2nCXs0e

Headache After Childbirth Epidural a Red Flag for Brain Bleed

Women who experience headaches following epidural anesthesia during childbirth have a greater risk of developing intracranial subdural hematoma

Batya Swift Yasgur, MA, LSW

Women who experience headaches following epidural anesthesia during childbirth have a greater risk of developing intracranial subdural hematoma, new research shows.

Using a large database to study over 22 million deliveries, investigators found a 100-fold increase in subdural hematoma in women who experienced a headache following epidural, compared with their counterparts with subdural hematoma who did not experience headaches.

"When a patient has a post-dural puncture headache, they are at risk for a subdural hematoma, which can result in serious morbidity and increased mortality and needs to be considered by any clinician looking after these patients," lead author Albert Moore, MD, associate professor, McGill University, Montreal, Canada, told *Medscape Medical News*.

"The risk is higher in patients who have coagulopathy, previous cerebral arteriovenous malformations, and hypertensive disease, and there is also a possibility that delaying a blood patch may increase the risk of developing a subdural hematoma," he said.

The study was published online September 16 in *JAMA Neurology*.

No Robust Evidence

"I had read and heard a lot of reports about women who had post-dural puncture headaches, who then developed a subdural hematoma," Moore noted.

"However, these were only case reports and there was no robust evidence to support any association of post-dural puncture headache with subdural hematoma and brain damage," he added.

Moore and his coinvestigators were concerned about this potential association because more than half of all women have epidurals during childbirth — and a significant percentage of them have post-dural puncture headaches.

"So if there really was an association of post-dural puncture headache with subdural hematoma, those who provide epidurals for labor and care for patients with post-dural puncture headaches should be aware," he said.

The goal of the study then was to determine whether there was an association of post-dural puncture headache and subdural hematoma. The investigators also looked at whether there were factors that could potentially increase or decrease the risk of subdural hematoma in these patients.

"The most important thing we were wondering about was the epidural blood patch, because a blood patch is something that can be offered and, if it is protective, could help a lot of these patients," he said.

The investigators analyzed data from the US Agency for Healthcare Research and Quality National Readmission Database, which included women who experienced childbirth from January 2010 to December 2016.

Patients (N = 26,469,771, mean [SD] age 28.1 [6.0] years) were required to have been admitted for childbirth, have 2 months of follow-up data, and not receive a diagnostic lumbar puncture (n = 22,130,815 patients who met the inclusion criteria).

Post-dural puncture headache within 2 months of childbirth was considered to be the primary exposure, and included either a reaction to spinal or lumbar puncture; a spinal and epidural anesthesia-induced headache during labor and delivery; or an

epidural anesthesia-induced headache during the immediate postpartum period.

The primary outcome was the incidence of subdural hematoma, while secondary outcomes were in-hospital mortality and the occurrence of neurosurgery.

Blood Patch Timing Important

Post-dural puncture headaches were identified in 68,374 deliveries, representing an overall rate of 309 (95% confidence interval [CI], 302 - 316) per 100,000 women.

Postpartum subdural hematoma (n = 342) represented an incidence of 1.5 (95% CI, 1.3 - 1.8) per 100,000 deliveries.

Of these, 25% (95% CI, 18% - 33%) and 75% (95% CI, 67% - 82%) were diagnosed during the birth admission and readmission, respectively.

Women with subdural hematoma were more likely to experience in-hospital mortality, compared with those without (2.9% vs .05%, representing a difference of 2.89%; 95% CI, 0.32% - 5.47%; *P* = .02).

Of those with subdural hematoma, 21.9% underwent neurosurgery compared to .003% of patients who had not experienced subdural hematoma (difference, 21.9% [95% CI, 14.1% - 30.0%]; *P* < .001).

The crude absolute increase was calculated as 145 (95% CI, 117 – 174) cases per 100,000 population.

When the researchers adjusted for an array of potential confounders (eg, age, comorbidities, vaginal vs cesarean delivery, hypertension, and preeclampsia), they found that post-dural puncture headache had an odds ratio (OR) for subdural hematoma of 199 (95% CI, 126 - 317; *P* < .001) and an adjusted absolute risk increase of 130 (95% CI, 90 - 169; *P* < .001) per 100,000 deliveries.

Coagulopathy, arteriovenous malformation, and delayed blood patch were found to have the highest level of association with subdural hematoma (adjusted ORs of 3.35 [95% CI, 1.55 - 7.22); 32 [95% CI, 5 - 215]; and 39 [95% CI, 14 - 108], respectively).

On the other hand, obesity and cesarean delivery without labor had negative adjusted absolute risk differences for subdural hematoma (−0.6 [95% CI, −1.3 to 0.0] and −0.6 [95% CI, −1.2 to 0.0] per 100,000 population, respectively).

There were statistically significant interactions between post-dural puncture headache and severe preeclampsia and chronic hypertension (β, −3.154 [SE, 1.123]; *P* = .005 and β, −1.581 [SE, 0.473]; *P* < .001, respectively).

Notably, a delayed blood patch was associated with an adjusted OR of 39 (95% CI, 14 - 108; *P* < .001 and an adjusted risk difference of 4659 (95% CI, 306 - 9011; *P* < .03) per 100,000.

"When we looked at other risk factors, we found some interesting things," Moore commented.

"Patients with hypertension, either before the pregnancy or pregnancy induced, [and] patients with coagulopathies and preexisting arteriovenous malformations in the brain had higher rates of subdural hematoma."

After adjusting for other risk factors, the researchers found that a blood patch performed at any time following the diagnosis of post-dural puncture headache did not appear to protect against subdural hematoma.

However, when looking specifically at the association with later blood patches — which were defined as "any happening in a readmission after post-dural puncture headache diagnosis" — the researchers found "much higher rates of subdural hematoma, suggesting that earlier blood patches are associated with lower rates of subdural hematoma and delayed blood patches with higher rates," Moore said.

A Major Contribution

Commenting on the findings for *Medscape Medical News*, Edward Riley, MD, professor of anesthesiology, perioperative and pain medicine at Stanford University School of Medicine in California, described the study as a "major contribution to the field."

"[This study] shows that dural puncture is not benign," Riley said.

Riley, who was not involved with the research, emphasized that there is "no take-home message suggesting that women should avoid epidurals during childbirth or that other individuals should avoid spinal anesthesia, since the benefits still outweigh the risks of these procedures."

He recommended "diligent follow-up and treatment of post-dural puncture headaches, because they are significant."

The authors point out that their study is observational, and therefore can only assess an association between post-dural puncture headache and subdural hematoma.

"Further research is needed to establish if this association is causal for this rare outcome," they write.

The financial costs of the study were paid for by a grant from the McGill University Health Center Department of Anesthesia research fund. Moore and coauthors and Riley have disclosed no relevant financial relationships.

JAMA Neurology. Published online September 16, 2019. Abstract

http://bit.ly/2mEfI9A

Woman Who Ate 'Unusually Large' Amount of Wasabi Developed Broken-Heart Syndrome

The woman mistook a serving of wasabi for avocado.

By Rachael Rettner - Senior Writer

A woman got more than a burning mouthful when she mistook a serving of wasabi for avocado — the spicy food appeared to cause her to develop "broken-heart syndrome," according to a new report of the case.

The 60-year-old woman was attending a wedding in Israel when she ate "a large amount of wasabi," which she thought was avocado, according to the report, published Sept. 20 in the journal BMJ Case Reports.

A few minutes later, she felt a "sudden pressure in her chest radiating to her arms," the report said.

Despite this symptom, the woman decided to stay at the wedding, and the pain subsided. But the next day, she felt general weakness and discomfort, which prompted her to go to the doctor.

At the hospital, tests revealed that the woman had broken-heart syndrome, also known as Takotsubo cardiomyopathy, according to the report authors, from Soroka University Medical Center in Beer Sheva, Israel.

Broken-heart syndrome is a condition in which the heart's main pumping chamber, the left ventricle, becomes enlarged and weakened so that it doesn't pump properly, Live Science previously reported. Symptoms can resemble those of a heart attack, and include chest pain and shortness of breath. Unlike damage from a heart attack, however, broken-heart syndrome is temporary, and most patients recover within a month.

The condition is often triggered by emotional stress, such as the death of a loved one or the loss of a job, according to the Mayo Clinic. But it may also be triggered by physical stress, such as an asthma attack or major surgery.

In the woman's case, it appears that eating about a teaspoon of wasabi triggered broken-heart syndrome. This isn't the first report of broken-heart syndrome triggered by food, but most other cases emerge after a severe allergic reaction to the food.

"To the best of our knowledge, this is the first report of Takotsubo cardiomyopathy triggered by wasabi consumption," they wrote.

Still, the authors don't think that wasabi is dangerous, at least in the small amounts that people typically consume. Some studies even suggest the food has benefits, including antioxidant activity, the authors wrote in the study.

The woman was treated with heart medications, including ACE inhibitors and beta blockers, both of which lower blood pressure. One month later, her heart tests appeared normal, indicating she had recovered from her condition, the report said.

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Trial finds high-dose radiation effective for men whose prostate cancer has spread

Phase II, randomized trial data show targeted radiation sparks immune system response similar to vaccination

A randomized clinical trial of targeted, high-dose radiation for men with oligometastatic prostate cancer has shown the treatment to be an effective and safe option for patients who wish to delay hormone-suppression therapy. The phase II trial found that radiation therapy can generate an immune system response not previously believed possible in this type of cancer. Findings will be presented today at the 61st Annual Meeting of the American Society for Radiation Oncology (ASTRO) in Chicago.

Previous research has shown high-dose radiation to be safe and effective for men with localized or non-metastatic prostate cancer, but patients with oligometastatic disease – whose cancer has been treated but then returned to a limited number of other parts of the body – generally have been considered incurable. "Single-institution studies and limited prospective data have recently suggested that high-dose, targeted radiation may be effective for men whose prostate cancer had spread, and now these ORIOLE randomized data confirm those observations," explained Ryan Phillips, MD, PhD, chief resident in radiation oncology at the Johns Hopkins School of Medicine in Baltimore, and lead author on the study.

The study, also known as the ORIOLE trial, randomized 54 patients whose cancer had spread to a limited number of sites outside the prostate after treatment with surgery or radiation. The patients were placed in one of two arms: those who were observed but received no further treatment for six months, and those who were treated with stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), to the metastatic sites outside of the prostate. SABR/SBRT is a form of high-precision cancer therapy that delivers substantially higher doses of radiation to the tumor site in just one or a few treatment sessions.

Men treated with SABR were significantly less likely to experience increases in their PSA levels and lived significantly longer without any detectable disease progression than patients who received no additional treatment. Six months later, just 19% of patients treated with SABR saw their disease progress, compared to 61% of those in the observation arm (p=0.005). The median progression-free survival (PFS) time for those in the observation arm was 5.8 months (HR 0.30, p=0.002), whereas more than half of the patients in the SABR-treated arm were still progression-free more than a year after treatment.

“ORIOLE provides additional randomized trial data to support what previous studies have been suggesting,” said Dr. Phillips. “Compared to retrospective reports, our study provides a higher level of evidence that SABR benefits these patients (as compared to observation for six months) because we can see how the patients who didn’t get SABR did in comparison.”

The ORIOLE trial, only the second randomized clinical trial to report findings on SABR for oligometastatic prostate cancer, has also shed light on what happens to the immune system when the disease is treated with high-dose radiation therapy.

The research team looked at blood cells sampled before radiation therapy and 90 days after treatment; they found “significant, measurable changes” in the T cells of patients on the SABR arm, but no change in the T cells of those in the observation arm. “The magnitude of change in the immune system response was similar to

what you see after a vaccination" said Dr. Phillips, suggesting that radiation may spark the immune system to more aggressively fight the cancer.

"This is the first bit of evidence that I'm aware of showing that SABR can induce a systemic immune response in patients with prostate cancer," said Phuoc Tran, MD, PhD, principal investigator of the trial and an associate professor of radiation oncology and molecular radiation sciences at the Johns Hopkins Kimmel Cancer Center. "Other studies have made similar observations, but these are probably the most robust, sensitive and controlled observations that SABR can excite a systemic immune response."

"Cancer of the prostate is a tumor that does not typically incite a response from the immune system, so seeing this response is exciting," he added. "There is still much work to be done to understand how radiation and the immune system interact."

Using a sophisticated type of imaging largely accessible only to research institutions, the study also shed light on how high-dose radiation therapy may alter the course of prostate cancer spread or metastasis.

Typically, metastatic prostate cancer lesions are detected using conventional imaging technologies such as bone scans, MRIs and/or CT scans. The ORIOLE trial used these conventional imaging techniques to identify patients eligible for their study (eligibility was based upon the detection of one to three metastatic lesions), but also made use of a more sensitive, advanced imaging technology known as a prostate-specific membrane antigen (PSMA) PET scan. This scan detects proteins that are overexpressed in prostate cancer and can reveal the presence of otherwise undetectable tumor growth.

Patients randomized to the SABR arm (n=36) received radiation to all lesions detected by conventional imaging. However, they also underwent PSMA PET scans prior to and 180 days after treatment. The results of those scans were not made available to the physicians developing their treatment plans; they were used only for further analysis and comparison of cancer growth.

What they showed, said Dr. Phillips, was that patients with no additional untreated lesions detected by the PSMA PET scan at baseline (a state referred to as total consolidation) were significantly less likely to develop new metastatic lesions at six months (16% vs. 63%, p=0.006) than those whose PSMA PET scan showed at least one additional lesion at baseline (a state referred to as subtotal consolidation). Patients with total consolidation of lesions also had significantly better (4.8 times greater) progression-free survival than patients whose PSMA PET scans showed additional lesions.

What this suggests, said Dr. Tran, is that the high-dose radiation treatments are not just destroying the tumors targeted by SABR, but they are changing the course of metastatic disease.

"Importantly, patients with subtotal consolidation had more new lesions," he said. "It isn't just that the untreated lesions are continuing to grow. This phenomenon suggests that treating macroscopic metastatic disease alters the natural history of the disease; that existing macroscopic metastases can influence the non-visible or microscopic disease development into new visible metastases."

Currently, PSMA PET scans are not widely available for physicians to use in treatment planning, said Dr. Phillips, but this study should add to the growing body of evidence of their usefulness. "That extra imaging information gave us extra power to prevent disease progression and new metastases," he said. "In our experience, these scans add to our ability to control the disease."

Finally, the trial also analyzed circulating tumor DNA (ctDNA) using an ultra-sensitive liquid biopsy test developed by Max Diehn, MD, PhD, an associate professor of radiation oncology at Stanford

University. Using ctDNA, the group identified a specific mutational signature that predicted which men most benefited from SABR.

"There is now accumulating evidence that SABR is effective for patients with oligometastatic disease, but there are currently no biomarkers that help us to determine who benefits most from this treatment. Our findings represent the first molecular marker that may predict a benefit of SABR in patients with oligometastatic disease. If additional validation of this mutational signature bears out in other cohorts, then we could potentially use it to personalize which patients with oligometastatic prostate cancer should receive SABR," commented Dr. Diehn.

The abstract, "Primary outcomes of a phase II randomized trial of observation versus stereotactic ablative radiation for oligometastatic prostate cancer (ORIOLE)," will be presented in detail at ASTRO's 61st Annual Meeting in Chicago. To schedule an interview with Dr. Phillips and/or outside experts, contact ASTRO's media relations team.

https://nyti.ms/2mNlrd6

These Ants Use Germ-Killers, and They're Better Than Ours

Parasitic fungi do not seem to develop resistance to the chemicals, suggesting new ways to prevent antibiotic resistance.

By Carl Zimmer

As a microbiologist, Massimiliano Marvasi has spent years studying how microbes have defeated us. Many pathogens have evolved resistance to penicillin and other antimicrobial drugs, and now public health experts are warning of a global crisis in treating infectious diseases. These days, Dr. Marvasi, a senior researcher at the University of Florence in Italy, finds solace in studying ants.

About 240 species of ants grow underground gardens of fungi. They protect their farms against pathogens using powerful chemicals secreted by bacteria on their bodies. Unlike humans, ants are not facing a crisis of antimicrobial resistance.

Writing in the journal Trends in Ecology and Evolution, Dr. Marvasi and his colleagues argue that fungus-farming ants could serve as a model for drug development. It's not just that they have antimicrobials — it's how they use their drugs.

Leafcutter ants carry bacteria that produce chemicals needed to kill a parasitic fungus. The chemicals may help scientists learn how to dodge antimicrobial resistance. **Frank Rumpenhorst/dpa, via Associated Press**

Fungus-farming ants bring leaves or other debris to gardens in their nests, where certain kinds of fungi thrive. The fungi — which can flourish nowhere else — grow into dense webs that the ants feed to their larvae. But the crops are also attractive to a parasitic fungus called Escovopsis. It attacks the gardens and starves the ants.

"It's a war between the ants and the pathogens for the same food," Dr. Marvasi said.

The ants have powerful allies in this war: bacteria that live on their thoraxes. Worker ants coat eggs with certain strains of these bacteria. As an ant matures, it feeds its personal supply of bacteria with secretions from glands on its thorax. The bacteria pay the ants back for this special care by making powerful antimicrobials that kill Escovopsis, protecting the gardens from destruction.

The fact that bacteria make antimicrobials is hardly surprising. The ones that doctors prescribe today were mostly discovered in the soil, made by microbes. What is surprising is that the chemicals used by the ants work so well. Escovopsis has evolved defenses against the bacteria, producing compounds that inhibit their growth. And yet the ants still manage to keep these pathogens in check.

Dr. Marvasi and his co-authors — Ayush Pathak of Imperial College London and Steve Kett of Middlesex University London — argue that we would do well to look more closely at the ants to figure out the secrets to their success. One important advantage is that the bacteria on ants make several antimicrobials at once. “It’s an impressive chemical factory,” said Dr. Marvasi.

Powerful evolutionary forces create this variety, said Sarah Worsley, a senior research associate at the University of East Anglia in England, who was not involved in the new study.

When the ants forage for garden fertilizer, they pick up random bacteria from the ground. These compete fiercely with the resident microbes for the nutrients provided by the ant glands. Natural selection favors the residents that make powerful antimicrobials that ward off the newcomers.

“These antimicrobials are being produced as a result of this warfare on the ant’s surface,” said Dr. Worsley. “The ants get in on the competition and use those antimicrobials to look after their fungus gardens.”

Researchers are also learning how new antimicrobials evolve. “We’re accumulating so much new information on the molecular level now,” said Katrin Kellner, a molecular ecologist at the University of Texas at Tyler.

Sometimes resident bacteria on ants take up a gene from competitors. The protein made by the new gene may then alter the shape of an existing antimicrobial.

Other mutations may shuffle genetic switches in the bacteria’s DNA. As a result, it may produce new antimicrobial compounds.

But Ulrich Mueller, an evolutionary biologist at the University of Texas at Austin, warned that scientists may not yet understand the ants well enough to learn from their success.

Some antimicrobials that kill Escovopsis, for example, also seem to defend the ants from their own infections. It’s possible that their evolution has little to do with protecting fungal gardens.

“That dimension has been completely ignored,” Dr. Mueller said.

Dr. Marvasi and his colleagues are investigating the evolutionary competition between the bacteria on ants and Escovopsis, pitting the organisms against one another in Petri dishes.

They want to see if the combination of related antimicrobials is the secret to the ants’ success. Mimicking that strategy might help keep our own antimicrobial drugs potent.

“The idea is maybe to have one main antibiotic, but in a mixture of similar antibiotics,” Dr. Marvasi said.

Dr. Worsley and her colleagues are reproducing the evolution of the bacteria living on the ants. The scientists are tweaking the bacterial genes that produce antimicrobials, hoping to discover new compounds that might work on human diseases, rather than garden parasites. “We’re shortcutting evolution by taking inspiration from these arms races in the past,” she said.

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Why viruses like Herpes and Zika will need to be reclassified, and its biotech impact

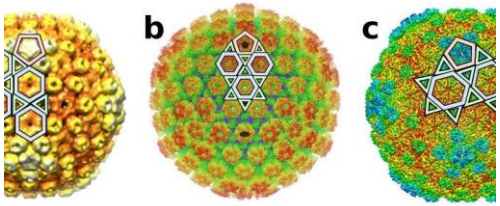
New research reveals that the way viruses were perceived in terms of their architecture will need to be retooled

New research reveals that the way viruses were perceived in terms of their architecture will need to be retooled, because they are actually structured in many more patterns than previously understood. The findings could have significant impact on how they are classified, our understanding of how they form, evolve and infect hosts, and strategies to identify ways to design vaccines to target them.

In the 1950s and '60s as scientists began to obtain high resolution images of viruses, they discovered the detailed structure of the

capsid—an outer protective layer composed of multiple copies of the same protein—which protects the virus' genetic material. The majority of viruses have capsids that are typically quasi-spherical and display icosahedral symmetry—like a 20-sided dice for instance.

The capsid shell is what protects them, and as scientists discovered their structure, they proposed that capsids could have different sizes and hold different amounts of genome, and therefore could infect hosts differently.



Evolutionary related viruses infecting bacteria and humans adopting one of the newly established protein layouts of icosahedral capsids. Bacillus phage Basilisk (a), herpes simplex virus 1 (b), and bacteriophage lambda (c). **Antoni Luque, San Diego State University and Reidun Twarock, University of York.**

Why this matters

When designing drugs to target viruses, scientists can now take their varying structural shapes into account to improve efficacy.

Two researchers who study the structures of viruses, Antoni Luque, a theoretical biophysicist at San Diego State University and a member of its Viral Information Institute, and Reidun Twarock, a mathematical biologist from the University of York, UK, and a member of York's Cross-disciplinary Centre for Systems Analysis, show that many viruses have essentially been misclassified for 60 years, including common viruses such as Herpes simplex and Zika.

This was because despite having the structural images from cryo-electron microscopy, we did not have the mathematical description of many of the architectures of different viruses.

"We discovered six new ways in which proteins can organize to form icosahedral capsid shells," Luque said. "So, many viruses don't adopt only the two broadly understood capsid architectures. There are now at least eight ways in which their icosahedral capsids could be designed."

They used a generalization of the quasiequivalence principle to see how proteins can wrap around an icosahedral capsid.

Their study, which will be published in *Nature Communications* on Friday, September 27, also shows that viruses that are part of the same structural lineage, based on the protein that they're composed of, adopt consistent icosahedral capsid layouts, providing a new approach to study virus evolution.

Biotech applications

Structural biologists can now take this information and reclassify the structure of the viruses, which will help unveil molecular and evolutionary relationships between different viruses.

It will also provide a guide to engineer new molecular containers for nanotech and biotech applications, and it will help scientists to identify specific strategies to target the assembly of proteins in the capsid. This can eventually lead to a more systematic approach to developing antiviral vaccines.

"We can use this discovery to target both the assembly and stability of the capsid, to either prevent the formation of the virus when it infects the host cell, or break it apart after it's formed," Luque said. "This could facilitate the characterization and identification of antiviral targets for viruses sharing the same icosahedral layout."

This new framework accommodates viruses that were previously outliers, provides new predictions of viral capsid architectures, and has identified common geometrical patterns among distant evolutionary related viruses that infect everyone from humans to bacteria.

Twarock said the new blueprints also provide "a new perspective on viral evolution, suggesting novel routes in which larger and more complex viruses may have evolved from simple ones at evolutionary timescales."

Architectural applications

The geometries could be also used in new architectural designs in buildings and construction.

Since the 1960s, these viral capsids have been classified using the geometrical framework introduced by structural biologist Donald Caspar and biophysicist Aaron Klug, which were inspired by the geodesic domes designed by the renowned architect R. Buckminster Fuller. However, as molecular imaging techniques have advanced, an increasing number of 3-D viral capsid reconstructions that included viruses like Herpes or Zika have fallen out from this classical geometrical framework.

"This study introduces a more general framework than the classic Caspar-Klug construction. It is based on the conservation of the local vertices formed by the proteins that interact in the capsid," Luque explained. "This approach led to the discovery of six new types of icosahedral capsid layouts, while recovering the two classical layouts from Caspar-Klug based on Goldberg and geodesic polyhedra."

"Structural puzzles in virology solved with an overarching icosahedral design principle" is published in *Nature Communications*.

More information: *Structural puzzles in virology solved with an overarching icosahedral design principle, Nature Communications (2019).* *doi.org/10.1038/s41467-019-12367-3*

http://bit.ly/2nPyZoJ

Analyses of newborn babies' head odors suggest importance in facilitating bonding

First to identify the chemical makeup of the odors produced by newborn babies' heads

日本のニュース

A team led by Kobe University Professor Mamiko Ozaki (Department of Biology, Graduate School of Science) has become the first to identify the chemical makeup of the odors produced by newborn babies' heads. The results shed more light on the olfactory importance of newborns' heads in mother-baby and kin recognition. They also developed a non-invasive and stress-free method of sampling these odors directory from heads of the babies.

The research team consisted of professors and researchers from Hamamatsu University of Medicine, Iwate University, Tsukuba University and Kobe University.

The study looked at both the chemical and psychological aspects of the odors of babies' heads and how this provides an important way for newborns to attract the attention of caregivers. Research into these odors can hopefully be utilized in the prevention of issues such as infant neglect and attachment disorders.

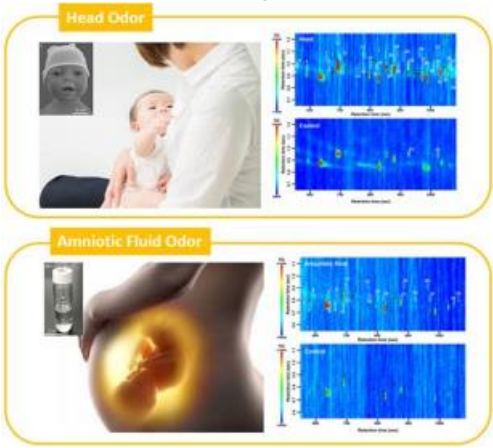


Figure 1: Odor sampling and GCxGC-MS chemical analysis **Kobe University**

The scientific paper for this study was first published in English in the online journal 'Scientific Reports'.

Research aims and methodology:

The role of olfactory information in forming connections between humans is not well understood. Although there have been studies into the importance of olfactory cues in the formation and development of mother-infant relationships, there have been very few investigations to analyze and identify the essential chemical components of such cues.

The main aim of this study was to understand more about the odor produced by newborn babies, which may facilitate caregiving. The following research was carried out:

1. Chemical analysis of newborn babies' head odors and amniotic fluid odors

Head odor samples were obtained from 5 babies born at Hamamatsu University Hospital. A stress-free method using monosilica beads was used to trap the odors. The beads were wrapped inside a cap-shaped net bandage and then placed on the babies' heads. The babies were with their mothers for the duration of the 20 minute sampling period and showed no signs of distress. Two samples of the mothers' amniotic fluid odor were also taken by suspending monosilica beads in the headspace of the glass bottle containing the fluid.

Thirty seven volatile odor components were identified in the GCxGC-MS analytical results aggregated for all the odor samples (five babies' heads and two amniotic fluid samples) (Figure 1).

2. Chemical similarities and variations in the odors

Aldehydes, carbonic oxides and hydrocarbons were among the 37 volatile odor components identified in the babies' head and amniotic fluid samples. The composition contents of these odors were calculated and the patterns for all the samples were compared (Figure 2).

It was discovered that the odor samples from babies' heads are more distinct from each other than those obtained from amniotic fluid. Furthermore, the odor profiles of Babies 1 and 2, which were collected within an hour after birth, looked less similar to each other than those of Babies 3, 4 and 5, which were collected 2 to 3 days after birth. These results suggest that a baby can strongly express its individuality through the odor soon after birth compared to a few days later.

3. Similarities and variations in sensory recognition of the odors

A total of 62 Kobe University students aged 18-24 (31 female and 31 male) were asked to smell one of three samples. The samples were artificial odor mixtures based on the baby's head and amniotic fluid samples taken at Hamamatsu University Hospital. Fifteen minutes later they were then asked to determine which of the four test samples (three artificial odor mixtures and the control solvent) was identical to the odor they had smelled earlier. Participants were also requested to rate their level of confidence in their decision. These were blind experiments; the participants were unaware of the type and origin of the samples.

The results suggested that the participants were able to distinguish between the odor samples (Figure 3). When the target odor was one of the mixtures based on the odor of babies' heads, the identification rate was over 70% for all participants. However, the identification rate for the amniotic fluid odor was lower than that (55%), and there was also a difference in the identification rate between female (73%) and male participants (36%).

Further Development:

The chemical analysis and olfactory recognition of babies' head odors in this study are potentially important contributions to the understanding of mother-infant bond formation and early non-verbal communication.

This research could be further developed by analyzing samples from a greater number of babies' heads. In addition, it may be worth investigating other factors, which can affect the odor recognizing ability of grownups, such as the marital status or child-care experience of the participants.

Acknowledgements:

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Study finds age hinders cancer development

A new study, published in* Aging Cell*, has found that human ageing processes may hinder cancer development.

Ageing is one of the biggest risk factor for cancer. However, the biological mechanisms behind this link are still unclear.

Each cell in the human body is specialised to carry out certain tasks and will only need to express certain genes. Gene expression is the process by which specific genes are activated to produce a required protein.

Gene expression analyses have been used to study cancer and ageing, but only a few studies have investigated the relationship between gene expression changes in these two processes.

In an effort to better understand the biological mechanisms researchers from the University of Liverpool's Integrative Genomics of Ageing Group, led by Dr Joao Pedro De Magalhaes, compared how genes differentially expressed with age and genes differentially expressed in cancer among nine human tissues.

Normally, a healthy cell can divide in a controlled manner. In contrast, senescent or 'sleeping' cells have lost their ability to divide. As we age, the number of senescent cells in our bodies increase, which then drive many age-related processes and diseases.

Genetic mutations triggered by things such as UV exposure can sometimes cause cells to replicate uncontrollably -- and uncontrolled cell growth is cancer. Cells are often able to detect these mutations and in response go to sleep to stop them dividing.

The researchers found that in most of the tissues examined, ageing and cancer gene expression 'surprisingly' changed in the opposite direction. These overlapping gene sets were related to several processes, mainly cell cycle and the immune system. Moreover, cellular senescence changed in the same direction as ageing and in the opposite direction of cancer signatures.

The researchers believe the changes in ageing and cellular senescence might relate to a decrease in cell proliferation, while cancer changes shift towards an increase in cell division.

Dr De Magalhaes, said: "One of the reasons our bodies have evolved to have senescent cells is to suppress cancers. But then it seems that senescent cells accumulate in aged human tissues and may contribute to ageing and degeneration. Importantly, our work challenges the traditional view concerning the relationship between cancer and ageing and suggests that ageing processes may hinder cancer development. While mutations accumulate with age and are the main driver of cancer, ageing tissues may hinder cell proliferation and consequently cancer. So you have these two opposite forces, mutations driving cancer and tissue degeneration hindering it. This may explain why at very advanced ages cancer incidence levels off and may even decline."

However, an alternative explanation comes from evolutionary biology. First author Kasit Chatsirisupachai, explains: "And aged tissue might actually be a better environment for a rogue cancer cell to proliferate because the cancer cell will have an evolutionary advantage."

Dr De Magalhaes: "Our results highlight the complex relationship between ageing, cancer and cellular senescence and suggest that in most human tissues ageing processes and senescence act in tandem while being detrimental to cancer. But more mechanistic studies are now needed."

The full study, entitled 'A Human Tissue-Specific Transcriptomic Analysis Reveals that Ageing Hinders Cancer and Boosts Cellular Senescence', can be found here *https://onlinelibrary.wiley.com/doi/10.1111/acel.13041*

http://bit.ly/2nTc9fG

Transplanting poop can be beneficial—swapping vaginal fluids may be even better

Transferring vaginal fluids could "revolutionize" women's health, researchers say.

Beth Mole

In the afterglow of successful fecal transplants, researchers are now sniffing around vaginal fluids for the next possible bodily product to improve health—and they're roused by the possibilities.

Vaginal fluid transplants could “revolutionize the way we view and treat conditions affecting the female reproductive tract,” researchers at Johns Hopkins wrote in a recent study on vaginal microbiota transplants (VMTs). If they work as researchers hypothesize, they could rub out many common problems at once. And based on what we know of vaginas, they could be far less messy than transplants involving poop.

Microbial muck

The basic idea behind VMTs is identical to that of poop transplants, aka fecal microbiota transplants (FMTs), which have been around for centuries. Generally, FMTs aim to use microbe-laden bodily products—in this case excrement—to introduce or restore rich, complex microbial communities into the innards of ailing recipients. In healthy human intestines, thriving microbial inhabitants are involved in everything from cycling hormones and influencing immune responses to protecting from pathogenic germs, not to mention helping extract nutrients from food. When these communities die off, get out of balance (a condition generally called dysbiosis), or become overrun by disease-causing germs, our health can wane. That’s where FMTs come in.

Some researchers say they can trace deuce-based remedies back centuries, to people slurping "yellow soup” to treat severe diarrhea in 4th century China, and Bedouin groups tossing back camel patties to cure dysentery centuries later. The idea plopped into western medicine in the 1950s but was largely dismissed until recently. The brown tide began to turn as researchers learned more about our microbial residents, and the rise of antibiotic-resistant infections spurred them to explore new treatment options.

Modern FMT recipients now take in the goods by piping them into their bowels, gulping them in capsules, or injecting them in enemas. And researchers are looking into using FMTs to treat a range of conditions including obesity, food allergies, inflammatory bowel disease, depression and multiple sclerosis.

But despite the fact that the medicine has come a long way from serving poopy soup, researchers are still straining to squeeze out all of FMTs potential. So far, the only condition for which there’s firm evidence that FMTs are effective is recalcitrant *Clostridium difficile* infections, which cause severe diarrhea—echoing the centuries-old uses of FMTs.

Against the life-threatening *C. diff* infections, FMTs have proven highly effective, clearing the infection in 80% to 90% of patients after one round. As such, FMTs are seen by many as a clear—albeit limited—success story, and they’ve garnered considerable attention from researchers and patients alike who hope they’ll be just as potent at treating other conditions.

Still, even with the focus on FMTs and microbiome research, our gut communities have remained enigmatic, proving extremely complex and variable. Researchers still don’t understand them enough to cure other conditions. We have yet to flush out what features, mixes, ratios, or microbial groups or species may be key to particular health outcomes. In other words, it’s unclear what makes for solid donor poop—let alone how to regulate and administer said poop.

On the flip side

Vaginal microbiota transplants, on the other hand, may not face such onerous hurdles. Based on what researchers have gathered so far, the microbial communities of a healthy vagina are relatively simple compared with that of the gut, and they play key roles in health.

As the Johns Hopkins researchers note in their recent study, “Although there has been increasing awareness of the broad spectrum of ‘normal,’ it is generally considered that the ‘optimal’

vaginal microbiota communities are dominated by one of only a handful of species of *Lactobacillus*" bacteria.

But if those communities get frisky, growing more diverse and ditching a dominant *Lactobacillus*, women can develop a common medical condition called bacterial vaginosis. This is linked to a range of problems including increased risk of urinary tract infections, greater susceptibility to getting and spreading sexually transmitted infections, issues with infertility, and preterm birth. Bacterial vaginosis is estimated to affect around 30% of US women aged 14 to 49, according to the Centers for Disease Control and Prevention. Other imbalances in vaginal microbes have been linked to recurrent yeast infections, some reproductive tract cancers, and the harboring of group B Streptococcus (bacteria that can cause severe infections in newborns).

A standard treatment for bacterial vaginosis is antibiotics, but the condition can relapse in as much as 70% of cases within 3 months. The hope of VMTs is that they could restore a healthy, simple vaginal microbiome and wipe out all of those risks in one clean stroke.

In anticipation of such a clinical peak, the researchers at Johns Hopkins set up a pilot study of 20 women to try to figure out how to screen potential donors of cervicovaginal secretions, which could then be used for transplants.

The pilot screening process first involved a questionnaire about sexual behavior, vaginal product use, infections, and vaginal symptoms. Researchers next did tests for active infections and past exposures, probed the genetics of vaginal microbes, and looked at the physicochemical properties of vaginal fluids. They determined, among other things, that a good cut-off point for the pH of transplantable vaginal fluids is ≤4.2.

Only seven of the 20 women in the study (35%) were considered potentially eligible to be VMT donors in the end, and the researchers expect that percentage to be even lower in larger screenings.

While few women may end up qualifying to be donors, the researchers note that "the idea of a 'super-donor' with no identified past or current infections and with favorable *Lactobacillus*-dominated microbiota is one that should be explored and is of potential high impact to the project and the field."

Once safe and desirable donors are identified, researchers face the real test of whether VMTs actually work. Based on epidemiological data of women who have sex with women, vaginal microbiota transfers are possible. But they still need to be proven and refined in clinical setting.

There are some key unknowns, for instance, whether aspects of the vaginal environment—such as mucus or lactic acid—might be critical for transplant success, or whether minority bacterial community members are key to overall health.

For now, the researchers "anticipate that the framework described [in the study] will help accelerate clinical studies of VMT." In the meantime, "the development of the FMT field is an obvious source of inspiration for initiating study of other forms of microbiota transplantation, such as VMT."

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http://bit.ly/2oyKZuZ

New blood test capable of detecting multiple types of cancer

In study, test proved able to detect and localize more than 20 types of cancer with a high degree of accuracy

Test detected methylation patterns associated with cancer in free-floating DNA in blood

A new blood test in development has shown ability to screen for numerous types of cancer with a high degree of accuracy, a trial of

the test shows. Dana-Farber Cancer Institute investigators will present the results of the multi-center trial during a session today at the European Society for Medical Oncology (ESMO) 2019 Congress.

The test, developed by GRAIL, Inc., uses next-generation sequencing technology to probe DNA for tiny chemical tags (methylation) that influence whether genes are active or inactive. When applied to nearly 3,600 blood samples - some from patients with cancer, some from people who had not been diagnosed with cancer at the time of the blood draw - the test successfully picked up a cancer signal from the cancer patient samples, and correctly identified the tissue from where the cancer began (the tissue of origin).

The test's specificity - its ability to return a positive result only when cancer is actually present - was high, as was its ability to pinpoint the organ or tissue of origin, researchers found.

The new test looks for DNA, which cancer cells shed into the bloodstream when they die. In contrast to "liquid biopsies," which detect genetic mutations or other cancer-related alterations in DNA, the technology focuses on modifications to DNA known as methyl groups. Methyl groups are chemical units that can be attached to DNA, in a process called methylation, to control which genes are "on" and which are "off."

Abnormal patterns of methylation turn out to be, in many cases, more indicative of cancer - and cancer type - than mutations are. The new test zeroes in on portions of the genome where abnormal methylation patterns are found in cancer cells.

"Our previous work indicated that methylation-based assays outperform traditional DNA-sequencing approaches to detecting multiple forms of cancer in blood samples," said the study's lead author, Geoffrey Oxnard, MD, of Dana-Farber. "The results of the new study demonstrate that such assays are a feasible way of screening people for cancer."

In the study, investigators analyzed cell-free DNA (DNA that had once been confined to cells but had entered the bloodstream upon the cells' death) in 3,583 blood samples, including 1,530 from patients diagnosed with cancer and 2,053 from people without cancer.

The patient samples comprised more than 20 types of cancer, including hormone receptor-negative breast, colorectal, esophageal, gallbladder, gastric, head and neck, lung, lymphoid leukemia, multiple myeloma, ovarian, and pancreatic cancer.

The overall specificity was 99.4%, meaning only 0.6% of the results incorrectly indicated that cancer was present. The sensitivity of the assay for detecting a pre-specified high mortality cancers (the percent of blood samples from these patients that tested positive for cancer) was 76%. Within this group, the sensitivity was 32% for patients with stage I cancer; 76% for those with stage II; 85% for stage III; and 93% for stage IV.

Sensitivity across all cancer types was 55%, with similar increases in detection by stage. For the 97% of samples that returned a tissue of origin result, the test correctly identified the organ or tissue of origin in 89% of cases.

Detecting even a modest percent of common cancers early could translate into many patients who may be able to receive more effective treatment if the test were in wide use, Oxnard remarked.

The senior author of the study is Minetta C. Liu, MD, of the Mayo Clinic. Co-authors are: Eric A. Klein, MD, and Mikkael A. Sekeres, MD, of the Cleveland Clinic; Michael V. Seiden, MD of US Oncology Research; Earl Hubbell, PhD, Oliver Venn, DPhil, Arash Jamshidi, PhD, Nan Zhang, PhD, John F. Beausang, PhD, Samuel Gross, PhD, Kathryn N. Kurtzman, MD, Eric T. Fung, MD, PhD, Brian Allen, MS, Alexander M. Aravanis, MD, PhD, and Anne-Renee Hartman, MD, of GRAIL, Inc.; Donald Richards, MD, PhD, of Texas Oncology; and Peter P. Yu, MD, of Hartford HealthCare Cancer Institute, Hartford, Conn.

http://bit.ly/2oCdqbH

Earliest life found in ancient Aussie rocks

The Pilbara's famous stromatolites finally give up their secret.

Mark Bruer reports.

Australian scientists have unearthed traces of the oldest life form ever found in 3.5 billion-year-old rocks in Western Australia.

In a major advance in the field, the University of New South Wales team says its discovery of microbial remains hidden in the famous Dresser Formation stromatolites offers clues for how life on Earth started, and where to look for signs of life on Mars.

Ever since they were discovered in the East Pilbara region in the 1980s, scientists have believed the stromatolites were created in areas of hydrothermal activity from layers of living organisms such as cyanobacteria, a single-cell microbe.

However, that theory has been unproven for nearly four decades, because time and weathering of the rocks has altered their mineralogy and prevented the identification of organic matter – until now.

To get a clearer picture of how these ancient rocks came into being, lead researcher Raphael Baumgartner and colleagues needed to study parts of the stromatolites that had not been affected by weathering.

Photomicrograph of stromatolites from the 3.5 billion-year-old Dresser Formation. They are delineated by the mineral pyrite, also known as fool's gold. **University of South Australia**

They obtained samples extracted by diamond drilling from deep within the stromatolites, below the exposed area. The team analysed the samples with cutting-edge micro-analytical tools and techniques including high-powered electron microscopy, spectroscopy, ion mapping and isotope analysis. The works, in other words. Late one night they found what they were looking for: organic matter. It was there in the pyrite – a mineral also known as "fool's gold" – from which the stromatolites are composed.

For Baumgartner, it was a "Eureka moment".

"The organic matter that we found preserved within pyrite of the stromatolites is exciting – we're looking at exceptionally preserved coherent filaments and strands that are typically remains of microbial biofilms. "This is an exciting discovery – for the first time, we're able to show the world that these stromatolites are definitive evidence for the earliest life on Earth."

The scientists say their findings, combined with earlier work on the Pilbara stromatolites that suggested life may have begun on land rather than in the ocean, are helping us answer a central question: where did we come from?

"Understanding where life could have emerged is really important in order to understand our ancestry. And from there, it could help us understand where else life could have occurred – for example, where it was kick-started on other planets," Baumgartner says.

As it happens, last month NASA and European Space Agency (ESA) scientists, including the heads of the Mars 2020 missions, spent a week in the Pilbara with UNSW team leader Martin Van Kranendonk for specialist training in identifying signs of life in these same ancient rocks.

"It is deeply satisfying that Australia's ancient rocks and our scientific know-how is making such a significant contribution to our search for extra-terrestrial life," says Van Kranendonk.

"This represents a major advance in our knowledge of these rocks, in the science of early life investigations generally, and – more specifically – in the search for life on Mars. We now have a new target and new methodology to search for ancient life traces."

The team's findings are published in the journal *Geology*.

http://bit.ly/2nQLT5J

Type 2 diabetes remission possible with 'achievable' weight loss, say researchers

People who achieve weight loss of 10% or more in the first five years following diagnosis with type 2 diabetes have the greatest chance of seeing their disease go into remission,

according to a study led by the University of Cambridge. The findings suggest that it is possible to recover from the disease without intensive lifestyle interventions or extreme calorie restrictions.

Type 2 diabetes affects 400 million people worldwide and increases the risk of heart disease, stroke, blindness and amputations. While the disease can be managed through a combination of positive lifestyle changes and medication, it is also possible for the high blood glucose levels that define diabetes to return to normal - through significant calorie restriction and weight loss. An intensive low-calorie diet involving a total daily intake of 700 calories (less than one cheeseburger) for 8 weeks has been associated with remission in almost nine out of ten people with recently diagnosed diabetes and in a half of people with longstanding disease.

However, there is little evidence to show whether the same effect can be achieved by people undergoing less intensive interventions, which are more feasible and potentially scalable to the wider population. To answer this question, a team led by researchers at the University of Cambridge studied data from the ADDITION-Cambridge trial, a prospective cohort study of 867 people with newly diagnosed diabetes aged 40 and 69 years recruited from general practices in the eastern region.

The research was funded by Wellcome, the Medical Research Council and the National Institute for Health Research.

The researchers found that 257 participants (30%) participants were in remission at five-year follow-up. People who achieved weight loss of 10% or more within the first five years after diagnosis were more than twice as likely to go into remission compared to people who maintained the same weight.

"We've known for some time now that it's possible to send diabetes into remission using fairly drastic measures such as intensive weight loss programmes and extreme calorie restriction," says Dr Hajira Dambha-Miller from the Department of Public Health and Primary Care.

"These interventions can be very challenging to individuals and difficult to achieve. But, our results suggest that it may be possible to get rid of diabetes, for at least five years, with a more modest weight loss of 10%. This will be more motivating and hence more achievable for many people."

Senior author Professor Simon Griffin of the MRC Epidemiology Unit added: "This reinforces the importance of managing one's weight, which can be achieved through changes in diet and increasing physical activity. Type 2 diabetes, while a chronic disease, can lead to significant complications, but as our study shows, can be controlled and even reversed."

In order to clarify the best way to help patients with type 2 diabetes achieve sustained weight loss, the team is currently undertaking a study called GLoW (Glucose Lowering through Weight management). The study compares the current education programme offered by the NHS to people after they have been diagnosed, with a programme delivered by WW (formerly Weight Watchers®). The team is looking to recruit individuals who have been diagnosed with type 2 diabetes within the last three years, have not attended a structured education programme and are able to visit one of our testing centres in Wisbech, Ely or Addenbrooke's Hospital. Further details can be found at the GLOW Study website.

Reference *Dambha-Miller, H* et al. *Behaviour change, weight loss and remission of type 2 diabetes: a community based prospective cohort study. Diabetic Medicine; DOI: 10.1111/dme.14122*