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2 Infants Were Buried Wearing Helmets Made from Kids' Skulls. And Archaeologists Are Puzzled.

Two infants were buried some 2,100 years ago wearing "helmets" made from the skulls of other children, archaeologists have discovered.

By Owen Jarus - Live Science Contributor

The remains of the two infants were found with nine other burials at a site called Salango, on the coast of central Ecuador. The archaeologists who excavated the burials between 2014 and 2016 recently published the details of their findings in the journal Latin American Antiquity.

The infants were buried wearing helmets made from the skulls of children. **© Sara Juengs)**

The team says this is the only known case in which children's skulls were used as helmets for infants being buried. The scientists don't know what killed the infants and children.

Putting the "helmets" on

The helmets were placed tightly over the infants' heads, the archaeologists found. It's likely that the older children's skulls still had flesh on them when they were turned into helmets, because without flesh, the helmets likely would not have held together, the archaeologists noted.

One infant's "face looked through and out of the cranial vault" — the space in the skull that holds the brain — the archaeologists wrote.

Interestingly a "hand phalanx," a type of bone, was found wedged between the infant's head and the helmet. They don't know whom the hand phalanx belonged to, said Sara Juengst, lead author of the paper and an anthropology professor at the University of North Carolina, Charlotte. Juengst noted that other tests, such as those using DNA and strontium isotopes (variations of an element with different numbers of neutrons), may help to identify the owner of the bones.

Infant bone helmets

The archaeologists are not certain why helmets made from children's skulls were placed on the infants' heads. It "may represent an attempt to ensure the protection of these 'presocial and wild' souls," the archaeologists wrote. Near the infants, the archaeological team also discovered ancestor figurines, which depict ancestors, made of stone. This finding supports this protection idea, as their presence indicates a "concern with protecting and further empowering the heads," the archaeologists wrote.

Previous work suggests that a volcanic eruption covered the area in ash not long before the infants were buried. This eruption may have affected food production, and the newly discovered bones suggest the infants and children suffered from malnutrition, the researchers said.

It's possible that "the treatment of the two infants was part of a larger, complex ritual response to environmental consequences of the eruption," the archaeologists wrote, noting that "more evidence is needed to confirm this."

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Borderline personality disorder has strongest link to childhood trauma

People with Borderline Personality Disorder are 13 times more likely to report childhood trauma than people without any mental health problems, according to University of Manchester research.

The analysis of data from 42 international studies of over 5,000 people showed that 71.1% of people who were diagnosed with the serious health condition reported at least one traumatic childhood

experience. The study was carried out by researchers at The University of Manchester in collaboration with Greater Manchester Mental Health NHS Foundation Trust. It is published in the journal Acta Psychiatrica Scandinavia.

In the latest of a series of Meta-analyses by the team on the effects of childhood trauma on adult mental health, they show it is much more likely to be associated with BPD than mood disorders, psychosis and other personality disorders.

The most common form of adverse experience reported by people with BPD was physical neglect at 48.9%, followed by emotional abuse at 42.5%, physical abuse at 36.4%, sexual abuse at 32.1% and emotional neglect at 25.3%.

BPD is often a debilitating mental health problem that makes it hard for someone a control their emotions and impulses. The disorder, often linked to self-harm and substance abuse, is hard to treat and associated with significant costs to sufferers and society as a whole. Some of the characteristics of this condition -such as experiencing extreme, overwhelming emotions over what might be seen to others as a minor issue - are common, but become chronic and exaggerated after childhood trauma.

Dr Filippo Varese, from The University of Manchester, said: "During childhood and adolescence, our brain is still undergoing considerable development and we are also refining strategies to deal with the challenges of everyday life, and the negative feelings that come with them.

"In some people who have experienced chronic, overwhelming stress in childhood, it is likely that these responses do not develop in the same way. People can become more sensitive to 'normal' stress. They are sometimes unable to deal with intense negative thoughts and feelings, and they might resort to dangerous or unhelpful measures to feel better, such as taking drugs or self-harming. This can lead to various mental health difficulties, including the problems commonly seen in people who receive a diagnosis of BPD. "We found a strong link between childhood trauma and BPD, which is particularly large when emotional abuse and neglect was involved."

He added: "Borderline is a slightly misleading term - as it implies that this condition only has a mild impact. Far from that, BPD can be very distressing and difficult to treat.

"The term BPD was originally used to indicate mental health problems that were not a psychosis nor an anxiety or depressive disorder - but something in the middle. Another term used in modern times is 'emotionally unstable personality disorder', which perhaps gives a clearer picture of the kind of problems typically described by these people.

"We hope these findings underline the importance of trauma informed care for people accessing mental health services, where prevalence rates of BPD are high. "But further research is needed to explore the complex factors also likely to be involved such as biology, experiences in later life, and psychological processes."

An embargoed copy of the paper, Childhood Adversity and Borderline Personality Disorder: A Meta-Analysis is available.

http://bit.ly/35m9L1t

New finding on origin of avian predentary in Mesozoic birds

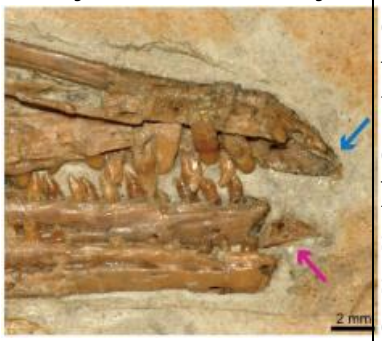
Also provides evidence the predentary was proprioceptive and mobile

The predentary bone is one of the most enigmatic skeletal elements in avian evolution. Located at the tip of the lower jaw, this bone is absent in more primitive birds and in living birds; it is thought to have been lost during evolution. For over 30 years, the origin and function of the avian predentary has remained mysterious.

Now, however, Alida Bailleul, LI Zhiheng, Jingmai O'Connor and ZHOU Zhonghe from the Institute of Vertebrate Paleontology and

Paleoanthropology (IVPP) of the Chinese Academy of Sciences have made significant progress towards solving this long-standing mystery. Their findings were published in Proceedings of the National Academy of Sciences *of the United States of America (PNAS)* on November 18.

Using a battery of analytical methods, the team, led by Dr. Bailleul, presents strong evidence that the avian predentary was covered by a keratinous beak - a horny sheath that covers the bones of the rostrum in all living birds, all of which are edentulous and have beaks. It also provides evidence the predentary was proprioceptive, i.e., it was able to detect external mechanical stimuli; and was mobile - thus representing a now extinct form of cranial kinesis.



The pink arrow points to the predentary and the blue arrow points to the upper portion of the jaw, which has no teeth. Together, they may have been covered by a keratinous beak, and the predentary was most likely mobile
Credit: IVPP

Cranial kinesis occurs when joints are able to move within the skull - mainly between the upper jaw and the braincase. This feature is widespread in living birds; however, it is thought to be mostly absent in Mesozoic birds.

Based on her examination of the fossilized tissues of the predentary and other jaw elements of Yanornis martini from the Jehol Biota, Dr. Bailleul identified a specific type of cartilage inside the joint between the predentary and dentary that strongly suggests some movement between these elements.

The team noticed that the predentary is only found in ornithuromorphs that have teeth. However, the tip of the premaxilla - the bone of the upper bill that would have occluded with the predentary - is without teeth. This suggests that the tip of the upper jaw, like the predentary, was also covered with a keratinous beak.

The tiny beak at the tip of the skull, combined with the sensitive and mobile predentary bone and teeth that were most likely also proprioceptive, represents a unique feeding adaptation that allowed greater dexterity when manipulating food. Although bizarre and now extinct, this unique feeding apparatus persisted in the ornithuromorph clade for at least 58 million years, from the Early to the Late Cretaceous.

Using information from the fossilized tissues and preexisting data on the embryology of living birds, the team also formulated a hypothesis regarding the origin of this bone, suggesting it is a sesamoid, similar to the human knee cap. Identification as a sesamoid means this bone is a novel skeletal innovation unique to one lineage of ornithuromorphs, and that it did not arise from a preexisting skull bone.

Although additional research on fossil birds (and also extant birds) is required to confirm some of these hypotheses, the predentary is such a small bone that it is only rarely preserved, thus making it very difficult - if not impossible - to find specimens that can shed light on the remaining pieces of this mystery.

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Statins not associated with memory or cognition decline in elderly, may be protective in some patients

Study offers reassurance to consumers with concerns on statins' effects

Given consumer concern that statins may be associated with memory or cognitive decline, a new study published today in the Journal of the American College of Cardiology may offer reassurance, as no difference was found in the rate of memory or cognitive decline of elderly statin-users compared to never-users.

"Not only are statins one of the most prescribed medications in the world, there is strong evidence that they reduce mortality in our patients with heart disease, stroke, diabetes, renal disease and other lipid disorders. Most importantly, statins aren't associated with a risk for major adverse health advents," said Katherine Samaras, MBBS, PhD, an endocrinologist at St. Vincent's Hospital in Australia and the study's lead author. "These findings will hopefully go a long way toward reducing consumers' concerns about memory and cognition from statins, so they don't stop taking these lifesaving medications."

The researchers examined changes in the memory and global cognition regarding statin-use over a six-year observation period and two years of brain volume studies using the Sydney Memory and Ageing Study, a longitudinal observation study of cognition of community-dwelling, non-demented elderly participants conducted at the Centre for Healthy Brain Ageing (CHeBA), University of New South Wales, Sydney, Australia. Data were collected every two years on four occasions over the six-year period by psychologists and nurses. Clinicians diagnosed the presence of heart disease, cerebrovascular disease, hypertension and Type 2 diabetes.

Participants' medications and duration of use were categorized as statin ever-use versus never-use; continuous statin-use during observation versus never-use; specific statins (simvastatin, pravastatin and atorvastatin) versus never-use; and statin initiation during observation period versus never-use.

The 1,037 participants were aged 70 to 90 years and were 98% Caucasian and Australian- (67%) or European- (18%) born. There were 395 statin never-users and 642 statin ever-users, which included ever-users at baseline and those who commenced taking statins during the study period. On average, participants had been on statins for nine years.

To measure their primary endpoints--memory and global cognition--a comprehensive assessment of global cognition and memory was developed. Five memory tests were employed by the researchers to assess new learning and short and long-term recall using verbal and visual memory tasks. Global cognition evaluated memory plus processing speed, language, visuospatial ability and executive function.

All participants were offered brain magnetic resonance imaging (MRI) at baseline, with 529 patients accepting and 408 undergoing a repeat MRI two years later. Statin ever-users and never-users were found to have similar total brain volume, hippocampal and parahippocampal brain volumes at baseline with no significant differences two years later.

Statin ever-users and never-users were similar at baseline for both memory and global cognition, the researchers found no significant difference in rate of decline in either memory or global cognition. Participants who took statins continuously over the study period had significantly higher baseline performance in memory and global cognition compared to never-users; the rate of decline in memory and global cognition for this subgroup was similar over the six-year observation period. When researchers compared the 99 participants who started statins during the study period, they found statin initiation was associated with a lessening in the rate of decline of memory. Overall, no associations between statin use and cognition were found between baseline and the six years of observation.

The researchers did find a protective interaction between statin ever-use, heart disease and the six-year change in the total learning memory test score. Among patients with heart disease, statin ever-users displayed a slower rate of decline on this test compared to never-users. However, in patients without heart disease, there was a comparable rate of decline between statin ever-users and never-

users. The study also found a protective interaction between statin ever-use and the rate of decline in long-delayed recall performance for patients carrying the APOE-4 genotype. Carriers of this genotype are at high risk of Alzheimer's disease. In secondary analyses, male statin users did display a significantly faster logical memory decline compared to male never-users, but there was no significant difference between female statin users and never-users.

"We must acknowledge some limitations of the study, in particular the observational design and potential for selection and survivor bias," said Perminder Sachdev, MBBS, PhD, senior author who, along with Henry Brodaty, MBBS, MD, leads the Sydney Memory and Ageing Study. "Additionally, as participants with more advanced cognitive impairment were excluded from the study, no conclusions can be made for statin benefits in that group."

In an accompanying editorial, Costantino Iadecola, MD, and Neal S. Parikh, MD, MS, from Weill Cornell Medicine in New York City said, "These data support the view that worries about cognitive impairment should not limit statin use and raise the possibility that statins may favorably alter cognitive trajectories in a group of elders at high risk of Alzheimer's disease."

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Patients with advanced breast cancer are being denied access to life-prolonging drug

Experts also call for better access to opioid pain relief for patients

Lisbon, Portugal: Survival for patients with the most common forms of advanced breast cancer could be substantially improved if both younger and older patients had access to a group of anti-cancer drugs called CDK4/6 inhibitors, according to experts at the Advanced Breast Cancer Fifth International Consensus Conference (ABC5) in Lisbon today (Saturday). [1]

In a session agreeing new guidelines for treating advanced breast cancer, they said there was now enough evidence that this class of medicines helps patients live longer and with the same or better quality of life. However, they said the medicines were not being offered to the majority of patients who could benefit.

The experts also highlighted that difficulties with access to opioid pain relief around the world, including a lack of supply in poorer countries and a backlash against opioid addiction in the USA, are leading to breast cancer patients suffering unnecessarily and dying in pain.

A key aim of the Advanced Breast Cancer Conferences and the ABC Global Alliance [2] is to double survival among patients with the disease by 2025. Chair of the ABC5 Conference, Professor Fatima Cardoso, Director of the Breast Unit of the Champalimaud Cancer Centre in Lisbon, Portugal, said: "We now have a family of drugs, CDK4/6 inhibitors, that can substantially prolong life in the most common subtype of breast cancer.

"These drugs bring us much closer to our aim of doubling the time patients with advanced breast cancer live without their disease progressing, but we can only achieve that if they are available to everyone who needs them."

Around 70% of advanced breast cancers are oestrogen receptor positive (ER+) and HER2 negative - also called hormone dependent cancers. ER+ cancers are driven by the hormone oestrogen.

"For these cancers, CDK4/6 inhibitors should be the standard of care, both for younger, pre-menopausal and older, menopausal women, as well as men with advanced breast cancer," said Prof Cardoso. "However, the major problem is the cost of these medicines and, at present, only a small proportion of patients around the world are being treated with them. The same occurs with anti-HER2 therapies, which can prolong survival substantially for another subtype of advanced breast cancer - HER2 positive breast cancer.

"There is unequal access to these medicines not only between countries, but within countries as well, and between pre- and post-menopausal women. Our panel of world experts on the treatment of breast cancer agrees that CDK4/6 inhibitors should be make available to every patient who could benefit from them, not just a small percentage."

The experts also called on policy-makers worldwide to ensure that fears about the abuse of opioids should not limit cancer patients' access to adequate pain control.

In the new guidelines, they state: "The advanced breast cancer (ABC) community is aware of limitations that are being imposed worldwide, as a consequence of the perceived abuse of opioids in certain areas of the world. The ABC community is united in insisting that cancer patients should not have restrictions placed that will limit their access to adequate pain control."

Professor Eric Winer, Director of the Breast Cancer Program at Dana-Farber and the Dana-Farber/Harvard Cancer Center, Boston, USA, and co-chair of the conference, said: "Patients with advanced breast cancer can suffer pain and other symptoms, particularly towards the end of their lives. We need to ensure that appropriate pain medications and other symptom interventions are available to them.

"We acknowledge that the misuse of opioids is a big problem, particularly in the United States, but we need to make sure that in trying to deal with this problem we do not interfere with pain management in cancer patients. In addition, in some low- and middle-income countries, such as some in Africa, there are problems with patients being able to access any form of pain relief, and this needs to be addressed urgently."

The panel of experts also called for further research into the use of cannabis for managing symptoms and pain in patients with advanced breast cancer. However, they stressed that it should never replace existing medicines that have been proven to work, such as morphine.

"The panel encourages research on the potential role of cannabis to assist in pain and symptom control but strongly stresses that it cannot replace proven medicines, such as morphine, for adequate pain control," say the experts in their new guidelines.

These issues were among several addressed by 1,500 experts and patients from approximately 90 countries around the world at the conference as they agreed new and modified guidelines for the treatment and management of all types of advanced breast cancer. The new guidelines will be published in *Breast* and *Annals of Oncology* in 2020.

There are no reliable figures for the numbers of women (and men) living with advanced breast cancer. However, there are over two million new cases of breast cancer a year in the world and 0.6 million deaths. About 5-10% of cases are either locally advanced or have spread to other parts of the body (metastasised) at diagnosis, and these figures reach almost 80% in developing countries. About a third of all early breast cancer cases will become metastatic even with the best care, and the average overall survival for these patients is around three years.

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Living Great Apes are Smarter than Australopithecines, New Research Suggests

New research challenges the long-held idea that, because the brain of human ancestors called australopithecines was larger than that of many modern great apes, they were smarter.

University of Adelaide's Professor Roger Seymour and colleagues measured the rate of blood flow to the cognitive part of the brain, based on the size of the holes in the skull that passed the supply arteries.

The research team calibrated this technique in humans and other mammals and then applied it to 96 great ape skulls and 11 *Australopithecus* fossil skulls.

***Forensic facial reconstruction of* Australopithecus afarensis. Image credit: Cicero Moraes / CC BY-SA 3.0.**

"Our study revealed a higher rate of blood flow to the cognitive part of the brain of living great apes compared to *Australopithecus*," Professor Seymour said.

"The results were unexpected by anthropologists because it has been generally assumed that intelligence is directly related to the size of the brain."

"At first, brain size seems reasonable because it is a measure of the number of neurons. On second thought, however, cognition relies not only on the number of neurons, but also on the number of connections between them, called synapses. These connections govern the flow of information within the brain and greater synaptic activity results in greater information processing."

The human brain uses 70% of its energy on synaptic activity, and that amount of energy relies on a proportionately high blood supply to deliver oxygen. Although our brain occupies only 2% of our body weight, it uses 15-20% of our energy and requires about 15% of the blood from the heart.

"The great apes were known to be very intelligent and included the gorilla Koko, who was taught to communicate with over 1,000 signs, a chimpanzee called Washoe who learned about 350 signs, and Kanzi, a bonobo, who not only developed good English comprehension and syntax but also made stone tools," Professor Seymour said.

"How does the intelligence of modern great apes stack up against that in our 3 million-year-old relatives, the australopithicines such as Lucy? Non-human great apes have smaller or equal sized brains compared to the size indicated by the fossil braincases of *Australopithecus* species, so Lucy is generally considered to have been smarter."

"It is known that the large human brain looks like a scaled-up primate brain in terms of size and neuron number. However, the study shows that cerebral blood flow rate of human ancestors falls well below the data derived from modern, non-human primates."

"Based on the results, it is estimated that blood flow to Koko's cerebral hemispheres was about twice that of Lucy," Professor Seymour said. "Because blood flow rate might be better measure of information processing capacity than brain size alone, Koko seems to have been smarter." The findings were published online in the *Proceedings of the Royal Society B*.

Roger S. Seymour *et al*. 2019. Cerebral blood flow rates in recent great apes are greater than in *Australopithecus* species that had equal or larger brains. *Proceedings of the Royal Society B* 286 (1915); doi: 10.1098/rspb.2019.2208

http://bit.ly/2KJarGp

A Rare Genetic Disorder Turned These Siblings' Blood 'Milky' White

Three siblings all carried two copies of a mutated gene, which caused their blood to run white with fat.

By Nicoletta Lanese - Staff Writer 3 days ago Health

A rare genetic disorder caused three siblings' blood to flood with fat and turn "milky" white, according to a new report of the unusual case.

The three siblings consisted of one set of fraternal twins (a daughter and son) and an older son, all born to a first-cousin couple in a Pennsylvania Dutch family. In their teens and early 20s, all three siblings experienced mysterious symptoms, including bouts of

abdominal pain. They had all been diagnosed with hypertriglyceridemia, a fairly common disorder that causes fatty molecules called triglycerides to build up in the blood.

Now in their 50s, the siblings recently underwent genetic testing and learned that they have a condition that's much more rare, affecting only 1 in every million people, according to the case report, published today (Nov. 18) in the journal Annals of Internal Medicine.

Those with the ultrarare disorder, known as familial chylomicronemia syndrome (FCS), may accumulate more than 1,000 milligrams of triglycerides per deciliter (mg/dL) of blood. For comparison, normal blood levels of the fat should fall below 150 mg/dL, and 500 mg/dL would be considered "very high" in a healthy person, according to the National Institutes of Health.

Indeed, in people with FCS, blood fat levels are so high that the normally crimson fluid turns the color of milk. (FCS is not the only condition that can cause milk-colored blood; the symptom may also appear in people with severe hypertriglyceridemia.)

The three siblings had long struggled to keep their triglyceride levels under control and suffered frequent inflammation of the pancreas, also known as pancreatitis — a serious condition that can cause abdominal pain, fever and vomiting. At the hospital, the male twin's triglyceride levels reached as high as 5,000 mg/dL, while the other brother's levels peaked at around 6,000 mg/dL. The female twin's triglyceride levels soared highest of all, reaching 7,200 mg/dL at maximum. The siblings hoped their doctors could help subdue those aggressive symptoms.

To confirm the sibling's rare diagnosis, the doctors looked to their patients' genes. Triglycerides typically build up in the blood due to multiple malfunctioning genes and other related health conditions, such as diabetes or high-blood pressure, according to the Journal of the American Board of Family Medicine. But when doctors probed the siblings' genetic code, the researchers spotted only one mutated gene that was key for breaking down triglycerides in the body.

In healthy people, the gene contains instructions to build a protein called lipoprotein lipase (LPL), which typically coats the blood vessels that run through muscles and fatty tissues in the body, according to the Genetics Home Reference. LPL breaks down fats carried in the blood; without an adequate supply, the siblings' blood plasma ran thick with excess triglycerides.

Each sibling carried two copies of the mutated LPL gene, meaning both their parents passed down the mutated genetic code to the children, the case report noted. What's more, the particular genetic mutation in the siblings had never been seen before, the authors said. The doctors placed the siblings on a fat-restricted diet, which successfully stabilized their triglyceride levels and quelled their bouts of pancreatitis. Sometimes, when triglyceride levels spike, doctors must manually replace the fat-filled blood of their patients with healthy blood from donors, Live Science previously reported. Thankfully, the siblings' condition could be curtained with diet alone.

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Brain scans reveal how the human brain compensates when one hemisphere is removed

Remaining half of the brain formed unusually strong connections between different functional brain networks

Researchers studying six adults who had one of their brain hemispheres removed during childhood to reduce epileptic seizures found that the remaining half of the brain formed unusually strong connections between different functional brain networks, which potentially help the body to function as if the brain were intact. The case study, which investigates brain function in these individuals with hemispherectomy, appears November 19 in the journal *Cell Reports*.

"The people with hemispherectomies that we studied were remarkably high functioning. They have intact language skills; when I put them in the scanner we made small talk, just like the hundreds of other individuals I have scanned," says first author Dorit Kliemann, a post-doc at the California Institute of Technology. "You can almost forget their condition when you meet them for the first time. When I sit in front of the computer and see these MRI images showing only half a brain, I still marvel that the images are coming from the same human being who I just saw talking and walking and who has chosen to devote his or her time to research."

Study participants, including six adults with childhood hemispherectomy and six controls, were instructed to lay down in an fMRI machine, relax, and try not to fall asleep while the researchers tracked spontaneous brain activity at rest. The researchers looked at networks of brain regions known to control things like vision, movement, emotion, and cognition. They also compared the data collected at the Caltech Brain Imaging Center against a database of about 1,500 typical brains from the Brain Genomics Superstruct Project.

They thought they might find weaker connections within particular networks in the people with only one hemisphere, since many of those networks usually involve both hemispheres of the brain in people with typical brains. Instead, they found surprisingly normal global connectivity--and stronger connections than controls between different networks.

All six of the participants were in their 20s and early 30s during the study, but they ranged from 3 months old to 11 years old at the time of their hemispherectomies. The wide range of ages at which they had the surgeries allowed the researchers to home in on how the brain reorganizes itself when injured. "It can help us examine how brain organization is possible in very different cases of hemispherectomy patients, which will allow us to better understand general brain mechanisms," says Kliemann.

Moving forward, the hemispherectomy research program at Caltech, led by Lynn Paul (senior research scientist and principal investigator) in the laboratory of Ralph Adolphs (Bren Professor of Psychology, Neuroscience, and Biology and the director of the Caltech Brain Imaging Center) hopes to replicate and expand this study in order to better understand how the brain develops, organizes itself, and functions in individuals with a broad range of brain atypicalities.

"As remarkable as it is that there are individuals who can live with half a brain, sometimes a very small brain lesion like a stroke or a traumatic brain injury like a bicycle accident or a tumor can have devastating effects," says Kliemann. "We're trying to understand the principles of brain reorganization that can lead to compensation. Maybe down the line, that work can inform targeted intervention strategies and different outcome scenarios to help more people with brain injuries."

This work was supported by the Brain Recovery Project: Childhood Epilepsy Surgery Foundation, the National Institutes of Health, and the National Science Foundation.

Cell Reports, Kliemann author et al.: "Intrinsic functional connectivity of the brain in adults with a single cerebral hemisphere"

http://bit.ly/2OfHmVe

Long spaceflights found to lead to blood flowing in the wrong direction in some cases

People in space for long durations can experience blood flowing in the wrong direction in the jugular vein

by Bob Yirka , Phys.org

An international team of researchers has found that people in space for long durations can experience blood flowing in the wrong direction in the jugular vein. In their paper published on *JAMA Network Open*, the group describes their study of blood flow in astronauts.

As astronauts have come to spend longer periods in space, scientists have been studying what the effects of freefall on the body. Prior studies have shown that it can lead to weakened muscles, which is why astronauts have to use exercise machines. Long space flights have also been found to cause bone loss, a loss of blood volume and a weakened immune system. Researchers also report that extended freefall deconditions cardiovascular health—the system weakens when it does not have to work as hard against gravity's influence on blood flow. More recently, astronauts have reported that after spending six months or more in space, they begin experiencing blurred vision. In this new effort, the researchers were looking into these new reports to find out what might be behind it.

Suspecting that changes to blood flow might be behind changes to vision, the researchers tested blood flow in the left jugular vein of 11 astronauts—its job is to move blood out of the head when lying down. When standing or sitting, blood moves out of the head through other veins—the jugulars mostly prevent too much blood loss. The researchers measured blood volume passing through the left jugular vein both before and after several astronauts carried out extended missions on the International Space Station—the astronauts also carried out tests of their own at 50 and 150 days into their missions.

Once the astronauts returned to Earth, the researchers analyzed all of the data from all of the tests. They found instances blood stagnation and reverse blood flow. They also found two instances of small blood clots. The researchers suggest the reversed blood flow was likely due to organs in the chest shifting positions, resulting in one or more of them pressing on the jugular vein. It is not deemed a serious problem at this time. They note also that testing of pressure suits aboard the space station has met with mixed results in improving blood flow.

More information: *Karina Marshall-Goebel et al. Assessment of Jugular Venous Blood Flow Stasis and Thrombosis During Spaceflight, JAMA Network Open (2019). DOI: 10.1001/jamanetworkopen.2019.15011*

http://bit.ly/35rzCoQ

Your RNA May Have Come from Space, Meteor Study Suggests

The discovery of ribose sugar in ancient meteorites just made space rocks a little sweeter.

By Brandon Specktor

A new study suggests that when some ancient meteorites crash-land on Earth, they bring a dash of extraterrestrial sugar with them.

To be clear, this is not table sugar (sadly, scientists still have no insight into whether aliens prefer their coffee black or sweetened). Rather, in the powdered samples of two ancient, carbon-filled meteorites, astronomers have found traces of several sugars that are key to life — including ribose, the sugary base of RNA (ribonucleic acid).

According to lead study author Yoshihiro Furukawa, this is the first time that these bioessential sugars have been detected in meteorites. The find gives fresh fuel to the idea that the essential building blocks of life on Earth were forged in space, before crash-landing on our young planet billions of years ago, Furukawa said.

"Other important building blocks of life have been found in meteorites previously, including amino acids (components of proteins) and nucleobases (components of DNA and RNA), but sugars have been a missing piece," Furukawa, an associate professor at Tohoku University in Japan, said in a statement.

In the new study, Furukawa and his colleagues analyzed powder collected from two ancient meteorites: the Murchison meteorite, which fell near Murchison, Australia, in 1969, and meteorite NWA 801, which was discovered in Morocco in 2001. Both space rocks are believed to be older than Earth itself (more than 4.5 billion

years old) and have been shown in previous studies to carry organic matter, including amino acids.

The researchers analyzed the meteorite samples using gas chromatography mass spectrometry, which allows scientists to categorize molecules by their mass and electric charge. The team found small amounts of ribose in both meteorites — up to 11 parts per billion in NWA 801 and up to 180 parts per billion in Murchison — plus trace amounts of other sugars, including xylose and arabinose.

Ribose is a crucial component of RNA, a versatile molecule carried by all known life-forms. RNA is perhaps best known as a master messenger, responsible for copying the genetic information stored in DNA and delivering that data to the cellular structures responsible for making the proteins that humans and other organisms need to survive. Other types of RNA actively aid in protein synthesis by moving amino acids around the cell, while still other types play a role in gene expression or in igniting or speeding up chemical reactions.

RNA is, in a word, essential — and some researchers suspect that it was the first molecule to carry genetic information in Earth's earliest lifeforms, well before DNA and proteins became commonplace. Now that ribose has been detected in two 4.5-billion-year-old meteorites (but 2-deoxyribose, the primary sugar in DNA, has not), scientists can make a stronger case that sugar from space bombarded early Earth and helped life take shape.

"This is important since there could have been a delivery bias of extraterrestrial ribose to the early Earth, which is consistent with the hypothesis that RNA evolved first," study co-author Danny Glavin, of NASA's Goddard Center for Astrobiology, said in the statement. In other words, meteorites may have delivered more ribose to early Earth than deoxyribose, which may explain why RNA appeared before other genetic molecules.

Scientists will soon have another chance to skim the sugar off of some ancient space rocks, when Japan's Hayabusa2 and NASA's OSIRIS-Rex spacecraft return samples of the asteroids Bennu and Ryugu to Earth. These asteroids, which have never come in contact with Earth and are between a few hundred million and a billion years old each, could help scientists prove which types of molecules truly originate off of our planet and which showed up only after the sugar was served.

The study was published Nov. 18 in the journal Proceedings of the National Academy of Sciences.

http://bit.ly/2sddd0f

Bram Stoker's Vampire Victim Shows 'Textbook' Leukemia Symptoms

One example in "Dracula" was "a textbook case."

By Mindy Weisberger - Senior Writer

***A real and deadly disease may have inspired the symptoms described in novels about vampires.* (Image: © Alamy)**

Victims of vampire attacks in 19th-century novels didn't just turn pale, swoon and waste away; they displayed a wide range of symptoms that hinted at deadly attacks by a fanged, bloodsucking predator.

However, the descriptions of those symptoms were likely grounded in observations of real medical conditions. In fact, the hallmarks of a so-called vampire attack strongly resemble physical symptoms caused by cases of acute leukemia, according to a new study.

At the time, leukemia had not yet been identified as a disease among the medical community. Perhaps this is why its particular array of symptoms, the cause of which was then unknown, inspired writers to assign a supernatural explanation, researchers recently reported.

Leukemia is a type of cancer that affects white blood cells. It originates in bone marrow; the cancer cells quickly multiply and overwhelm the production and activity of normal white blood cells, leading to anemia and vulnerability to infections. In acute leukemia, the disease progresses very quickly if untreated, according to the National Cancer Institute.

For their blood-chilling study, the researchers looked to three novels that formed the foundation of the popular vampire genre: "The Vampyre" by John William Polidori (1819), "Carmilla" by J. Sheridan Le Fanu (1879) and "Dracula" by Bram Stoker (1897). The scientists documented all characters that were identified as vampire victims, compiling a list of symptoms and the length of time those symptoms lasted. Then, the researchers compared the symptoms with those produced by a range of illnesses.

"The Vampyre" portrayed just two victims, describing no symptoms leading up to their deaths. "Carmilla" had three victims, all female; they displayed "persistent exhaustion, fever, pallor, dyspnoea [difficulty breathing] and chest pain," as well as red marks on the skin of their chests, the scientists reported.

Published more than a decade after "Carmilla," "Dracula" was brimming with even more details of the ailments plaguing the novel's three vampire victims, one of whom — Lucy Westenra — eventually died (and then revived as a vampire). Each of the victims suffered from "malaise, paleness, fatigue, anorexia, dyspnoea and weight loss," accompanied by a trance-like, delirious state, according to the study.

'Bloodless, but not anemic'

Some of those symptoms could be explained by other diseases, such as tuberculosis (TB), a bacterial lung infection. However, TB was a well-known disease by the 19th century, and none of the fictional doctors in the vampire novels diagnosed their patients with TB. This suggests that there were other symptoms that didn't match what doctors would expect to see in a TB patient, the researchers wrote.

Diphtheria, a bacterial infection that affects breathing and swallowing, also produces similar symptoms to acute leukemia. But it additionally causes coughing and discolored patches around the mouth and throat, which weren't described in any of the novels.

Another possible diagnosis for a vampire victim could be anemia, a deficiency in red blood cells that can lead to fatigue and unusual pallor. Again, this condition was known to 19th-century doctors, and yet none of the doctors in the three novels suggest it for the vampire victims. In fact, Westenra in "Dracula" is described as "bloodless, but not anemic," and her symptoms overall provided "a textbook example" of a patient suffering from acute leukemia, according to the study.

"None of the other diseases considered matched as well as acute leukemia," the study authors said.

"We therefore conclude that real-life acute leukemia patients very likely were the inspiration for the symptoms of victims in the Gothic vampire literature." The findings were published online Nov. 12 in the Irish Journal of Medical Science.

http://bit.ly/2QLQ27j

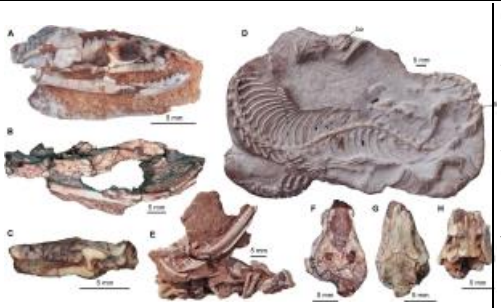
New fossils shed light on how snakes got their bite and lost their legs

New fossils of an ancient legged snake, called Najash, shed light on the origin of the slithering reptiles.

The fossil discoveries published in *Science Advances* have revealed they possessed hind legs during the first 70 million years of their evolution.

They also provide details about how the flexible skull of snakes evolved from their lizard ancestors.

The evolution of the snake body has captivated researchers for a long time—representing one of the most dramatic examples of the vertebrate body's ability to adapt—but a limited fossil record has obscured our understanding of their early evolution until now.



Najash specimens from LBPA as published in Science Advances. **Credit: Science Advances**

Dr. Alessandro Palci, from Flinders University, was part of the international research team that performed high-resolution (CT) scanning and light microscopy of the preserved skulls of Najash to reveal substantial new anatomical data on the early evolution of snakes.

"Snakes are famously legless, but then so are many lizards. What truly sets snakes apart is their highly mobile skull, which allows them to swallow large prey items. For a long time we have been lacking detailed information about the transition from the relatively rigid skull of a lizard to the super flexible skull of snakes".

"Najash has the most complete, three-dimensionally preserved skull of any ancient snake, and this is providing an amazing amount of new information on how the head of snakes evolved. It has some, but not all of the flexible joints found in the skull of modern snakes. Its middle ear is intermediate between that of lizards and living snakes, and unlike all living snakes it retains a well-developed cheekbone, which again is reminiscent of that of lizards."

Flinders University and South Australian Museum researcher Professor Mike Lee, was also part of the study, and adds "Najash shows how snakes evolved from lizards in incremental evolutionary steps, just like Darwin predicted."

The new snake family tree also reveals that snakes possessed small but perfectly formed hind legs for the first 70 million years of their evolution.

"These primitive snakes with little legs weren't just a transient evolutionary stage on the way to something better. Rather, they had a highly successful body plan that persisted across many millions of years, and diversified into a range of terrestrial, burowing and aquatic niches," says Professor Lee.

A render of Najash by Raúl O. Gómez, Universidad de Buenos Aires, Buenos Aires, Argentina. **Credit: Render of Najash by Raúl O. Gómez, Universidad de Buenos Aires, Buenos Aires, Argentina**

More information: *F.F. Garberoglio el al., "New skulls and skeletons of the Cretaceous legged snake Najash, and the evolution of the modern snake body plan," Science Advances (2019). DOI: 10.1126/sciadv.aax5833 ,*
https://advances.sciencemag.org/content/5/11/eaax5833

http://bit.ly/2roLjOd

Only eat oysters in months with an 'r'? Rule of thumb is at least 4,000 years old

Foodie tradition dictates only eating wild oysters in months with the letter "r"—from September to April—to avoid watery shellfish, or worse, a nasty bout of food poisoning.

by Halle Marchese

Now, a new study suggests people have been following this practice for at least 4,000 years.

An analysis of a large shell ring off Georgia's coast revealed that the ancient inhabitants of St. Catherines Island limited their oyster harvest to the non-summer months.

How can scientists know when islanders were collecting oysters? By measuring parasitic snails.

Snails known as impressed odostomes, Boonea impressa, are common parasites of oysters, latching onto a shell and inserting a stylus to slurp the soft insides. Because the snail has a predictable 12-month life cycle, its length at death offers a reliable estimate of when the oyster host died, allowing Florida Museum of Natural History researchers Nicole Cannarozzi and Michal Kowalewski to use it as a tiny seasonal clock for when people collected and ate oysters in the past.

The impressed odostome, Boonea impressa, is a tiny marine snail that parasitizes oysters by perching atop and piercing their shells and sucking their insides. Because the snails have a predictable 12-month life cycle, their length can record the time of death of their oyster host, allowing researchers to date ancient oyster harvesting. **Credit: Kristen Grace/Florida Museum**

Stowaways on discarded oyster shells, the snails offer new insights into an old question about the shell rings that dot the coasts of Florida, Georgia, South Carolina and Mississippi.

"People have been debating the purpose of these shell rings for a very long time," said Cannarozzi, the study's lead author and Florida Museum environmental archaeology collection manager. "Were they everyday food waste heaps? Temporary communal feasting sites? Or perhaps a combination? Understanding the seasonality of the rings sheds new light on their function."

Cannarozzi and Kowalewski, Thompson Chair of Invertebrate Paleontology, analyzed oysters and snails from a 230-foot-wide, 4,300-year-old shell ring on St. Catherines Island and compared them with live oysters and snails. They found that island inhabitants were primarily harvesting oysters during late fall, winter and spring, which also suggested the presence of people on the island tapered off during the summer.

The seasonality of the shell ring may be one of the earliest records of sustainable harvesting, Cannarozzi said. Oysters in the Southeast spawn from May to October, and avoiding oyster collection in the summer may help replenish their numbers.

"It's important to look at how oysters have lived in their environment over time, especially because they are on the decline worldwide," she said. "This type of data can give us good information about their ecology, how other organisms interact with them, the health of oyster populations and, on a grander scale, the health of coastal ecosystems."

Cannarozzi said using impressed odostomes to gauge what time of year oysters were harvested offers an independent way to assess ancient patterns of oyster gathering. This approach can complement other archaeological methods, including stable isotope analysis and examining shell growth rings.

Kowalewski said the method could be applied to other marine invertebrate studies if the "timepiece" organism's life cycle meets several key requirements.

"If you have species with a lifespan of one year or less, consistent growth patterns and predictable spawning behavior, you could potentially use them as clocks as well," he said. "We might be able to use this type of strategy to reconstruct population dynamics or the natural history of various species, especially those that are extinct."

Cannarozzi and Kowalewski emphasized the importance of interdisciplinary collaboration in addressing longstanding research questions in new ways. Their project combined paleontology, the study of fossils and other biological remains, with archaeology, which emphasizes human history. Cannarozzi's specialization—environmental archaeology—also explores the close connections between humans and their natural resources.

"People have affected the distributions, life cycles and numbers of organisms over time," Cannarozzi said. "Understanding how people in the past interacted with and influenced their environment can inform our conservation efforts today."

The researchers published their findings in *PLOS ONE*.

More information: *Nicole R. Cannarozzi et al, Seasonal oyster harvesting recorded in a Late Archaic period shell ring, PLOS ONE (2019). DOI: 10.1371/journal.pone.0224666*

Journal information: PLoS ONE

http://bit.ly/34jYX3W

The other use for feathers

Research reveals they make pretty useful armour.

A bird's feathers play an important role in mating, flight and insulation, but new research suggests they also help protect its body. After analysing the elastic properties of the contour feathers of the Northern Gannet (*Morus bassanus*), researchers from Cornell University, US, say the feathers act much like armour, shielding the body from solid objects such as tree branches – or water, in the case of extreme plunge divers like *M. bassanus.*

"The presence of feathers on the gannet's skin, particularly around the chest, is likely to have a significant effect on spreading the impact force of water over a much larger area on the skin and in turn minimise the pressure on the chest area, thereby, protecting integument," they write in the *Journal of the Royal Society Interface.*

Their model suggests the feathers reduce the pressure on the skin by as much as three times.

The researchers acknowledge that as bird-diving is highly dynamic, the forces a bird experiences in the wild could be different to those created in the study. However, they believe their model would still hold.

https://bbc.in/37vsutq

Premature baby's cuddle 'saved twin brother's life'

A very premature baby who doctors thought was going to die made a dramatic improvement after his twin brother was put into his incubator.

Hannah Zimunya believes her son Dylan saved brother Deiniol's life simply by giving him a cuddle after the twins were reunited in hospital.

The boys, from Wrexham, had been born 15 weeks early and were rushed 60 miles (96km) to a neonatal unit in Bolton. Dylan improved and was transferred to Wrexham, but Deiniol deteriorated.

Deiniol and Dylan Zimunya were born 15 weeks early **Mercury Press**

Hannah, 28, had gone into premature labour in October 2018 when she was 25 weeks pregnant, and despite best efforts by doctors at Wrexham Maelor Hospital to delay birth, the twins were delivered two days later. Dylan weighed 2lbs (0.9kg) while Deiniol was even tinier at just 1lb 9oz (0.7kg).

They were transferred to the Royal Bolton Hospital, the nearest unit catering for extremely premature babies with two incubators available, and placed on ventilators to breathe for them.

Hannah, who has three other children with her husband Xavi, said: "We were expecting the boys to be born early with them being twins, but I don't think anyone expects or can prepare themselves to go through that. "The whole experience was terrifying."

Dylan's condition improved and he was moved back to Wrexham Maelor, but Deiniol remained in Bolton still needing 100% oxygen to survive, and showing no sign of improvement.

When the twins were 14 weeks old, medical staff were worried Deiniol's condition was fatally deteriorating and they brought Dylan back to the hospital to say goodbye. The twins spent just five minutes together in the incubator having a cuddle, but hours later Deiniol's condition had stabilised, and his oxygen support was reduced to 50%.

Hannah said: "It wasn't until I phoned later that night to ask how Deiniol was doing that they told me his oxygen support had been halved. "It was incredible. Somehow Dylan, by just being there, managed to help Deiniol - he made him better. "I wasn't expecting that at all and neither were the nurses and doctors.

'Saved his life with a cuddle'

"The next day his oxygen [support] levels had gone back up to 100% and he was showing signs of deterioration again, so the nurses suggested bringing Dylan back for another cuddle.

"Within two days Deiniol was taken off his ventilator completely. It really was a miracle. "He saved his life with a cuddle. It was brilliant to watch and it showed all of us that they should never have been separated."

Dylan remained in Bolton with Deiniol for a further two months before being discharged in January this year. Deiniol followed his brother home in April. He still needs smaller amounts of round-the-clock oxygen until his lungs become strong enough to breathe independently. The boys celebrated their first birthday with a big party with their brother TJ, eight, sisters Lily, six, and Thandi, three.

"I can't explain how happy I am both boys have celebrated their first birthdays, because there was a time where we didn't know if both of them would get the chance to," said Hannah. "It was the scariest time we have been through. "We couldn't be more thankful to all the staff at both The Wrexham Maelor and Royal Bolton hospitals."

The practice of placing twins in incubators together in an attempt to improve their condition is carried out at UK hospitals but evidence as to whether there are proven benefits is inconclusive.

http://bit.ly/2qInQYp

A new antibiotic has been hiding in the gut of a tiny worm. It may be our best weapon against drug-resistant bacteria.

New class of antibiotics could help fight drug-resistant gram-negative bacteria

by Roberto Molar Candanosa

Researchers at Northeastern have discovered a new antibiotic that could treat infections caused by some of the nastiest superbugs humanity is facing in the antibiotic resistance crisis.

After two years of work, a team of researchers led by Kim Lewis, University Distinguished Professor of biology, announced their discovery of darobactin, which can kill resistant microbes known as gram-negative bacteria.

The discovery, published today in *Nature*, promises to be a much-needed weapon in the war on drug-resistant bacteria, which are estimated to cause 700,000 deaths each year worldwide.

"We are running out of antibiotics," says Lewis, who directs the Antimicrobial Discovery Center, where the discovery of darobactin was made. "We need to be looking for novel compounds with no pre-existing resistance in the clinic or the population."

Yu Imai, a postdoctoral research associate in Lewis' lab, discovered the compound from Photorhabdus bacteria that live inside the gut of a nematode, a tiny parasitic worm found in soil.

It's the first time, Lewis says, that the animal microbiome was found to harbor an antibiotic that promises to be useful for humans.

In experiments using mice conducted by Kirsten Meyer, also a postdoctoral research associate in Lewis' lab, darobactin cured E. coli and Klebsiella pneumoniae infections, with no signs of toxicity.

The newly discovered compound breathes new life into the search for a solution to the antimicrobial resistance crisis. The molecule has a unique structure and an unusual mode of action that make it particularly effective against gram-negative bacteria.

"We have never seen anything remotely similar to that before among antibiotics," Lewis says.

Gram-negative bacteria, which include E. coli and Salmonella, have an additional, outer membrane that shields them from many types of antibiotics.

This extra protection is why gram-negative bacteria are at the top of a list of "priority" pathogens that need to be targeted with new antibiotics, compiled by the World Health Organization.

Bacteria can also acquire additional resistance mechanisms from other microorganisms, which can make them largely impervious to currently available antibiotics. In a process biologists call horizontal gene transmission, bacteria pick up DNA from the environment and incorporate it into their genomes. These new genes can then be passed down to future generations.

This ability to pick and choose DNA is also how Photorhabdus bacteria, which have been around for hundreds of millions of years, acquired the genes coding for darobactin, Lewis says.

"What were they doing for the last 370 million years?" Lewis says. "I think these bacteria screened the entire biosphere for antibiotics of use to us."

Nematodes and Photorhabdus bacteria have a symbiotic relationship that helps them prey on different kinds of insects, such as caterpillars. Inside a caterpillar, nematodes release Photorhabdus bacteria, which in turn release toxins that kill the caterpillar and turn it into dinner.

But as the symbionts dine, the Photorhabdus also have to fend off freeloaders from the environment, which might also want to feast on the dead caterpillar. These opportunistic microbes can come from the nematode's own gut, which happens to be full of the same gram-negative bacteria that attack humans.

"Since Photorhabdus bacteria live in the nematode, and the nematode is an animal just like we are, whatever they make has to be non-toxic [for us]," Lewis says. "These compounds also have to move through and survive in the tissues of the caterpillar, which is also an animal and is actually very similar to us."

More than 50 years have passed since the introduction of the last class of antibiotics that target gram-negative bacteria.

The restrictive outer membrane of gram-negative bacteria is built with the help of an essential protein that sits on the surface of the cell.

This protein, called BamA, works like a gumball machine that opens and closes a gate to dispense chewing gum. In these bacteria, BamA opens and closes a gate periodically, taking in freshly made proteins and inserting them into the protective membrane. That open-and-close mechanism is the vulnerability of these bacteria, Lewis says.

"Darobactin binds to that [BamA] protein and jams it, so it cannot open anymore," he says. "The bacteria cannot build a proper cell envelope, and that causes death."

When Lewis' team tested E. coli that had developed resistance to darobactin, the bacteria lost their ability to infect mice. That means gram-negative bacteria cannot change the BamA protein without losing their ability to infect.

Eric Brown, Distinguished University Professor of biochemistry and biomedical sciences at McMaster University in Hamilton, Ontario, says the discovery of darobactin is an example of research "from soup to nuts" in terms of finding a compound from natural sources, figuring out a target, doing animal studies, and sorting out the way the organism makes that compound.

"They didn't set out to find the BamA inhibitor, they just kind of stumbled on it," Brown says. "It's just kind of a master class on how to find a unique natural product antibiotic."

It's not the first time Lewis' lab has made a remarkable find by digging up soil bacteria. In 2015, Lewis and Slava Epstein, a professor of biology at Northeastern, working with NovoBiotic Pharmaceuticals, a biotech startup they founded together, announced the discovery of teixobactin, another promising class of antibiotics. Teixobactin targets gram-positive bacteria, another major class of microbes that includes MRSA, a deadly strain of staph.

Brown, who emphasized that darobactin shows promise as a potential new antibiotic, says it's difficult to predict whether the newly discovered compound will be safe and effective in people.

"It's pretty promising to see efficacy in infection models with more than one pathogen, and they report a lack of toxicity in those experiments, at least apparent, because it's not an extensive toxicity test by any stretch," Brown says.

"It certainly is a very long road to a new antibiotic [for humans], but I'm of the view that you really need shots on goal. [And this] is another shot on goal for a field that desperately needs options."

Lewis expects darobactin to follow in the steps of teixobactin, which is on track to enter clinical trials. And, he says, there might be more antibiotics waiting to be discovered, including additional ones that target BamA.

"There's a trillion species of bacteria on the planet," Lewis says. "It is hard for me to imagine that we found the only molecule that exists on the planet that targets this [BamA] protein."

More information: *Yu Imai et al. A new antibiotic selectively kills Gram-negative pathogens, Nature (2019).* *DOI: 10.1038/s41586-019-1791-1*

http://bit.ly/2XGoi5H

Dengue infections dive where Wolbachia established in mosquitoes in parts of Asia, Australia, and Brazil

First large-scale evidence that infecting mosquitoes with common bacteria could dramatically reduce dengue infections; near Rio, chikungunya cases fall as well

National Harbor, MD, USA - Amid a global surge of infections with dengue and fears climate change will make it worse, an international alliance of researchers presented new evidence today showing reports that the disease fell dramatically in communities in Indonesia, Vietnam, Brazil and Australia. The reduction in dengue cases occurred in communities where they had released lab-grown mosquitoes carrying *Wolbachia*, a naturally occurring bacteria that prevents mosquitoes from transmitting infections when they bite humans.

Presenting today at the Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH), researchers at the World Mosquito Program (WMP) reported a key finding: a 76% reduction in dengue transmission in a community in Indonesia that endures frequent dengue outbreaks and a similar reduction in cases of dengue and chikungunya in an urban area near Rio de Janeiro, Brazil.

"We are very encouraged by the public health impact we are seeing - it highlights the potential of this approach to fight dengue and related mosquito-borne diseases at a global scale," said Professor Cameron Simmons, Director of Impact Assessment and an expert in the epidemiology of dengue at WMP. "Evidence is rapidly accumulating that areas where *Wolbachia*-infected mosquitoes have been deployed have fewer reports of dengue than untreated areas."

Often called break-bone fever for the searing joint pain it produces, dengue also can lead to fatal complications. There are no drugs to treat the disease. The only licensed dengue vaccine has been

saddled with safety issues. The ASTMH Annual Meeting will feature a highly-anticipated update from a late-stage trial with a new dengue vaccine, but experts stress that many tools are needed to control the disease.

The WMP *Wolbachia* trials are ongoing and, given the promising results thus far, are being rapidly expanded to Colombia, Sri Lanka, India and Western Pacific island nations. These trials are driven by a large body of evidence indicating that establishing *Wolbachia* in local mosquito populations could offer a safe way to reduce dengue infections. *Wolbachia*-infected mosquitoes can be created in the laboratory by injecting it into their eggs. *Wolbachia* also has been shown to inhibit chikungunya and Zika.

While presenting at the ASTMH conference today, Katie Anders, PhD, an expert in the epidemiology of dengue at WMP, and her colleagues noted that the work in Indonesia involved an experimental release in 2016 of *Wolbachia*-infected mosquitoes in an area of about 65,000 people adjacent to Yogyakarta City, Indonesia. The city on the island of Java is home to about 400,000 people who routinely face risks of dengue infections. The 76% reduction represented notifications of dengue among the targeted population recorded by local health authorities, compared with an untreated control area nearby.

Anders reported results from a smaller field study near Nha Trang, Vietnam where very few cases of dengue were reported during the year following the 2018 release of *Wolbachia*-infected mosquitoes. This low case incidence in the intervention area was documented at a time in which Nha Trang itself was experiencing one of its largest dengue outbreaks ever.

Anders also presented results published earlier this year showing local dengue transmission ceased in Far North Queensland, Australia. Beginning eight years ago, releases of *Wolbachia*-infected mosquitoes in local communities in this region led to a 96% reduction in cases of dengue-transmission.

The researchers stressed that all of the mosquito releases have been preceded by intensive community outreach and education efforts to inform local communities about the safety of *Wolbachia* bacteria and the potential impact of the releases on the surrounding ecosystem. Advocates of this approach to fighting dengue noted that it has several advantages over other methods. *Wolbachia* has none of the toxicity of conventional insecticides and it does not require genetically modifying the mosquitoes. It is also self-sustaining, which should make it highly cost effective.

Wolbachia is naturally present in the majority of insects. But it's not found in the Aedes aegypti mosquitoes that are the main carriers, or vectors, of dengue, chikungunya and Zika--all of which belong to a class of viruses called arboviruses.

"This is exciting work, carried out in the midst of an explosion in dengue infections that health authorities are finding very difficult to control," said ASTMH President Chandy C. John, MD, MS, FASTMH. "The combination of advanced science and committed community engagement is impressive--and essential to its success."

Using *Wolbachia* to Target Both Chikungunya and Dengue in Brazil

Luciano Moreira, PhD, WMP's Program Lead in Brazil, reported preliminary results showing cases of dengue and chikungunya fell by more than 70% in 2018 - 2019 among 100,000 people in two different areas Niterói, a city near Rio, following the release of *Wolbachia*-infected mosquitoes in their neighborhoods.

Moreira and his team at Fundação Oswaldo Cruz (Oswaldo Cruz Foundation) also noted, however, that because dengue incidence was generally low throughout Rio and Niteroi during the field trials, it was more difficult to show a comparative reduction in

Wolbachia-treated areas. There was, though, a clear difference compared to untreated areas.

"There has been an epidemic of chikungunya in these areas," Moreira said. "And disease surveillance by the Ministry of Health is showing there was 75% less chikungunya in Niteró where we released the mosquitoes compared with areas where we are not working." Chikungunya is a disease that can lead to chronic, debilitating joint pain and, while native to sub-Saharan Africa, it is becoming a growing problem across Latin America and the Caribbean.

Meanwhile, dengue is once again surging in Brazil, with infections in 2019 up almost 600% and deaths rising by 220%. It's part of a trend in which, last year, dengue infections globally reached near record highs, with especially large outbreaks in Asia and Latin America. Dengue is common in Puerto Rico, the U.S. Virgin Islands and American Samoa, and local transmission has occurred in Florida, Texas and Hawaii.

Moreira said Brazil's Ministry of Health is keen to expand efforts to test the capacity of *Wolbachia*-infected mosquitoes as a tool for controlling outbreaks of dengue and chikungunya. There is also interest in using *Wolbachia* to help protect people from Zika as well. While the intense Zika outbreak of 2016 is over, there are concerns it could return in Brazil and elsewhere. Moreira said plans are now underway to target 1.5 million people with releases of *Wolbachia*-infected mosquitoes in Brazil. Meanwhile, Anders said work is also underway in Yogyakarta City to conduct a gold-standard trial that involves a population of about 350,000.

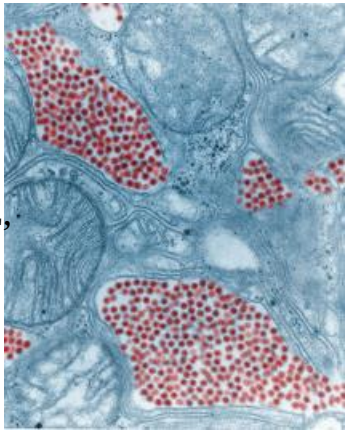
Existing evidence of reductions in dengue linked to the *Wolbachia* mosquitoes is entirely consistent with earlier modelling predictions of the likely impact. There have been no safety concerns in any of the communities where *Wolbachia* has been deployed. "We are very excited that this self-sustaining and cost-effective method has been embraced by communities and is delivering the public health benefits we expected it would," said the WMP's Simmons. "Our challenge now is to work with partners and governments to bring the method to 100 million people by 2023."

http://bit.ly/2KNeEsw

Eastern equine encephalitis virus poses emergent threat, say NIAID officials

As of November 12, 36 confirmed cases of EEE had been reported by eight states; 13 of these cases were fatal

WHAT: Although eastern equine encephalitis (EEE), a mosquito-borne illness, has existed for centuries, 2019 has been a particularly deadly year for the disease in the United States. As of November 12, 36 confirmed cases of EEE had been reported by eight states; 13 of these cases were fatal. In a new commentary in *The New England Journal of Medicine*, officials from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, describe the eastern equine encephalitis virus (EEEV) that causes EEE, current research efforts to address EEE, and the need for a national strategy to address the growing threat of EEEV and other emerging and re-emerging viruses spread by mosquitoes and ticks (known as arboviruses).



Colorized electron microscope image of mosquito salivary gland tissue infected by the eastern equine encephalitis virus. Viral particles are red.
CDC/Fred Murphy/Sylvia Whitfield

There were 12 documented U.S.-based EEE epidemics between 1831 and 1959. The virus is spread between *Culiseta melanura* mosquitoes and various tree-perching birds found in forested wetlands. Occasionally, other mosquito species transmit the virus to

people and other mammals. In people, EEEV takes roughly 3 to 10 days to cause symptoms. The virus initially causes fever, malaise, intense headache, muscle aches, nausea and vomiting; specific diagnostic testing may not reveal anything as EEEV is difficult to isolate from clinical samples, and testing for EEEV antibodies may be negative. Neurologic signs of EEE, which may appear within 5 days of infection, initially are nonspecific but rapidly progress. Most people (96%) infected with EEEV do not develop symptoms; however, of those who do, one-third or more die, and the others frequently suffer permanent and severe neurologic damage.

Although point-of-care diagnostics for EEE and many other mosquito-borne causes of encephalitis are not available, currently they would be of limited value in the absence of effective treatment, the authors write. So far, no antiviral drug has proven safe and effective against EEE, but many compounds are being assessed. Monoclonal antibodies have been found effective in an experimental animal model but only when given prior to infection. Patients with EEE are currently treated with supportive care, which often includes intensive care in a hospital and ventilator assistance. Patients with EEE are not infectious, and social support and counseling for both the patient and the family are vitally important given the seriousness of the disease, the authors write.

Several EEE vaccine candidates are in development but may have trouble reaching advanced development and licensure, according to the authors. EEE outbreaks are rare, brief and focal, and occur sporadically in unpredictable locations, making it difficult to identify an appropriate target population for vaccination. Efforts to develop mosquito-saliva vaccines that would be effective against multiple mosquito diseases, including EEE, are in early stages.

In the absence of effective EEE vaccines and treatments, state and local health departments can provide an early warning of imminent human infections by surveilling horses, birds and mosquitoes, but these efforts are threatened by insufficient funding, according to the authors. In recent years, the Americas have seen a growing number of emerging and re-emerging arboviruses, such as dengue, West Nile, chikungunya, Zika and Powassan. Although outbreaks of EEE disease thus far have been infrequent and focal, the spike in cases in 2019 and the looming presence of other, potentially deadly arboviruses in the United States and globally demand a national defense strategy for arboviruses and other vector-borne diseases, the authors write. Although the best way to address these viruses is not entirely clear, to "ignore them completely and do nothing would be irresponsible," say the authors.

ARTICLE: *DM Morens, GK Folkers, and AS Fauci. Eastern Equine Encephalitis Virus--Another Emergent Arbovirus in the United States. The New England Journal of Medicine. DOI: 10.10561/NEJMp1811661 (2019).*

https://wb.md/2DeqRt3

Age No Excuse Not to Treat Lung Cancer, Even in 'Oldest Old'

Even though treatment improves survival odds substantially, especially surgery for earlier-stage disease

Pam Harrison

Many patients aged 90 years or older who have non–small cell lung cancer (NSCLC) are not offered any treatment at all, even though treatment improves survival odds substantially, especially surgery for earlier-stage disease, say researchers reporting a nationwide retrospective analysis.

"It is unclear why patients are not receiving therapy, but we speculate that ageism may be a factor," lead author Chi-Fu Jeffrey Yang, MD, Stanford University Medical Center, California, said in a statement.

"But our study suggests that elderly patients with lung cancer who receive curative-intent, standard-of-care treatment in a multidisciplinary setting can have better outcomes than what you

might have initially expected," he added. "Surgery in carefully selected patients may not only be reasonable but also an optimal therapy," Yang emphasized. The study was published online November 19 in the *Annals of Thoracic Surgery*.

"Treatment should not be withheld from these 'oldest old' patients based on their age alone," the investigators conclude.

Reinforcing this sentiment, Brendon Stiles, MD, Weill Cornell Medicine, New York City, who was not directly involved with the study, said many patients who are 90 years or older can easily tolerate treatment for lung cancer without a significant decrease in their physical or mental quality of life.

"Obviously the authors aren't suggesting that we operate on every nonagenarian, but in that same light, we shouldn't refuse every nonagenarian a chance at curative therapy," Stiles said in a statement.

Analysis of More than 7000 Patients

The team analyzed data from the National Cancer Data Base from 2004 to 2014 to determine how treatment might benefit patients aged 90 years or older who have NSCLC.From the database, the investigators identified 7205 patients who were 90 years of age or older and who had been diagnosed with NSCLC.

Approximately 20% of the group had stage I NSCLC; 7.6% had stage II disease; about 21% had stage III disease; and 52% had stage IV disease. More than half (57.6%) of all these patients did not receive any therapy, Yang and colleagues report.

Approximately one quarter received radiotherapy alone; some 4% were treated with chemoradiotherapy; and about 5% received stereotactic body radiotherapy (SBRT). Only 3.7% were treated surgically; some 6% were treated with chemotherapy.

Five-Year Survival Rates

"The overall 5-year survival of the entire cohort was 4.9%," the investigators report.

However, 9.3% of patients who received some form of therapy were alive at 5 years, compared to 1.7% of those who received no treatment, they note.

For those with stage I disease, 15.7% were still alive at 5 years, as were 6.4% with stage II disease.

For those with stage III or IV disease, 5-year survival rates were 2.9% and 1.2%, respectively.

The most noticeable improvement in survival was seen for patients with stage I NSCLC.

In this group of patients, median survival was 63% better among those who received curative-intent treatment compared with patients who received no treatment, the investigators indicate.

Indeed, for patients who underwent curative-intent treatment — whether it was surgery or any type of radiotherapy — survival was about 17 months longer than it was for those who received no treatment at all.

No Treatment at All

A third of patients with stage I disease received no treatment at all, despite the fact that as a group, many patients with stage I disease were relatively healthy and had a low Charlson comorbidity index score, the authors point out.

For stage II patients, the survival benefit was associated with a 68% improvement in survival among those who received curative-intent therapy compared with those who received no treatment ($P < .001$).

For those with stage III disease, curative-intent treatment was associated with a 45% improvement in survival compared with no treatment ($P = .002$), as was palliative-intent treatment, which was associated with a 41% improvement in survival compared with no treatment ($P < .001$).

Even among patients with stage IV disease, treatment improved survival odds by 40% compared with no treatment ($P < .001$), the investigators note.

Table. Median Survival for the Oldest Old NSCLC Patients

	Stage I	Stage II	Stage III	Stage IV
No treatment	10 months	4.5 months	2.3 months	1.5 months
Palliative-intent Tx	16.6 months	9.5 months	7.7 months	NA
Curative-intent Tx	27.4 months	12.8 months	11.6 months	4.4 months

Best Outcomes

Perhaps not surprisingly, the best outcomes were for stage I patients whose lung cancer was amenable to surgery.

In this group of patients, 33.7% were alive at 5 years, compared to 17.1% of patients whose cancer was not amenable to surgery and 6.2% of stage I patients who were not treated.

Compared to SBRT, surgery was significantly associated with a 33% improvement in survival (P = .05), the study authors point out.

"More research needs to be done, but preliminarily, our study suggests that people in their 90s with early-stage lung cancer who undergo surgery live longer than patients who are healthy enough to undergo surgery but do not," Yang pointed out.

Should Be the Patient's Choice

Asked by *Medscape Medical News* for his thoughts on the study, Arthur Caplan, PhD, director, Division of Medical Ethics, New York University Langone Medical Center, New York City, noted that some of these patients may not want to be treated, but that should be their choice, not that of the healthcare provider.

"Treatment or surgery is not something that we should expect these patients to do, but we should be making an informed choice and not presume that patients don't want to be treated," Caplan observed. "There will be some healthy 90-year-olds with early-stage lung cancer who might say yes [to treatment]," he added.

He also suggested that with new approaches to treatment for lung cancer, such as immunotherapy, "it's important to keep in mind that therapies that are more drug based and not like radiation or chemotherapy are emerging and that we should not make any blind assumptions about treatment based solely on age," he said.

"Ninety may not be the new 60, but being 90 should not exclude you completely from consideration for treatment," Caplan emphasized.

Yang has disclosed no relevant financial relationships. A coauthor has a financial relationship with Scanlan International. Caplan has served as a director, officer, partner, employee, advisor, consultant, or trustee for Johnson & Johnson's panel for compassionate drug use and as a contributing author and advisor for Medscape.

https://bbc.in/2XGuoTD

Cancer: One in five cancer diagnoses 'in Emergency Departments'

One in five people in Northern Ireland receive their cancer diagnosis while attending an emergency department (ED), according to research by the NI Cancer Registry.

By Marie-Louise Connolly

The registry confirmed to BBC News NI that, at present, a quarter of bowel cancers are being diagnosed in EDs. It said mostly older patients are affected. Its research also found that a third of lung cancers in NI are diagnosed after a patient turns up at an ED.

According to senior health professionals and some cancer charities patients having to wait lengthy times to see a consultant is contributing to the problem. Earlier this week, BBC News NI revealed that a number of non-emergency operations across Northern Ireland have had to be suspended, as a result of staff shortages.

It has also emerged that the number of patients who waited more than 12 hours in Northern Ireland's emergency departments in September was double the same time last year.

Survival rate 'lowest'

The head of services at Macmillan Cancer Support, Heather Monteverde, said the statistics about diagnoses were "shocking and extremely worrying". She said emergency departments cannot provide the very specialist care needed by cancer patients.

Ms Monteverde added that only 55% of cancer patients in Northern Ireland are starting treatment within the 62-day target, a figure that was "deteriorating month-by-month". "Behind the statistics are individual people who are worried that they are very ill," she told the BBC's Good Morning Ulster programme.

"They have attended their GP and sometimes they are on very long waiting lists; their condition is deteriorating and they feel they have no other option but to pitch up in an emergency department.

"Or indeed, sometimes their GPs are so frustrated that they can't get them seen, their GPs are advising them to attend an emergency department."

The cancer survival rate is lowest for patients who present via emergency than any other route, although it is thought this is because those patients tend to have later-stage cancers than those who present via other medical routes.

Ms Monteverde said EDs are not the ideal environment to learn that you have the disease. "For most people, a cancer diagnosis is a fairly devastating event in their lives," she said.

"To be in a really busy A&E department which is quite often mayhem - it's noisy, it's crowded; there's no privacy."

Earlier this year, a report by the Northern Ireland Cancer Registry found that 74% of the 4,316 people who died from cancer in Northern Ireland in 2015 were admitted to Emergency Departments in the final years of their lives.

Also, one in six (17%) people died within seven days of their last emergency admission and almost all (95%) of these died in hospital.

Anna Gavin from the Northern Ireland Cancer Registry agreed with Ms Monteverde that longer waiting lists had added to the number of cancer patients being diagnosed in EDs.

"Unfortunately, the people who present through A&E present are at the later stage of disease and their survival [rate] is much lower than if they present through some of the other ways that you can come into the system."

Ms Gavin said when there are screening programmes in place, such as breast and bowel cancer screening, it led to a "wide variation" in the number of ED diagnoses, compared to conditions where no regular screening is carried out.

Breast assessment targets

However, the 14-day breast assessment target has not been met again in Northern Ireland. During March, 1,387 patients were seen by a breast cancer specialist for a first assessment following an urgent referral for suspected breast cancer. Of these, 85.6 % (1,187) were seen within 14 days compared with 100% in the previous year. Statistics published by the Department of Health show 69.4% of new referrals for suspected breast cancer were classified as urgent in March 2019. The department said the waiting times are "unacceptable". Previously the permanent health secretary said that it would take £1bn to tackle Northern Ireland's hospital waiting lists.

http://bit.ly/2KQk2LK

Weird Triassic 'Dragons' Had Massive Heads. Here's Why.

These reptiles had enormous heads in proportion to their bodies.

By Mindy Weisberger - Senior Writer

Millions of years before the dinosaurs, tank-like predators that looked like Komodo dragons with absurdly huge heads roamed the planet. And it turned out that these reptiles, known as erythrosuchids (eh-rith-roe-SUE-kids) may have evolved their

enormous noggins as they became "hypercarnivores," a new study suggests.

With their powerful jaws and "steak-knife like teeth," they were likely "at the top of the food chain" in their ecosystems, said lead study author Richard Butler, a professor of paleobiology with the School of Geography, Earth and Environmental Sciences at the University of Birmingham in the United Kingdom.

The erythrosuchid species Garjainia madiba, illustrated here, was native to South Africa. **(Image: © Copyright Mark Witton)**

In fact, erythrosuchids' heads were proportionally larger — relative to body size — than the head-to-body ratio of even the biggest carnivorous dinosaurs, according to the study.

Burly, big-headed erythrosuchids lived between 250 million and 238 million years ago, during the early part of the Triassic period (251 million to 199 million years ago).

"They are close to the ancestral lineage of archosaurs — the group including birds, dinosaurs, crocodilians and pterosaurs," Butler told Live Science in an email. Even to an untrained eye, these ancient beasts' heads look unusually huge, and researchers hoped that a more thorough investigation of erythrosuchids fossils could shed light on why they evolved such bizarrely huge heads.

The scientists compared data on head and femur length in erythrosuchids to those measurements from other four-limbed animals, living and extinct. Their findings confirmed that erythrosuchids' massive heads were, in fact, proportionally larger than any reptiles'. This feature likely evolved as the group adapted to fill ecological niches as hypercarnivores — animals that eat only meat.

With such huge skulls, erythrosuchids' jaws and teeth would have had a greater reach than their smaller-headed competitors, and larger muscles could have lent them a more powerful bite, said paleontologist and freelance paleoartist Mark Witton. Witton, who was not involved with the new study, reconstructed one of the species of erythrosuchid, *Garjainia madiba*, in an illustration for a prior study on the creature.

"It's not just their head size that is interesting: their jawlines and dental configuration are also quite sophisticated," Witton told Live Science in an email. And while questions remain about how these ancient "dragons" used their jaws, one thing is certain: Their heads weren't as heavy as they looked. Skulls in this reptile group were full of air pockets, which made them relatively light. And in any case, they would have been held up by robust neck muscles, Witton explained.

"They likely wielded their heads with precision and finesse, despite their size," he said. "The head might be huge, but we can see that it's well supported and mounted to a powerful, muscular body."

The findings were published online Nov. 20 in the journal Royal Society Open Science.

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

A near-hopeless childhood cancer succumbs to drug duo

Mass screening turns up a therapy that holds promise for treating a highly aggressive class of tumours.

A combination of drugs has shown promise in laboratory tests against an inevitably fatal nervous-system cancer that mostly strikes children.

Diffuse midline gliomas are tumours of the central brain and spinal cord. The only available treatment is radiation, and the median survival for one type of this cancer, diffuse intrinsic pontine glioma, is 9–11 months. Previous work has suggested that the drug

panobinostat kills these tumour cells, but they ultimately become resistant to the treatment.

Michelle Monje at Stanford University in California and her colleagues looked for drugs that could be used alone or in combination to kill diffuse midline glioma cells. The team tested 2,706 single compounds and 9,195 drug combinations in cell cultures grown from patients' tumours.

A combination of two drugs, panobinostat and marizomib, increased survival in mice bearing tumours grown from the samples. This drug combination altered when genes in the cancer cells turn on and off, and interfered with cellular metabolism.

Sci. Transl. Med. (2019)

https://wb.md/2XIfz2O

From Licorice to Slippery Elm: What Works for GI Symptoms?

Up to 85% of patients with gastrointestinal symptoms or diseases use complementary/alternative medical therapies

David A. Johnson, MD

This transcript has been edited for clarity.

Hello. I'm Dr David Johnson, professor of medicine and chief of gastroenterology at Eastern Virginia Medical School in Norfolk, Virginia. Welcome back to another GI Common Concerns.

Alternative or complementary medical therapies, particularly those available over the counter, are increasingly used in the United States. A recent survey suggested that up to 85% of patients with gastrointestinal (GI) symptoms or diseases were using these complementary/alternative medical therapies.

It is very important that we don't blow off patients when they bring up these therapies by saying that there is no evidence to support them or that we've never heard of them. Therefore, I wanted to bring some of these traditional therapies to your attention by discussing a recently published review of their use and, where available, the evidence surrounding it.

Apple Cider Vinegar

Many patients take and swear by apple cider vinegar for reflux disease. Intuitively, it makes little sense because it's an acetic acid, which can be toxic to the GI system in concentrations greater than 20%. When used for consumption, most vinegars, in particular apple cider vinegar, are diluted down to 5%. When taken as therapies, they are perhaps diluted even more with a little bit of water after a meal.

The evidence on this really is pretty slim. It has been suggested that this works therapeutically by balancing pH. Again, this makes no sense because reflux isn't related to a lack of acid but is due to an *excess* of acid, potentially in the wrong place.

Although this doesn't make much therapeutic sense, it is something that patients seek out. I always tell them that if they use it and find that it helps, the evidence doesn't really support this, although it hasn't been well studied in trials.

Melatonin

We may underestimate the power of melatonin.

As a supplement, melatonin is traditionally used as a sleep aid. But we also have to remember that the foregut produces melatonin, and the GI tract contains melatonin at levels at least 400 times greater than the pineal gland.

In upper GI disease, melatonin is used for its ability to potentially strengthen the esophageal barrier, although data are very limited on this topic. Some data on the use of melatonin (3 or 6 mg) have suggested that it may be better alone or in conjunction with a proton pump inhibitor (PPI).

Many of our patients with gastroesophageal reflux disease may have nocturnal symptoms, so don't dismiss the appropriate control of their reflux.

I find the argument for melatonin to be inordinately powerful in some of the other GI diseases, in particular inflammatory bowel disease, as it does change some reactivity for colonic mucosa in an animal study.

Although rare, melatonin can cause nightmares, so you should make sure your patients are aware. Also, most patients don't take melatonin correctly. I ask patients to take it 15-30 minutes before bedtime. I recommend melatonin quite regularly and see little downside to its use.

Rikkunshito

One traditional therapy that is more common outside the United States, in particular Japan, is rikkunshito, a product composed of eight different herbal medicines.

A couple of years ago, rikkunshito was the focus of a number of abstracts at Digestive Disease Week, which studied it as a potential remedy in a variety of GI diseases. It has been suggested to have value for non-ulcer dyspepsia and reflux disease in particular. Evidence that it does improve reflux symptoms comes from very limited studies to date conducted primarily in Japan. Your patients may not be able to get rikkunshito easily unless they order it from overseas, but it's nonetheless something to stay aware of.

Slippery Elm

This botanical product derived from the bark of the slippery elm tree can be formulated in capsules, lozenges, and liquid preparations, including teas. Its constituent carbohydrate becomes viscous in contact with water, and it might offer increased viscosity and potential mucosal protection similar to what we would see with something like sucralfate. However, this has not been well studied for slippery elm.

Slippery elm appears to have only limited data surrounding its therapeutic use. One study[1] assessed its use in a very small cohort of 24 healthy volunteers, who reported a relative perception of having better outcomes of throat soothing. However, this was not a placebo-controlled study.

There is a need to heighten our awareness of this product, as it does increase the rate of miscarriage. This necessitates that it be avoided among women who are or may become pregnant.

Licorice

Patients may also be trying licorice as an alternative therapy.

It has some potential value in patients with gastric ulcer. Glycyrrhizin is the active component and is something that's been studied, particularly in ulcer healing. However, the clinical utility is limited by the fact that it does have a mineralocorticoid-like activity and therefore may change blood pressure, electrolytes, and a variety of other things.

There has been some investigation into deglycyrrhizinated versions of this product. Deglycyrrhizinated licorice (DGL) has been studied in dyspepsia. The evidence surrounding DGL for reflux disease is very limited. We have to be aware that licorice is out there and potentially being used by our patients, even though it is not something that we recommend.

Peppermint Oil

One treatment that I think we need to pay special attention to is peppermint oil.

Peppermint oil is a popular treatment for a variety of GI illnesses and has been studied in irritable bowel syndrome. I think peppermint oil as a smooth muscle relaxant has some potential advantage in the upper GI tract, particularly as it relates to noncardiac chest pain and nonobstructive-type dysphagia.

A very recent study looked at using peppermint oil in 38 patients and suggested that it does have a benefit. In this study, 63% of patients with nonobstructive dysphagia with chest pain responded. They took two Altoid-type mints before a meal, whereas those with just chest pain used it on an as-needed basis.

I find that peppermint oil is pretty easy to add in, with very limited downside or risk associated with its use as an alternative therapy. I usually have my patients try some Altoids with a little warm water first so it dissolves easily in their mouth, if they're having noncardiac chest pain.

Acupuncture

Acupuncture is obviously well recognized as a traditional Chinese approach to a variety of different medical disorders. It is not something I dismiss. I find that it has some intriguing adjunctive benefits beyond just the acupuncture, via manipulating the needles by adding heat or vibration—almost a kind of TENS [transcutaneous electrical nerve stimulation] type of strategy.

Acupuncture has been studied in noncardiac chest pain and also in reflux disease. The results suggest that it may be an adjunct to decreasing the PPI dose and it may be potentially therapeutic.

We are not sure exactly how it works, though it has been proposed that it does so by promoting changes in visceral hypersensitivity. There has been some research done showing that acupuncture changes the balloon distension pressure in patients with noncardiac chest pain.

Limited Evidence on Use of These Remedies

There has been a lot in the recent literature questioning the established medical therapies we use for GI conditions. These include concerns over the carcinogen potential of the H2-receptor antagonist ranitidine. We've also seen a plague of so-called "fake news" relating to the PPIs and concerns for a variety of adjunctive risks that don't seem to hold up to the rule of evidence.

As a result, more patients may be coming to you to ask about these complementary/alternative therapies, which we need to be aware of. We also need to be frank with our patients about the limited evidence surrounding their use and point out those they may want to avoid entirely, given the potential risks I've outlined. However, we should not be dismissive of things that patients bring to us and instead ask them the right questions.

Hopefully you will find this overview helpful in your next conversations on alternative medical therapies for upper GI disease. I'm Dr David Johnson. Thanks again for listening, and see you next time.

David A. Johnson, MD, is professor of medicine and chief of gastroenterology at Eastern Virginia Medical School in Norfolk, Virginia, and a past president of the American College of Gastroenterology. His primary focus is the clinical practice of gastroenterology. He has published extensively in the internal medicine/gastroenterology literature, with principal research interests in esophageal and colon disease, and more recently in sleep and microbiome effects on gastrointestinal health and disease.

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http://bit.ly/34myym4

Rare Flesh-Eating Bacteria Invaded Woman's Eye Sockets

This is a highly unusual place for the life-threatening infection to take hold.

By Rachael Rettner - Senior Writer

A woman developed an infection with "flesh-eating" bacteria in her eye sockets — a highly unusual place for the life-threatening infection to take hold, according to a new case report.

The 58-year-old woman went to the emergency room after she developed eye pain and swelling that had become progressively worse over five days, according to the report, published Nov. 7 in The Journal of Emergency Medicine.

A woman developed severe swelling around both her eye sockets, as well as pus discharging from her eyes, as a result of an infection with "flesh-eating" bacteria. **(Image credit: Reprinted with permission of Elsevier (2019).)**

An eye exam showed she had severe swelling around both her eye sockets as well as pus discharging from her eyes.

At first, it appeared that she could have cellulitis, a bacterial infection of the skin and underlying tissues.

But when the patient's symptoms worsened even after she received antibiotics, doctors suspected she could have a more serious condition — necrotizing fasciitis, an infection that destroys skin and muscle tissue and spreads quickly in the body.

These "flesh-eating" infections are rare overall, and necrotizing fasciitis of the eye socket is rarer still, with only a handful of cases ever reported in the medical literature, the authors wrote.

A tissue sample taken from the women's eye socket — known medically as the orbit — confirmed that she had orbital necrotizing fasciitis.

Study co-author Dr. Ryan Walsh, an assistant professor in the Department of Emergency Medicine at Vanderbilt University Medical Center in Tennessee, said he had never seen a case like this before. It's "probably a once in a career case," Walsh told Live Science.

Although rare, people can get necrotizing fasciitis when bacteria enter the body through breaks in the skin, including cuts and scrapes, burns and surgical wounds, according to the Centers for Disease Control and Prevention (CDC).

Necrotizing fasciitis can occur anywhere in the body, but is most commonly seen in the limbs or the abdominal wall, according to the University of Iowa. The rich blood supply in the face and eyes generally helps reduce the risk of flesh-eating infections in these areas, Walsh said. (Flesh-eating infections tend to thrive in low-oxygen environments with reduced blood supply, Walsh added.)

When cases of orbital necrotizing fasciitis do occur, they are most often seen after surgery or trauma in people with conditions that make them more susceptible to infection, such as diabetes. In the current case, it's unclear how the woman acquired the infection, but she was taking a medication for rheumatoid arthritis that weakened her immune system, which increased her risk of severe infections, Walsh said.

Several types of bacteria can cause necrotizing fasciitis. In the woman's case, tests showed she was infected with methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus pyogenes*.

But regardless of the cause, the condition is usually very serious, even fatal. Up to one-third of patients with necrotizing fasciitis die from their infection, according to the CDC. The fatality rate from orbital necrotizing fasciitis is about 12%, the authors said.

The woman underwent repeated surgeries to remove damaged or dead tissue from the area, and received antibiotics to treat the specific strains of bacteria she was infected with.

After 13 days in the hospital, she was well enough to go home. She was released in stable condition, Walsh said, and to his knowledge she does not have vision loss.