

http://www.eurekalert.org/pub_releases/2014-01/uocm-don010714.php

Discovery of new Tiktaalik roseae fossils reveals key link in evolution of hind limbs

Hind legs actually began as enhanced hind fins

The discovery of well-preserved pelvis and a partial pelvic fin from Tiktaalik roseae, a 375 million-year-old transitional species between fish and the first legged animals, reveals that the evolution of hind legs actually began as enhanced hind fins. This challenges existing theory that large, mobile hind appendages were developed only after vertebrates transitioned to land. The fossils are described by scientists in the Proceedings of the National Academy of Sciences, online on Jan. 13.

"Previous theories, based on the best available data, propose that a shift occurred from 'front-wheel drive' locomotion in fish to more of a 'four-wheel drive' in tetrapods," said Neil Shubin, PhD, Robert R. Bensley Distinguished Service Professor of Anatomy at the University of Chicago and corresponding author of the study, which marks his inaugural article as a member of the National Academy of Sciences. "But it looks like this shift actually began to happen in fish, not in limbed animals."



This is an updated illustration of Tiktaalik roseae in its natural environment. University of Chicago, Neil Shubin
Discovered in 2004 by Shubin and co-authors Edward Daeschler, PhD, Associate Curator of Vertebrate Zoology at the Academy of Natural Sciences of Drexel University, and the late Farish A. Jenkins, Jr., PhD, of Harvard University, Tiktaalik roseae represents the best-known transitional species between fish and land-dwelling tetrapods.

A lobe-finned fish with a broad flat head and sharp teeth, Tiktaalik looked like a cross between a fish and a crocodile, growing up to a length of 9 feet as it hunted in shallow freshwater environments. It had gills, scales and fins, but also had tetrapod-like features such as a mobile neck, robust ribcage and primitive lungs. In particular, its large forefins had shoulders, elbows and partial wrists, which allowed it to support itself on ground.

However, only specimen blocks containing the front portion of Tiktaalik have been described thus far. As the researchers investigated additional blocks recovered from their original and subsequent expeditions to the dig site in northern Canada, they discovered the rear portion of Tiktaalik, which contained the pelvis as well as partial pelvic fin material.

The fossils included the complete pelvis of the original 'type' specimen, making a direct comparison of the front and rear appendages of a single animal possible.

The scientists were immediately struck by the pelvis, which was comparable to those of some early tetrapods. The Tiktaalik pelvic girdle was nearly identical in size to its shoulder girdle, a tetrapod-like characteristic. It possessed a prominent ball and socket hip joint, which connected to a highly mobile femur that could extend beneath the body.

Crests on the hip for muscle attachment indicated strength and advanced fin function. And although no femur bone was found, pelvic fin material, including long fin rays, indicated the hind fin was at least as long and as complex as its forefin.

"This is an amazing pelvis, particularly the hip socket, which is very different from anything that we knew of in the lineage leading up to limbed vertebrates," Daeschler said.

"Tiktaalik was a combination of primitive and advanced features. Here, not only were the features distinct, but they suggest an advanced function. They appear to have used the fin in a way that's more suggestive of the way a limb gets used."

Tiktaalik pelvis were still clearly fish-like, with primitive features such as an undivided skeletal configuration, as opposed to the three-part pelvic girdle of early tetrapods. However, the expanded size, mobility and robusticity of the pelvic girdle, hip joint and fin of Tiktaalik made a wide range of motor behaviors possible.

"It's reasonable to suppose with those big fin rays that Tiktaalik used its hind fins to swim like a paddle," Shubin said. "But it's possible it could walk with them as well. African lungfish living today have similarly large pelvis, and we showed in 2011 that they walk underwater on the bottom."

(For a video of a walking lungfish see: <http://www.uchospitals.edu/news/2011/20111212-lungfish.html>).

"Regardless of the gait Tiktaalik used, it's clear that the emphasis on hind appendages and pelvic-propelled locomotion is a trend that began in fish, and was later exaggerated during the origin of tetrapods," Shubin said.

<http://phys.org/news/2014-01-toxicologists-explanation-alexander-great-death.html>

Toxicologists offer possible explanation for cause of Alexander the Great's death

Alexander the Great possibly died as a result of ingesting white hellebore

Phys.org - Leo Schep and fellow toxicologist Pat Wheatley are suggesting in a paper they've had published in the journal *Clinical Toxicology*, that Alexander the Great possibly died as a result of ingesting *Veratrum album*, more commonly known as white hellebore—a common plant with white flowers on it. The two researchers, both from New Zealand, suggest that other common types of poisons would have killed the famous military leader very quickly—while white hellebore, on the other hand, would have killed the man very slowly.

Schep has been on the case for a decade, after being approached by a group working on a BBC documentary about the man that forged one of the largest empires in the ancient world—all before his 32th birthday. He and Wheatley note that there are differing and sometimes conflicting reports of what happened to Alexander the Great, aka Alexander III of Macedon, but most accounts agree that the man grew ill after drinking for several days, remained sick (with a lot of pain) for 12 days, and then died. Schep and Wheatley point out that common poisons of the time such as strychnine or arsenic would have killed Alexander almost right away.

White hellebore, the two researchers note, was very well known by people of Alexander's time—it was used to cause people to vomit after ingesting something that might cause harm. Given in a large enough dose, however, the plant could have proven deadly—but it would take time. Schep and Wheatley suggest it could have been caused to ferment into a type of very bitter wine, then mixed with regular wine and given to Alexander—as reports suggest he was quite drunk, he wouldn't have noticed. They note also that the symptoms of white hellebore poisoning match relatively closely with symptoms described by witnesses who wrote down what they saw—severe stomach pain, fever, nausea and vomiting.

Of course, too much time has passed, (over 2000 years) for historians or scientists such as toxicologists to prove that any one thing killed Alexander, thus, this new theory will have to remain just that, though it might be given more credence as it appears to have more evidence backing it up than many ideas put forth by others through the years.

More information: Was the death of Alexander the Great due to poisoning? Was it Veratrum album? January 2014, Vol. 52, No. 1, Pages 72-77. informahealthcare.com/doi/abs/10.3109/15563650.2013.870341

Abstract

*Objective. To investigate the death of Alexander the Great to determine if he died from natural causes or was poisoned and, if the latter, what was the most likely poison. Methods. OVID MEDLINE (January 1950–May 2013) and ISI Web of Science (1900–May 2013) databases were searched and bibliographies of identified articles were screened for additional relevant studies. These searches identified 53 relevant citations. Classical literature associated with Alexander's death. There are two divergent accounts of Alexander's death. The first has its origins in the Royal Diary, allegedly kept in Alexander's court. The second account survives in various versions of the Alexander Romance. Nature of the terminal illness. The Royal Diary describes a gradual onset of fever, with a progressive inability to walk, leading to Alexander's death, without offering a cause of his demise. In contrast, the Romance implies that members of Alexander's inner circle conspired to poison him. The various medical hypotheses include cumulative debilitation from his previous wounds, the complications of alcohol imbibing (resulting in alcohol hepatitis, acute pancreatitis, or perforated peptic ulcer), grief, a congenital abnormality, and an unhealthy environment in Babylon possibly exacerbated by malaria, typhoid fever, or some other parasitic or viral illness. Was it poisoning? Of all the chemical and botanical poisons reviewed, we believe the alkaloids present in the various *Veratrum* species, notably *Veratrum album*, were capable of killing Alexander with comparable symptoms to those Alexander reportedly experienced over the 12 days of his illness. *Veratrum* poisoning is heralded by the sudden onset of epigastric and substernal pain, which may also be accompanied by nausea and vomiting, followed by bradycardia and hypotension with severe muscular weakness. Alexander suffered similar features for the duration of his illness. Conclusion. If Alexander the Great was poisoned, *Veratrum album* offers a more plausible cause than arsenic, strychnine, and other botanical poisons.*

<http://www.sciencedaily.com/releases/2014/01/140113100449.htm>

Natural Substance Studied for Future Treatment of Possibly Incurable Childhood Cancer

In a recent doctoral thesis submitted at Karlstad University, Christina Fjæraa Alfredsson shows how the substance ellagic acid found in red berries and nuts, for instance, can stop cell division in cultivated cells from the childhood cancer neuroblastoma and induce cell death.

In their laboratory experiments Christina Fjæraa Alfredsson and her colleagues have studied how ellagic acid affects the growth and survival of cultivated neuroblastoma cells. An important discovery was that adding ellagic acid resulted in a so-called programmed cell death. "The number of tumour cells in our model system was drastically reduced after the addition of ellagic acid. The effect was dose dependent, so at the rate of reduced cell growth and cell adhesion, and thus less potential for growth, the number of cell deaths increased considerably," says Christina Fjæraa Alfredsson.

Research on cancer treatment

The results are expected to form the basis for further research on ellagic acid and the possibility to use the substance in the future as a complement to current treatments of neuroblastoma and other forms of cancer.

"Many years of research remain before we know if ellagic acid can be used clinically," says Christina Fjæraa Alfredsson.

Strong antioxidant for use in future medicinal products

Ellagic acid is a naturally occurring substance and belongs to the group of phytochemicals, which are substances that can be extracted from plants. Pomegranates, raspberries, strawberries, and walnuts are rich in ellagic acid. Ellagic acid and similar substances are mostly known as strong antioxidants and therefore potentially effective against various diseases, but today researchers are also interested in how ellagic acid can be used in future medicinal products for treating cancer, for example.

The third most common childhood cancer disease

Neuroblastoma is the third most common childhood cancer type in children under the age of one. Aggressive neuroblastoma is a difficult cancer type to treat, and in spite of intensive research, the death rate for this type of neuroblastoma is still very high compared with other cancer types. It is therefore crucial to develop complementary alternatives to the current methods of treatment.

<http://www.sciencedaily.com/releases/2014/01/140113100610.htm>

Study: At-Home Test Can Spot Early Alzheimer's

The first at-home test to spot early signs of conditions like Alzheimer's disease has been developed, shown to be effective in spotting the early signs of cognitive decline

The Self-Administered Gerocognitive Examination (SAGE test), which takes less than 15 minutes to complete, is a reliable tool for evaluating cognitive abilities. Findings by researchers at The Ohio State University Wexner Medical Center confirming the feasibility and efficiency of the tool for community screening large numbers of people are published in the January issue of The Journal of Neuropsychiatry and Clinical Neurosciences.

Memory disorders researchers visited 45 community events where they asked people to take a simple, self-administered test to screen for early cognitive loss or dementia. Of the 1047 people who took the simple pen-and-paper test, 28 percent were identified with cognitive impairment, said Dr. Douglas Scharre, who developed the test with his team at Ohio State.

The SAGE test can also be taken at home by patients, who can then share the results with their physicians to help spot early symptoms of cognitive issues such as early dementia or Alzheimer's disease, said Scharre, who is director of the Division of Cognitive Neurology and heads the Memory Disorders Research Center at Ohio State's Wexner Medical Center. Often physicians may not recognize subtle cognitive deficits during routine office visits, he said.

"What we found was that this SAGE self-administered test correlated very well with detailed cognitive testing," Scharre said. "If we catch this cognitive change really early, then we can start potential treatments much earlier than without having this test."

While the test does not diagnose problems like Alzheimer's, it does allow doctors to get a baseline of cognitive function in their patients, so they can follow them for these problems over time. "We can give them the test periodically and, the moment we notice any changes in their cognitive abilities, we can intervene much more rapidly," Scharre said.

The SAGE test could also provide health care providers and caregivers an earlier indication of life-changing events that could lie ahead. Earlier research by Scharre found that four out of five people (80 percent) with mild thinking and memory (cognitive) issues will be detected by this test, and 95 percent of people without issues will have normal SAGE scores.

In this study, researchers found that SAGE's self-administered feature, pen-and-paper format, and four equivalent interchangeable forms allows it to be given in almost any setting, doesn't require any staff time to administer or to set up a computer, and makes it practical to rapidly screen large numbers of individuals in the community at the same time.

Study participants were ages 50 or older who had been recruited from a wide variety of community locations and events, including senior centers, health fairs, educational talks to lay public, independent and assisted-living facilities, and free memory screens through newspaper advertisement. The study excluded individuals who indicated that they had taken SAGE previously.

Participants are tested on orientation (month + date + year); language (verbal fluency + picture naming); reasoning/computation (abstraction + calculation); visuospatial (three-dimensional construction + clock drawing); executive (problem solving) and memory abilities.

Participants were provided their score and written information about SAGE, and were advised to show it to their physician for interpretation and potential further screening or evaluation based on their health history. All were told that this test represented their baseline to be compared to future re-screening by their physician. Missing six or more points on the 22-point SAGE test usually warrants additional follow-up by the physician. Scharre, who specializes in treating Alzheimer's disease, said treatments for Alzheimer's and dementia are more effective when started in the earliest stage of the disease. Unfortunately, patients with Alzheimer's disease often wait three to four years after their symptoms first appear to seek treatment.

Some 5 million Americans have Alzheimer's disease, and those numbers are expected to almost triple by 2050. An additional 3 percent to 22 percent of those over 60 years of age are thought to currently meet criteria for Mild Cognitive Impairment as well, Scharre said.

"Hopefully, this test will help change those situations," Scharre said. "We are finding better treatments, and we know that patients do much better if they start the treatments sooner than later."

Douglas W. Scharre, Shu Ing Chang, Haikady N. Nagaraja, Jennifer Yager-Schweller, Robert A. Murden. Community Cognitive Screening Using the Self-Administered Gerocognitive Examination (SAGE). Journal of Neuropsychiatry, 2014; DOI: 10.1176/appi.neuropsych.13060145

<https://www.sciencenews.org/article/green-tea-may-sabotage-blood-pressure-medication>

Green tea may sabotage blood pressure medication

Drink may keep intestinal cells from taking up drug

by Beth Mole

Green tea chemicals linked to reducing the risk of cancer and cardiovascular disease may also thwart a blood pressure medication by preventing it from getting into the blood stream.

In a preliminary study, researchers gave 10 healthy adults the blood pressure medication nadolol after the volunteers drank about two glasses of green tea a day for two weeks and again after they stopped drinking tea for two weeks. Compared with taking the medication after they avoided drinking tea, the volunteers had just 24 percent as much nadolol in their blood after consuming tea, the researchers found. What's more, after drinking tea, the drug was less effective at lowering blood pressure.

In lab-dish studies, the team, led by Shingen Misaka of Fukushima Medical University in Japan, found that antioxidants in green tea called catechins shut down the cellular machinery that pumps nadolol into cells.

The findings, appearing January 13 in *Clinical Pharmacology & Therapeutics*, suggest that green tea catechins may block uptake of nadolol in the intestines, where the drug gains access to the blood stream.

S. Misaka. et al. Green tea ingestion greatly reduces plasma concentrations of nadolol in healthy subjects. Clinical Pharmacology & Therapeutics. Published online January 13, 2014. doi:10.1038/CLPT.2013.241.

Further Reading

J. Raloff. Cancer fighting green tea may have a dark side. Science News Online, February 5, 2009.

J. Raloff. Tea yields prostate benefits. Science News Online, April 28, 2004.

http://www.eurekalert.org/pub_releases/2014-01/sp-ebm011014.php

Educated black men remembered as 'whiter'

Intellectually successful Black individuals may be susceptible to being remembered as "Whiter" and therefore 'exceptions to their race

Los Angeles, CA - A new study out today in SAGE Open finds that instead of breaking stereotypes, intellectually successful Black individuals may be susceptible to being remembered as "Whiter" and therefore 'exceptions to their race,' perpetuating cultural beliefs about race and intelligence. This new study shows that a Black man who is associated with being educated is remembered as being lighter in skin tone than he actually is, a phenomenon the study authors refer to as "skin tone memory bias."



These are images of skin tone used in the study. Avi Ben-Zeev, Tara Dennehy, Robin Goodrich, Branden Kolarik, and Mark Geisler

"When a Black stereotypic expectancy is violated (herein, encountering an educated Black male), this culturally incompatible information is resolved by distorting this person's skin tone to be lighter in memory and therefore to be perceived as "Whiter," the main researcher, Avi Ben-Zeev, stated.

Researchers Avi Ben-Zeev, Tara Dennehy, Robin Goodrich, Branden Kolarik, and Mark Geisler conducted a two-part experiment with a total of 160 university students. In the first experiment, participants were briefly exposed to one of two words subliminally: "ignorant" or "educated," followed immediately by a photograph of a Black man's face. Later, participants were shown seven photos that depicted the same face – the original as

well as three with darker skin tones and three with lighter skin tones. They were asked to determine which of these seven photographs was identical to the one that they had originally seen.

The researchers found that participants who were primed subliminally with the word "educated" demonstrated significantly more memory errors attached to lighter skin tones (identifying even the lightest photo as being identical to the original) than those primed subliminally with the word "ignorant." This skin tone memory bias was replicated in experiment two.

"Uncovering a skin tone memory bias, such that an educated Black man becomes lighter in the mind's eye, has grave implications," Avi Ben-Zeev stated. "We already know from past researchers about the disconcerting tendency to harbor more negative attitudes about people with darker complexions (e.g., the darker a Black male is, the more aggressive he is perceived to be). A skin tone memory bias highlights how memory protects this 'darker is more negative' belief by distorting counter-stereotypic Black individuals' skin tone to appear lighter and perhaps to be perceived as less threatening."

http://www.eurekalert.org/pub_releases/2014-01/lseh-rse011414.php

Research shows early promise of new drug for cancers caused by viruses

Specialized fat molecules, called sphingolipids, play a key role in the survival of aggressive lymphomas caused by viruses

New Orleans, LA – Christopher Parsons, MD, Director of the HIV Malignancies Program at LSU Health Sciences Center New Orleans, is the senior author of a paper that is the first to report that specialized fat (lipid) molecules, called sphingolipids, play a key role in the survival of aggressive lymphomas caused by viruses. The paper also reveals a new therapy for preventing production of sphingolipids by lymphoma cells, thereby killing these cells, which are often resistant to standard therapies.

The study is published in the January 2014 issue of *Molecular Cancer Therapeutics*, a journal of the American Association for Cancer Research.

The research team focuses on primary effusion lymphoma (PEL), an aggressive and deadly variant of diffuse large B-cell lymphoma that frequently occurs in people infected with HIV.

Though scientists have known that the Kaposi's sarcoma-associated herpesvirus (KSHV) causes PEL, development of effective therapies has proven difficult. PEL tumors arise within body cavities and progress rapidly with an average survival of around 6 months.

Combination chemotherapy represents the current standard of care for PEL, but side effects (including bone marrow suppression) and drug resistance (generated through virus-associated mechanisms) continue to limit the effectiveness of standard therapy.

After documenting the role of an enzyme called sphingosine kinase (SK), in the generation of biologically active sphingolipids in PEL tumors that keep the tumor cells alive, the researchers tested a novel clinical-grade small molecule that selectively targets SK. The molecule, called ABC294640, was developed by Apogee Biotechnology Corporation.

Previous studies found antitumor effects for ABC294640 with kidney, prostate, and breast cancer cell lines. In the current study, ABC294640 not only inhibited SK function and induced PEL cell death, it worked selectively for virus-infected cells while sparing uninfected cells.

"It is still early in our understanding of how these special lipids contribute to viral cancers, but this is a major potential advance.

There are no therapies available to fight viral tumors by selectively blocking these pathways, all while not harming normal, uninfected cells," notes Dr. Parsons, who is also a member of the LSUHSC Stanley S. Scott Cancer Center.

Dr. Parsons' research group partnered with Apogee several years ago to develop and test new small molecules targeting lipid synthesis pathways, especially those in viral lymphomas, which have high rates of relapse or failure with standard therapies and higher mortality than non-viral lymphomas.

"Our research thus far indicates that this molecule is safe, with the potential to stand alone as a single, orally administered drug with no need to combine it with other toxic drugs now routinely used but which fail to work for many patients," concludes Dr. Parsons.

In addition to Dr. Parsons, the LSUHSC research team also included Drs. Zhiqiang Qin, Lu Dai, Thomas Reske, Karlie Bonstaff, Luis Del Valle, and Paulo Rodriguez, who are all members of the Copeland-LSUHSC Partnership in Viruses, Cancer, and Immunotherapy. Researchers from the Medical University of South Carolina and Tongji University School of Medicine also participated. Charles D. Smith, President and CEO of Apogee Biotechnology Corporation, is a co-author.

The research was supported by grants from the National Institutes of Health, the LSUHSC New Orleans School of Medicine, and China's National Natural Science Foundation.

<http://nyti.ms/19CIYA2>

Over the Side With Old Scientific Tenets

Here are some concepts you might consider tossing out with the Christmas wrappings as you get started on the new year: human nature, cause and effect, the theory of everything, free will and evidence-based medicine.

Dennis Overbye

Those are only a few of the shibboleths, pillars of modern thought or delusions — take your choice — that appear in a new compendium of essays by 166 (and counting) deep thinkers, scientists, writers, blowhards (again, take your choice) as answers to the question: What scientific idea is ready for retirement?

The discussion is posted at edge.org. Take a look. No matter who you are, you are bound to find something that will drive you crazy.

John Brockman, the literary agent and provocateur who presides over intellectual bar fights at Edge, his online salon, has been posing questions like this one since 1998. The questions have included what you believe but can't prove, how the Internet is changing everything, and what you've changed your mind about.

"It's really the same thing every time," Mr. Brockman said over the phone, explaining that this year's question had arisen at a conference on the social sciences last summer and immediately engendered a debate about whether it was suitable for the Edge forum.

Mr. Brockman's contributors, many of whom are his clients, are a rambunctious lot who are unified by little more than a passion for ideas and the love of a good fight. (He represents several New York Times writers, although not this one.)

Some are boldface names in the pop-science firmament, like Freeman Dyson, the mathematician and futurist at the Institute for Advanced Study; Steven Pinker, the best-selling linguist from Harvard; Richard Dawkins, the evolutionary biologist and best-selling atheist from Oxford University; and Mihaly Csikszentmihalyi, the psychologist who invented the notion of flow, or being completely lost in what you are doing, and who says scientists need to let go of the idea that the truths they find are good for all time and place.

"Some are indeed true," Dr. Csikszentmihalyi says, "but others depend on so many initial conditions that they straddle the boundary between reality and fiction."

That thought was echoed by Alan Alda, the actor and science popularizer who criticizes the idea that things are either true or false, a staple of logic and math. Sometimes context matters.

Take death, which seems a pretty definitive state. "The body is just a lump," Mr. Alda says. "Life is gone. But if you step back a bit, the body is actually in a transitional phase while it slowly turns into compost — capable of living in another way."

Frank Wilczek of M.I.T., a Nobel Prize winner in physics, would retire the distinction between mind and matter, a bedrock notion, at least in the West, since the time of Descartes. We know a lot more about matter and atoms now, Dr. Wilczek says, and about the brain. Matter, he says, "can dance in intricate, dynamic patterns; it can exploit environmental resources, to self-organize and export entropy."

We can teach it to play chess.

But don't get too excited. Roger Schank, a computer scientist and psychologist for the nonprofit group Engines for Education, says that a chess-playing computer won't tell us anything about how or why humans play chess nor will it get interested in a new game when it gets bored. We should abolish the term "artificial intelligence," he says, adding: "There really is no need to create artificial humans anyway. We have enough real ones already." Stewart Brand, founder of the "Whole Earth Catalog," among many things, wants to talk about nuclear power, which he argues has been hampered by the unprovable notion that no level of radiation, no matter how low, is safe. As a result, billions of extra dollars have been spent to provide "meaningless levels of safety" around nuclear power plants — meaningless because our cells contain mechanisms for repairing radiation damage to DNA and because, moreover, "we all die."

Professor Dawkins and Lisa Feldman Barrett, a psychologist from Northeastern University, both attack the concept of essentialism, which holds that things like dogs and cats, triangles and trees, space and time, emotions and thoughts — all have an underlying essence that makes them what they are. This works great in math, Professor Dawkins argues, but is a disaster when applied to species or politics, disallowing the possibility of change or gradation.

"Florida must go either wholly Republican or wholly Democrat — all 25 Electoral College votes — even though the popular vote is a dead heat," he complains. (The number is now 29.) "But states should not be seen as essentially red or blue: they are mixtures in various proportions."

Max Tegmark, a cosmologist at M.I.T., claims we could get along just fine without the notion of infinity. The computer scientist W. Daniel Hillis of the technology company Applied Minds claims we can get along without

the notion of cause and effect, which he says is just an artifact of our brains' penchant for storytelling. Seth Lloyd, a computer scientist at M.I.T., says it's time to lose the notion of a universe.

Yes, nothing is sacred. Take evidence-based medicine, all the rage in the new age of health care. Gary Klein, a psychologist for the company MacroCognition, says the idea can impede medical progress by discouraging doctors from trying alternative treatments that have not been blessed by randomized controlled trials. He points out, for example, that many patients suffer from more conditions than experiments can control for.

Ian McEwan, the novelist, attacks this year's question itself. Retire nothing, he says; science needs to hang onto its traditions and ideas. "Aristotle ranged over the whole of human knowledge and was wrong about much," he says. "But his invention of zoology alone was priceless. Would you cast him aside? You never know when you might need an old idea."

The whole thing runs more than 120,000 words. You can dip into it anywhere and be maddened, confused or stirred. If there is an overall point, it is that there is no such thing as a stupid question.

The true currency of science, after all, is not faith or even truth, but doubt. It's hard to imagine a similar effort coming out of the College of Cardinals or the Politburo of the Chinese Communist Party. In science, as in democracy, everything has to be up for grabs. When the scientists and other intellectuals stop squabbling, then we will know we are in trouble.

<http://www.sciencedaily.com/releases/2014/01/140114102739.htm>

Fish Derived Serum Omega-3 Fatty Acids Help Reduce Risk of Type 2 Diabetes

High concentrations of serum long-chain omega-3 fatty acids may help reduce the risk of type 2 diabetes, High concentrations of serum long-chain omega-3 fatty acids may help reduce the risk of type 2 diabetes, according to a University of Eastern Finland study published recently in *Diabetes Care*. The sources of these fatty acids are fish and fish oils.

Type 2 diabetes is becoming increasingly widespread throughout the world, including Finland. Overweight is the most significant risk factor, which means that diet and other lifestyle factors play important roles in the development of type 2 diabetes. Earlier research has established that weight management, exercise and high serum linoleic acid concentrations, among other things, are associated with reduced risk of diabetes. However, findings on how fish consumption or long-chain omega-3 fatty acids affect the risk of diabetes have been highly contradictory. A protective link has mainly been observed in Asian populations, whereas a similar link has not been observed in European or US studies -- and some studies have even linked a high consumption of fish to increased diabetes risk.

Ongoing at the University of Eastern Finland, the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD) determined the serum omega-3 fatty acid concentrations of 2,212 men between 42 and 60 years of age at the onset of the study, in 1984-1989.

During a follow-up of 19.3 years, 422 men were diagnosed with type 2 diabetes.

Serum long-chain omega-3 fatty acid concentrations were used to divide the subjects into four categories. The risk of men in the highest serum omega-3 fatty acid concentration quarter to develop type 2 diabetes was 33% lower than the risk of men in the lowest quarter.

The study sheds new light on the association between fish consumption and the risk of type 2 diabetes. A well-balanced diet should include at least two fish meals per week, preferably fatty fish. Fish rich in long-chain omega-3 fatty acids include salmon, rainbow trout, vendace, bream, herring, anchovy, sardine and mackerel, whereas for example saithe and Atlantic cod are not so good alternatives. Weight management, increased exercise and a well-rounded diet built around dietary recommendations constitute the cornerstones of diabetes prevention.

Jyrki K. Virtanen, Jaakko Mursu, Sari Voutilainen, Matti Uusitupa, Tomi-Pekka Tuomainen. Serum Omega-3 Polyunsaturated Fatty Acids and Risk of Incident Type 2 Diabetes in Men: The Kuopio Ischaemic Heart Disease Risk Factor Study. Diabetes Care, January 2014

<http://www.medscape.com/viewarticle/818872?src=rss>

Nausea and Vomiting: What CAM Options Are Viable?

What Would You Do?

Désirée A. Lie, MD, MSEd

Case 1: Morning Sickness

Vicky is a 25-year-old primiparous woman in her 11th week of a normal pregnancy. She is experiencing excessive nausea and vomiting that is unrelieved by taking small frequent meals and eating crackers upon waking. Ultrasonography confirms a singleton pregnancy, and her hemoglobin level, metabolic panel, and urine tests are normal. She would like to avoid medications and asks whether she should try acupuncture, acupressure, or ginger for her symptoms.

Case 2: Motion Sickness

Mike is a 40-year-old man with a history of severe motion sickness induced by long car rides and boat trips. He is preparing to take a 2-week cruise. He would like a nonsedating alternative to antihistamines and anticholinergics to control motion sickness during his vacation. What might you suggest?

Nausea and Vomiting of Pregnancy: Does Anything Help?

Nausea and vomiting are common symptoms during the first trimester of pregnancy, occurring in almost one half of all women, and often persist until the fourth or fifth month (weeks 10-16) of pregnancy. Although typically self-resolving, these symptoms can lead to dehydration requiring hospitalization in a small minority of women. [Hyperemesis gravidarum](#), a condition characterized by persistent vomiting, weight loss, ketonuria, electrolyte abnormalities, and dehydration, can affect as many as 2 in 100 pregnant women.

Acupuncture and acupressure. Several reviews have examined the use of acupuncture or acupressure for symptom control.^[1-3] Acupuncture uses acupoint 6 (P6) proximal to the distal wrist crease for control of nausea, whereas acupressure can be applied manually or with wrist bands. Although studies have found acupressure to be more effective than sham acupressure,^[2] larger studies have not demonstrated efficacy of either acupressure or acupuncture over sham acupuncture or no treatment.^[2,3]

Ginger. Ginger (the rhizome *Zingiber officinale*) is a food condiment widely used in Asian cooking and as a traditional remedy for many conditions, such as dyspepsia, nausea and vomiting, constipation, bloating, and gingivitis, and for nongastroenterologic conditions such as fever and hypertension.^[4-6]

Both animal and human studies have supported the antiemetic properties of ginger. Ginger extract,^[7] ginger syrup,^[8] and ginger capsules^[9,10] have been reported in clinical trials to be superior to placebo for control of nausea and vomiting in pregnancy. A comparison^[11] of ginger capsules (1 g daily in 4 divided doses) with vitamin B₆ (pyridoxine) in early pregnancy found ginger to be more effective in reducing the severity of nausea but not in reducing the number of episodes of vomiting for women in early pregnancy, confirming findings from an earlier, smaller study.^[12]

An evidence-based review in 2011^[13] summarized the available evidence on the use of ginger. It concluded, on the basis of small heterogeneous trials comparing ginger with placebo and other comparators, that the effectiveness of ginger was similar to that of dimenhydrinate and pyridoxine, and ginger was probably as safe as placebo. Its safety has been shown in some trials,^[8] but other researchers have expressed concern about the potential risk for anticoagulant effects^[14,15] and advise caution in terms of the dosage used during pregnancy, suggesting that further studies are needed. Ginger should certainly be avoided by persons on anticoagulation therapy, those with duodenal ulcers, or those at risk for intestinal obstruction.^[11]

The American College of Obstetricians and Gynecologists (ACOG)^[16] and the National Institute for Health and Clinical Excellence^[17] both include ginger on their lists of acceptable therapies for the treatment of nausea and vomiting during pregnancy.

Hypnosis. Hypnosis has been recommended for nausea and vomiting during pregnancy as well as for symptoms associated with chemotherapy. However, a systematic review^[18] identified only 6 clinical studies on hypnosis, with the evidence for efficacy being weak. Better-designed studies should be conducted in the future to assess the efficacy of hypnosis for hyperemesis gravidarum.^[18]

A case report^[19] from 2011 provides some insight into the use of brief hypnosis for persistent nausea and vomiting throughout pregnancy. More data are needed before hypnosis can be recommended to patients.

Motion Sickness

Motion sickness is a normal response to real, perceived,^[20] or anticipated movement and can be triggered by the movement of a car, train, or airplane. It is experienced as seasickness by those on boats and is a concern of many persons who are contemplating a cruise.

The symptoms of motion sickness tend to be limited to the duration of the motion experienced. The symptoms, which include nausea and vomiting, dizziness, vertigo, cold sweat, disorientation, and fatigue, can be debilitating and particularly interfere with functioning at work for those whose jobs entail motion. Motion sickness can be visually induced (when there is no real motion) in virtual environments, such as simulators, cinemas, and video games. It is postulated that symptoms occur as a result of a mismatch among the visual, vestibular, and proprioceptive systems.

Pharmacologic approaches. Pharmacologic measures for vestibular or visually induced motion sickness include transdermal scopolamine, an anticholinergic agent worn as a patch behind the ear that is applied up to 8 hours before travel; its effects last up to 3 days. Oral promethazine can be taken 2 hours before travel, with effects lasting 6-8 hours. Over-the-counter treatments include antihistamines, such as dimenhydrinate, meclizine, and cyclizine, but these can be sedating, impair cognition, and interfere with daily function. The type of medication taken should be customized to the duration and purpose of travel.

Nonpharmacologic approaches. Nutritional tips to reduce motion sickness include avoiding fatty or spicy meals; staying well hydrated; drinking ginger ale; and eating small, frequent meals. Among alternative therapies, acupressure,^[21] wristbands,^[22] and ginger^[6,23,24] have been proposed as safe treatments. Other potential remedies include biofeedback training and relaxation,^[25] deep breathing techniques, and cognitive-behavioral therapy,^[26-29] modalities that have been tested on airplane pilots and were found to be helpful. More recently, the use of relaxing and pleasant music has been proposed as a noninvasive and inexpensive countermeasure to visually induced motion sickness.^[30,31] During a visually induced motion sickness experience, persons who listened to music that they self-reported as pleasant showed a significant reduction in motion sickness symptoms, with concomitant improved mood and emotion, compared with those who did not listen to pleasant music. The researchers postulated that the effect could be mediated by physiologic autonomic changes that promote relaxation and suggested more studies to examine the mechanism of this effect.

Case Resolution

After exclusion of more serious conditions, such as hyperemesis, multiple gestation, or diabetes, Vicky appears to have typical nausea and vomiting of early pregnancy. ACOG states that "treatment of nausea and vomiting of pregnancy with ginger has shown beneficial effects and can be considered as a nonpharmacologic option."^[16] Clinical trials have not confirmed the efficacy of acupuncture or acupressure for symptom control.

If Vicky does not have a bleeding diathesis and is not on anticoagulant medication, a trial of ginger capsules at 250 mg 4 times daily is warranted. She can also be reassured that these symptoms should subside as pregnancy progresses.

Mike has troublesome motion sickness that may prevent his enjoyment of his vacation, and he is eager to avoid anticholinergics and antihistamines. There are several nonsedating complementary and alternative medicine options with minimal side effects that he can try. The use of pleasant music, which he can enjoy on any digital device, could act as a countermeasure before and during travel. Wristbands that provide acupressure at the P6 point can be worn during the cruise. In addition, ginger capsules at a dose of 250 mg given 3 times daily may alleviate the symptoms of seasickness.

References

1. *Natural Standard*. www.naturalstandard.com Accessed January 2, 2014.
2. Anderson FW, Johnson CT. Complementary and alternative medicine in obstetrics. *Int J Gynaecol Obstet*. 2005;91:116-124. [Abstract](#)
3. Matthews A, Dowswell T, Haas DM, Doyle M, O'Mathúna DP. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev*. 2010;CD007575.
4. Haniadka R, Saldanha E, Sunita V, Palatty PL, Fayad R, Baliga MS. A review of the gastroprotective effects of ginger (*Zingiber officinale* Roscoe). *Food Funct*. 2013;4:845-855.
5. Palatty PL, Haniadka R, Valder B, Arora R, Baliga MS. Ginger in the prevention of nausea and vomiting: a review. *Crit Rev Food Sci Nutr*. 2013;53:659-669. [Abstract](#)
6. White B. Ginger: an overview. *Am Fam Physician*. 2007;75:1689-1691. [Abstract](#)
7. Keating A, Chez RA. Ginger syrup as an antiemetic in early pregnancy. *Altern Ther Health Med*. 2002;8:89-91. [Abstract](#)
8. Willetts KE, Ekangaki A, Eden JA. Effect of a ginger extract on pregnancy-induced nausea: a randomised controlled trial. *Aust N Z J Obstet Gynaecol*. 2003;43:139-144. [Abstract](#)
9. Vutyavanich T, Kraissarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. *Obstet Gynecol*. 2001;97:577-582. [Abstract](#)
10. Ozgoli G, Goli M, Simbar M. Effects of ginger capsules on pregnancy, nausea, and vomiting. *J Altern Complement Med*. 2009;15:243-246. [Abstract](#)
11. Ensiyeh J, Sakineh MA. Comparing ginger and vitamin B6 for the treatment of nausea and in pregnancy: a randomised controlled trial. *Midwifery*. 2009;25:649-653. [Abstract](#)
12. Chittumma P, Kaewkiattikun K, Wiriyasiriwach B. Comparison of the effectiveness of ginger and vitamin B6 for treatment of nausea and vomiting in early pregnancy: a randomized double-blind controlled trial. *J Med Assoc Thai*. 2007;90:15-20. [Abstract](#)
13. Maitre S, Neher J, Safranek S. FPIN's clinical inquiries: ginger for the treatment of nausea and vomiting in pregnancy. *Am Fam Physician*. 2011;84:1-2.
14. Ding M, Leach M, Bradley H. The effectiveness and safety of ginger for pregnancy-induced nausea and vomiting: a systematic review. *Women Birth*. 2013;26:e26-e30. [Abstract](#)
15. Tiran D. Ginger to reduce nausea and vomiting during pregnancy: evidence of effectiveness is not the same as proof of safety. *Complement Ther Clin Pract*. 2012;18:22-25. [Abstract](#)
16. American College of Obstetricians and Gynecologists. ACOG (American College of Obstetrics and Gynecology) practice bulletin: nausea and vomiting of pregnancy. *Obstet Gynecol*. 2004;103:803-814. [Abstract](#)
17. National Institute for Health and Clinical Excellence. Antenatal Care: Routine Care for the Healthy Pregnant Woman. NICE Clinical Guideline No. 62. London: National Collaborating Centre for Women's and Children's Health; 2008.
18. McCormack D. Hypnosis for hyperemesis gravidarum. *J Obstet Gynaecol*. 2010;30:647-653. [Abstract](#)
19. Madrid A, Giovannoli R, Wolfe M. Treating persistent nausea of pregnancy with hypnosis: four cases. *Am J Clin Hypn*. 2011;54:107-115. [Abstract](#)
20. Villard SJ, Flanagan MB, Albanese GM, Stoffregen TA. Postural instability and motion sickness in a virtual moving room. *Hum Factors*. 2008;50:332-345. [Abstract](#)

21. Hu S, Stritzel R, Chandler A, Stern RM. P6 acupressure reduces symptoms ofvection-induced motion sickness. *Aviat Space Environ Med.* 1995;66:631-634. [Abstract](#)
22. Miller KE, Muth ER. Efficacy of acupressure and acustimulation bands for the prevention of motion sickness. *Aviat Space Environ Med.* 2004;75:227-234. [Abstract](#)
23. Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *Br J Anaesth.* 2000;84:367-371. [Abstract](#)
24. Grontved A, Brask T, Kambskard J, Hentzer E. Ginger root against seasickness. A controlled trial on the open sea. *Acta Otolaryngol.* 1988;105:45-49. [Abstract](#)
25. Jozsvai EE, Pigeau RA. The effect of autogenic training and biofeedback on motion sickness tolerance. *Aviat Space Environ Med.* 1996;67:963-968. [Abstract](#)
26. Dobie TG, May JG, Fisher WD, Bologna NB. An evaluation of cognitive-behavioral therapy for training resistance to visually-induced motion sickness. *Aviat Space Environ Med.* 1989;60:307-314. [Abstract](#)
27. Schmid R, Schick T, Steffen R, Tschopp A, Wilk T. Comparison of seven commonly used agents for prophylaxis of seasickness. *J Travel Med.* 1994;1:203-206.
28. Sherman CR. Motion sickness: review of causes and preventive strategies. *J Travel Med.* 2002;9:251-256.
29. Shupak A, Gordon CR. Motion sickness: advances in pathogenesis, prediction, prevention, and treatment. *Aviat Space Environ Med.* 2006;77:1213-1223. [Abstract](#)
30. Yen Pik Sang FD, Billar JP, Golding JF, Gresty MA. Behavioral methods of alleviating motion sickness: effectiveness of controlled breathing and a music audiotape. *J Travel Med.* 2003;10:108-111.
31. Keshavarz B, Hecht H. Pleasant music as a countermeasure against visually induced motion sickness. *Appl Ergon.* 2013 Aug 16. [Epub ahead of print].

<http://www.bbc.co.uk/news/health-25712005>

Alcohol therapy: medicinal drinking through the ages

For hundreds of years alcohol claimed a prize place among the pills, potions and healing herbs of British pharmaceutical history.

By Smitha Mundasad BBC News

A drop of gin was once advised to ward off the plague, a glug of wine to "defend the body from corruption" and a sip of absinthe to cure the body of roundworms. Of course all this has changed. As our understanding of the harms of alcohol on society and the individual has grown, it has given up its place on prescription pads - instead to be superseded by advice to refrain from all but cautious use. An exhibition at the Royal College of Physicians in London traces its use and sometimes fatal misuse by medical men and women of the past, up to the calls for greater regulation today.

'Over-much guzzles'

One of the earliest records in the many leather-bound books on display is a translation of the work of Roger Bacon, a 13th Century English philosopher and writer on alchemy and medicine. According to the translation (published in 1683) Bacon suggests wine could: "Preserve the stomach, strengthen the natural heat, help digestion, defend the body from corruption, concoct the food till it be turned into very blood." But he also recognises the dangers of consuming ethanol in excess: "If it be over-much guzzles, it will on the contrary do a great deal of harm: For it will darken the understanding, ill-affect the brain... beget shaking of the limbs and bleareyedness."

Wine-based concoctions also make frequent appearances in the handwritten domestic cookery books of the 16th to 18th Centuries, sitting alongside tips on general food preparation. One recipe for the discerning 17th Century householder recommends an "excellent drink against the plague". Its ingredients include rue, sage and two pints of wine - much more than the UK's daily recommended limits today.

'The last drop'

Caroline Fisher, curator of the exhibition says: "While wine has its place in history as more of a fortifying tonic, spirits were seen in a different light. "While considered as therapies in their own right, they also served as carriers and preservatives for substances that would be otherwise difficult to bottle and sell." Absinthe, for example, distilled from herbs such as wormwood, has been documented for use against roundworms and other intestinal parasites for many years.

But according to Dr James Nicholls, of Alcohol Research UK, by the 18th Century spirits such as gin were considered by a growing number of people to be a major cause of drunkenness, poverty and crime.

'Intemperate habits'

In 1725, the first documented petition by the Royal College of Physicians expresses fellows' concerns about "pernicious and growing use of spirituous liquors". A gin craze was sweeping across England, as improved distillation methods together with lax regulation in comparison with wine and beer, meant the spirit was

Drinking levels



Current advice:

Women: **3 units** a day Men: **4 units** a day

Recommended limit if over 65:

Women and men: **1.5 units** a day

Source: Royal College of Psychiatrists

affordable to much of the population. Yet it was not until the 19th Century that alcohol was regarded as a problem in a consistent way, says Dr Virginia Berridge of the London School of Hygiene and Tropical Medicine.

As Britain became increasingly industrialised and urbanised it needed efficient and time-aware workers, making sobriety a virtue. Temperance movements began to emerge - at first some advised restrictions on certain drinks only, but over time their stance shifted to call for total abstinence. And by the mid-19th Century, physicians were involved in temperance movements of their own.

An 1871 statement from the British Medical Temperance Society, printed in the British Medical Journal said: "As it is believed that the inconsiderate prescription of large quantities of alcoholic liquids... has given rise, in many instances, to the formation of intemperate habits the undersigned while unable to abandon the use of alcohol in the treatment of certain cases of disease, are yet of the opinion that no medical practitioner should prescribe it without a grave sense of responsibility."

Society's views of alcohol and that of the medical community gradually changed, heralded, in part, by an increasing focus on efficiency as World War One dawned, and as scientific advances provided compounds with much greater medicinal potential.

'Cause of death'

Yet one of the most modern pieces to feature in the exhibition is a bottle of Atkinson's Infants Preservative, a remedy for teething babies, dated between 1919-1941. The packaging reassures parents it can be given "with the utmost confidence" as it had no narcotic content. It does however contain 50% alcohol among its ingredients. John Betts, Keeper at the Royal Pharmaceutical Society Museum says: "This is perhaps surprising considering what was known about the effects of alcohol by this time. "But it wasn't until 1941 that legislation in Great Britain forced pharmaceutical manufacturers to list all the ingredients in their medicines."

Over the years the Royal College of Physicians has had a long history of raising awareness of the health damage caused by alcohol. The college is currently calling for a range of measures, including a fifty pence minimum price per unit of alcohol in the UK and tighter restrictions on marketing and advertising, particularly where children may be exposed to it. The college says: "Alcohol is a factor in more than forty serious medical conditions, including liver disease and cancer, and one of the major preventable causes of death in the UK."

http://www.eurekalert.org/pub_releases/2014-01/jhm-ndc011014.php

New drug combo cures toughest cases of hepatitis C, hints to future injection-free therapies

Study shows safe and simpler treatment for potentially deadly, liver-damaging disease

Efforts to cure hepatitis C, the liver-damaging infectious disease that has for years killed more Americans than HIV/AIDS, are about to get simpler and more effective, according to new research at Johns Hopkins and elsewhere.

In a study to be reported in the Jan. 16 issue of the New England Journal of Medicine, researchers say combination treatments involving a pair of experimental, oral antiviral drugs, daclatasvir and sofosbuvir, were safe and highly effective in the treatment of hepatitis C. The combination therapy worked well even in the patients who are hardest to treat, in whom the conventional "triple therapy" with hepatitis C protease inhibitors, telaprevir or boceprevir, plus peginterferon and ribavirin had failed to cure the infection.

"This research paves the way for safe, tolerable and effective treatment options for the vast majority of those infected with hepatitis C," says study leader Mark Sulkowski, M.D., medical director of the Johns Hopkins Center for Viral Hepatitis. "Standard treatments for the disease are going to improve dramatically within the next year, leading to unprecedented advances for the treatment of patients infected with the hepatitis C virus." The research was conducted on 211 men and women with any of the three major types of the disease who were treated at 18 medical centers across the United States and Puerto Rico. Among patients with genotype 1 — the most common strain of the infection in the United States — 98 percent of the 126 previously untreated patients and 98 percent of 41 patients whose infections remained even after the triple therapy were considered cured, with no detectable virus in their blood three months after the treatment had stopped. Results were similar in study participants infected with genotypes 2 or 3, strains which are less common in the United States.

The study participants took a daily combination of 60 milligrams of daclatasvir and 400 milligrams of sofosbuvir, with or without ribavirin.

On Dec. 6, the U.S. Food and Drug Administration (FDA) approved sofosbuvir in combination with peginterferon and ribavirin for the treatment of genotype 1 infection and in combination with only ribavirin for genotype 2 and 3 infection. Daclatasvir has not yet been approved by the FDA.

Sulkowski says that if daclatasvir and other new drugs for hepatitis C win approval from the FDA, the dreaded weekly injections of peginterferon will be a thing of the past.

Sulkowski, a professor at the Johns Hopkins University School of Medicine, also says that the so-called "pill burden" of what had been standard therapy for genotype 1 could go down from some 18 pills per day and one injection per week to as few as one or two pills per day and no injections. Side effects from the new pill combination were generally mild, but included fatigue, headache and nausea, a safety profile that Sulkowski says compares favorably with that of the peginterferon-based therapy, which is tied to severe side effects which may include fatigue and depression.

The new study is one of the first to show that hepatitis C can be cured without the use of ribavirin, which is known to cause anemia.

The advent of simpler pill-only regimens, Sulkowski adds, should make it easier for those infected with hepatitis C to be cured, preventing the development of liver cancer and liver failure and obviating the need for liver transplant. Currently, he says, fewer than 5 percent of the estimated 3.2 million Americans with hepatitis C have been cured, according to the U.S. Centers for Disease Control and Prevention (CDC). Further, the CDC estimates that between 50 and 75 percent of people who live with chronic hepatitis C are unaware that they are infected.

Sulkowski says the arrival of simpler treatment regimens could not come soon enough. Many of the people diagnosed with the infection, mainly those born between 1945 and 1965, were infected during the 1970s and 1980s through injection drug use and tainted blood transfusions and are now suffering from cirrhosis and liver cancer tied to chronic infection. This is why, he says, the CDC recommended hepatitis C screenings in 2012 for all baby boomers.

Sulkowski says that further research is being performed by Gilead Sciences of Foster City, Calif., on a regimen that combines sofosbuvir with another experimental drug it manufactures, called ledipasvir, into a single tablet which can be taken once a day. Ledipasvir is similar to daclatasvir, which is made by Bristol-Myers Squibb of Princeton, N.J., in that it inhibits replication of the hepatitis nonstructural protein NS5A. The combination of sofosbuvir and ledipasvir has not yet been approved by the FDA.

The newly published study, which took two years to complete, was funded by Gilead Sciences and Bristol-Myers Squibb.

Sulkowski is a paid consultant to both Gilead Sciences and Bristol-Myers Squibb. The terms of his arrangements are managed by The Johns Hopkins University in accordance with its conflict of interest policies.

Besides Sulkowski, other study investigators involved in this study were Maribel Rodriguez-Torres, M.D., at the Fundacion de Investigacion in San Juan, Puerto Rico; K. Rajender Reddy, M.D., at the University of Pennsylvania; Tarek Hassanein, M.D., at Southern California Liver Center in Coronado, Calif.; Ira Jacobson, M.D., at Weill Cornell Medical College in New York; Eric Lawitz, M.D., at the University of Texas Southwestern Medical Center in San Antonio; Anna Lok, M.D., at the University of Michigan, Ann Arbor; Federico Hineostroza, M.D., at Orlando Immunology Center in Florida; Paul Tuluvath, M.D., at Mercy Medical Center in Baltimore, Md.; Howard Schwartz, M.D., at Miami Research Associates in Florida; David Nelson, M.D., at the University of Florida; and Gregory Everson, M.D., at the University of Colorado Denver.

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Heavy drinking in middle age may speed memory loss by up to 6 years in men

Study finds moderate drinking may not harm memory and executive function

MINNEAPOLIS – Middle-aged men who drink more than 36 grams of alcohol, or two and a half US drinks per day, may speed their memory loss by up to six years later on, according to a study published in the January 15, 2014, online issue of *Neurology*[®], the medical journal of the American Academy of Neurology. On the other hand, the study found no differences in memory and executive function in men who do not drink, former drinkers and light or moderate drinkers. Executive function deals with attention and reasoning skills in achieving a goal.

"Much of the research evidence about drinking and a relationship to memory and executive function is based on older populations," said study author Séverine Sabia, PhD, of the University College London in the United Kingdom. "Our study focused on middle-aged participants and suggests that heavy drinking is associated with faster decline in all areas of cognitive function in men."

The study involved 5,054 men and 2,099 women whose drinking habits were assessed three times over 10 years. A drink was considered wine, beer or liquor. Then, when the participants were an average age of 56, they took their first memory and executive function test. The tests were repeated twice over the next 10 years.

The study found that there were no differences in memory and executive function decline between men who did not drink and those who were light or moderate drinkers—those who drank less than 20 grams, or less than two US drinks per day.

Heavy drinkers showed memory and executive function declines between one-and-a-half to six years faster than those who had fewer drinks per day.

The study was supported by the British Medical Research Council, British Heart Foundation, the U.S. National Heart, Lung, and Blood Institute and the U.S. National Institute on Aging.

<http://www.sciencedaily.com/releases/2014/01/140115075624.htm>

Treating Chronic Kidney Disease Using Clay Minerals

A new agent in the treatment of chronic kidney disease

Clay has healing powers. This natural product is destined to help treat chronic kidney disease: a well-tolerated agent based on clay minerals lowers patients' excessive phosphate levels.

Miss M. spends around 15 hours a week in hospital. Her renal functions are limited, and her kidneys are no longer able to filter toxins from her blood. She is a dialysis patient, forced to rely on this artificial blood purification treatment that, although essential, greatly impairs her quality of life. She has to make three trips a week to the dialysis clinic and going away for longer than a few days is almost out of the question. And Miss M. is no exception: In Germany alone, over six million people suffer from some form of chronic renal disease. Around 70,000 depend on dialysis and they are joined by some 15,000 new dialysis patients every year. Poor diet and an aging population are contributing to the dramatic rise in chronic renal disease worldwide, with high blood pressure and diabetes the most significant risk factors related to renal failure.

When suffering from renal failure, the body is unable to filter out phosphates in sufficient quantities, and the resulting excess is then absorbed into the blood. This causes a build-up of calcium-phosphate deposits in the blood vessels, which can over an extended period lead to arteriosclerotic heart disease and premature death. Compared to people with healthy kidneys, those with compromised renal function are at least ten times more likely to suffer a heart attack or stroke. To counteract this increased risk, people suffering from chronic renal insufficiency are required to take phosphate binders with meals. In the stomach and intestines, these medications bind to phosphates from food so that they can be excreted undigested instead of being absorbed into the blood. The problem is that existing medications, such as calcium and aluminum salts, cause serious side-effects including constipation, hypercalcemia (an elevated level of calcium in the blood), and neurologic disorders.

Gentle alternatives to pharmaceutical treatments

But hope is in sight for sufferers of chronic renal disease. Scientists from the Fraunhofer Institute for Cell Therapy and Immunology IZI in Rostock teamed up with FIM Biotech GmbH to develop an effective therapeutic agent that patients can tolerate well. Formed by marine deposits of volcanic ash 60 billion years ago, clay minerals found in the Friedland area of north-east Germany provide the basis for the new agent. The clay first has to be processed before being refined using a special technical process.

In a series of laboratory trials and cell culture experiments, the cooperation partners were able to prove the high phosphate-binding capacity and tolerance rate of the clay minerals. "The phosphate binder obtained from pure mineralogical raw materials is just as effective as traditional pharmaceutical binders. It can lower renal patients' elevated phosphate levels. Our tests using animal models show that, unlike standard medications, our binder causes only mild side-effects," says Prof. Dr. Steffen Mitzner, head of the Working Group on Extracorporeal Immunomodulation in Rostock and Professor of Nephrology at the city's university. The scientists believe that their refined natural raw material could also be used in the treatment of inflammatory bowel disease. Another animal model trial is currently underway to determine the scope of using clay minerals to help heal artificially induced bowel inflammation.

http://www.eurekalert.org/pub_releases/2014-01/bs-w011514.php

World's largest animal genome belongs to locust

Offering new insight into explaining their swarming and long-distance migratory behaviors

Shenzhen, China - Researchers from Institute of Zoology, Chinese Academy of Sciences, BGI and other institutes have successfully decoded the whole genome sequence of Locust (*Locusta migratoria*), the most widespread locust species. The yielded genome is remarkably big- at 6.5 gigabytes, which is the largest animal genome sequenced so far. The latest study has been published online in the journal Nature Communications.

It surprises us that a single locust can eat its own bodyweight in food in a single day; this is, proportionately, 60 times a human's daily consumption. They are capable of inflicting famine and wiping out livelihoods when they swarm, which can cost countries billions of dollars in lost harvests and eradication efforts.

In this study, researchers sequenced *Locusta migratoria* using next-gen sequencing technology, totally yielding 721Gb of data, which covered $114 \times$ of the 6.3Gb locust genome size. They annotated and predicted about 17,307 gene models, and identified over 2,639 repeat gene families. Moreover, they discovered that the top ten repeat families only represented 10% of the total genome sequences, suggesting that there were no dominant families in the *L. migratoria* genome.

Compared with other reference insect genomes, researchers found the reason why locust has such large genome is transposable element proliferation combined with slow rates of loss for these elements. According to statistics, repetitive elements constituted 60% of the assembled genome. The transposable element in the Locust genome was expanded when comparing with the other insects. Besides, they also found that the locust genome exhibited the lowest rate of DNA deletions relative to the other insects.

To investigate the potential involvement of epigenetic regulation in locust phase change, researchers performed comparative methylome and transcriptome analysis. One interesting finding was that repetitive elements were highly methylated and introns had higher methylation levels than exons in locust genome. It was also noteworthy that there had changes in genes involved in the regulation of the cytoskeletal microtubular system and in neuronal activity during the onset of phase change in locusts from solitary to swarm.

As we all know, locust has an most distinguishing feature- the long-distance flight- which enables them can fly at speed of hundreds of kilometers an hour, or even cross the ocean. In this study, researchers found that locust had developed a highly efficient energy supply system by expansion genes in lipid metabolism and detoxification to fulfill the intensive energy consumption during their long-distance flight. The expansion of its gustatory and olfactory receptor gene families is for its strong adaptation to host plant recognition.

To advance the development of new effective insecticides, researchers identified the gene targets for pest control and new insecticides, such as cys-loop ligand-gated ion channels and G-protein-coupled receptors, which are considered to be major traditional insecticide targets, and the repertoire of several biological processes that may serve as mechanistic targets and lead to the development of specific and sustainable pest control methods.

<http://www.sciencedaily.com/releases/2014/01/140115095949.htm>

Some Families Would Consider Terminal Sedation for Brain Injured Relatives in Permanent Vegetative State, Study Shows

Allowing relatives to die with the help of terminal sedation a compassionate option once all treatment options are exhausted

The families of some very severely brain injured patients believe that once all treatment options are exhausted, allowing their relatives to die with the help of terminal sedation would be a humane and compassionate option, research carried out by the University of York and Cardiff University has revealed.

The study, based on interviews with the families of patients in a vegetative or minimally conscious state, found some relatives believed euthanasia by sedation would be preferable to withholding or withdrawing treatment. Currently, the withdrawal of treatment such as artificial nutrition and hydration is the only legal method guaranteed to allow death in patients in a vegetative state.

The research paper "Withdrawing Artificial Nutrition and Hydration from Minimally Conscious and Vegetative Patients: Family Perspectives" is published today in the *Journal of Medical Ethics*.

The study was carried out by Professor Celia Kitinger from the Department of Sociology at York and Professor Jenny Kitinger, at the School of Journalism, Media and Cultural Studies at Cardiff University. Celia Kitinger and Jenny Kitinger, who are sisters, are co-directors of the York-Cardiff Chronic Disorders of Consciousness Research Centre (CDoC) which explores the social and ethical challenges of the vegetative and minimally conscious state.

The researchers' sister, Polly, was severely brain injured in a car accident in 2009.

Celia Kitinger said: "At the moment it is legal to allow people to die by withdrawing artificial nutrition and hydration, but that can mean watching a long, slow death which many relatives just cannot bear the thought of. "If a court is going to take a decision to allow someone to die, why not do it in a way that's less prolonged for the patient, or, if the patient is entirely unaware, then at least less distressing for their family? There must be a more merciful way of allowing people to die. It's a message about being merciful and reducing suffering.

"We suggest that the lived reality of the families facing these decisions should be taken into account and that other ways of bringing about the death of severely brain damaged patients should be given full ethical consideration."

The study found that, although two thirds of 51 individuals questioned believed their relative would rather be dead than stay alive in a long-term vegetative or minimally conscious state, far fewer were willing to consider an application for withdrawal of artificial nutrition and hydration to allow death.

Celia and Jenny Kitzinger say the views of relatives should be given ethical consideration in legal and medical debates on treatment options.

Jenny Kitzinger explained: "The withdrawal of artificial nutrition and hydration is currently the only legally available and certain exit route for such severely brain injured patients. But failing to provide food or water to a loved one, even because of the conviction that they would prefer to be allowed to die, is a highly emotive issue with deep cultural resonance. Many of the people we interviewed were concerned that, even with a confirmed vegetative state diagnosis, their relatives would experience pain and suffering if nutrition and hydration were withdrawn or that it would be distressing for other family members to watch.

"There was a widespread perception that lethal injections would be more humane, compassionate and dignified than what they worried was 'death from neglect' as a result of treatment withdrawal."

One interviewee told the researchers: "I would view a lethal injection as a kinder decision, because if you stop feeding them, they are going to die. If you've made that decision, you might as well do it as humanely as you possibly can. To starve somebody to death seems a particularly cruel thing to do."

Some interviewees told the researchers they fought for medical interventions in the early stages of the injury or trauma in the hope their relative might recover. Some now regretted this believing the patient had suffered a fate worse than death.

Many said that, rather than actively seek withdrawal of artificial nutrition and hydration, they were waiting for a natural death with some working with doctors on agreements not to resuscitate patients if they suffered a cardiac arrest or not to treat life-threatening infections with antibiotics.

One interviewee said: "I don't feel it's my place to go to a court and say 'I want his nutrition withdrawn'. I don't think I could do that. But I don't think it's right or fair to actively take steps to prolong this life. I suppose I'm waiting for [him] to die naturally'."

C. Kitzinger, J. Kitzinger. Withdrawing artificial nutrition and hydration from minimally conscious and vegetative patients: family perspectives. Journal of Medical Ethics, 2014; DOI: 10.1136/medethics-2013-101799

<http://www.sciencedaily.com/releases/2014/01/140115122215.htm>

Later School Start Times Improve Sleep and Daytime Functioning in Adolescents

A new study links later school start times to improved sleep and mood in teens.

Julie Boergers, Ph.D., a psychologist and sleep expert from the Bradley Hasbro Children's Research Center, recently led a study linking later school start times to improved sleep and mood in teens.

The article, titled "Later School Start Time is Associated with Improved Sleep and Daytime Functioning in Adolescents," appears in the current issue of the Journal of Developmental & Behavioral Pediatrics.

"Sleep deprivation is epidemic among adolescents, with potentially serious impacts on mental and physical health, safety and learning. Early high school start times contribute to this problem," said Boergers. "Most teenagers undergo a biological shift to a later sleep-wake cycle, which can make early school start times particularly challenging. In this study, we looked at whether a relatively modest, temporary delay in school start time would change students' sleep patterns, sleepiness, mood and caffeine use."

Boergers' team administered the School Sleep Habits Survey to boarding students attending an independent high school both before and after their school start time was experimentally delayed from 8 to 8:25 a.m. during the winter term.

The delay in school start time was associated with a significant (29 minute) increase in sleep duration on school nights, with the percentage of students receiving eight or more hours of sleep on a school night jumping from 18 to 44 percent. The research found that younger students and those sleeping less at the start of the study were most likely to benefit from the schedule change. And once the earlier start time was reinstated during the spring term, teens reverted back to their original sleep levels.

Daytime sleepiness, depressed mood and caffeine use were all significantly reduced after the delay in school start time. The later school start time had no effect on the number of hours students spent doing homework, playing sports or engaging in extracurricular activities.

Boergers, who is also co-director of the Pediatric Sleep Disorders Clinic at Hasbro Children's Hospital, said that these findings have important implications for public policy. "The results of this study add to a growing body of research demonstrating important health benefits of later school start times for adolescents," she said. "If we more closely align school schedules with adolescents' circadian rhythms and sleep needs, we will have students who are more alert, happier, better prepared to learn, and aren't dependent on caffeine and energy drinks just to stay awake in class."

Boergers, Christopher J. Gable, Judith A. Owens. Later School Start Time Is Associated with Improved Sleep and Daytime Functioning in Adolescents. Journal of Developmental & Behavioral Pediatrics, 2013; : 1 DOI: 10.1097/DBP.000000000000018

<http://www.medscape.com/viewarticle/819215?src=rss>

Some Medical Schools Shaving Off a Year of Training

For Travis Hill, it was an offer too good to refuse.

Sandra G. Boodman *This KHN story was produced in collaboration with The Washington Post.*

Last year when the 30-year-old neuroscientist was admitted to a new program at the NYU School of Medicine that would allow him to complete medical school in only three years and guarantee him a spot in its neurosurgery residency, he seized it. Not only would Hill save about \$70,000 -- the cost of tuition and living expenses for the fourth year of medical school -- he would also shave a year off the training that will consume the next decade of his life.

"I'm not interested in being in school forever," said Hill, who earned a PhD from the University of California at Davis last June and started med school in Manhattan a few weeks later. "Just knowing where you're going to be for residency is huge." So is Hill's student loan debt: about \$200,000, dating back to his undergraduate days at the University of Massachusetts. And he won't begin practicing until he is 40.

The chance to finish medical school early is attracting increased attention from students burdened with six-figure education loans: The median debt for medical school graduates in 2013 was \$175,000, according to the Association of American Medical Colleges. This year, the combined cost of tuition and fees for a first-year medical student ranges from just over \$12,000 to more than \$82,000.

Need For More Primary Care Doctors

Some medical school administrators and policymakers see three-year programs as a way to produce physicians, particularly primary-care doctors, faster as the new health-care law funnels millions of previously uninsured patients into the medical system. Enormous student loans are cited as one reason some newly minted doctors choose lucrative specialties such as radiology or dermatology, which pay twice as much as pediatrics or family medicine.

But debt and the shortage of primary-care doctors are not the only factors fueling interest in accelerated programs.

Some influential experts are raising questions about the length of medical school in part because much of the fourth year is devoted to electives and applying for a residency, a process that typically takes months. (Similar questions are being raised about the third year of law school.)

In a piece published in the Journal of the American Medical Association in 2012, University of Pennsylvania Vice Provost Ezekiel Emanuel and Stanford economist Victor Fuchs proposed that a year of medical school could be eliminated "without adversely affecting academic performance." The overall time it takes to train physicians, they wrote, is an example of waste in medical education and could be shortened without affecting patient care or eroding clinical skills; students could be assessed on "core competencies rather than on time served."

A 2010 report by the Carnegie Foundation recommended that fast-tracking be considered.

So far, fewer than a dozen of the nation's 124 medical schools are offering or actively considering three-year programs, which typically involve the elimination of electives, attendance at summer classes and the provisional guarantee of a residency -- offered because three-year graduates might be at a disadvantage compared with other applicants.

NYU launched its program in September with Hill and 15 other students chosen from a pool of 50 applicants -- nearly a third of the medical school's 160-member class.

Texas Tech University Health Sciences Center in Lubbock graduated its first three-year class in 2013; its nine students are training in family medicine. Fifteen more students started this fall.

In September, Columbia University's College of Physicians and Surgeons launched a "fast track MD" for candidates who already hold doctorates in biology; there were 40 applicants for four slots.

Despite the growing popularity of such programs, critics question the wisdom of jettisoning the fourth year of medical school, which they say plays a crucial role in preparing doctors for residency and subsequent practice. Some note that the three-year track was offered by a few dozen medical schools in the late 1970s but subsequently abandoned, largely because of student burnout from trying to cram too much into three years. Supporters of the three-year option say that contemporary medical school programs are different from 1970s curricula, which relied more heavily on rote memorization, and that the new programs have been designed to minimize burnout.

"This has been tried before, and it was a miserable failure," said Stanley Goldfarb, associate dean for curriculum at the University of Pennsylvania's Perelman School of Medicine, who co-authored an essay opposing three-year programs in a recent *New England Journal of Medicine*.

"Since the 1970s things have gotten so much more complex in medicine," he said. The more relaxed fourth year, he said, gives students the chance to pick the field that best suits them and to carefully evaluate residencies. More than three-fourths of students, he said, enter medical school uncertain about their eventual specialty. Goldfarb said he favors enhancing the fourth year, not eliminating it.

Medical students have mixed feelings about three-year programs, said Nida Degesys, president of the Reston-based American Medical Student Association. While many are eager to reduce their debt, they are also concerned about missing opportunities; fourth-year electives can include ophthalmology, critical care and emergency medicine.

"I personally changed my mind" during med school, Degesys said. "In the first year I thought I was going to do OB-GYN, but I later found that emergency medicine is truly the right fit for me."

Century Old System

For more than a century, medical schools have largely designed their programs around a template: two years of preclinical or classroom work in basic medical science, followed by two years of clinical rotations, mostly in hospitals. After med school, students continue their training in residencies lasting from three to seven years, which increasingly is followed by a fellowship of one year or more.

"There have always been some individuals who wondered about the length of medical school," said John Prescott, former dean of the medical school at West Virginia University and chief academic officer at the Association of American Medical Colleges.

To speed the production of doctors, medical training during World War II was shortened to three years with no ill effect, he said.

Prescott calls the current three-year programs "well-designed experiments" that may provide models about how to prepare students "in the most cost-effective way." But he doubts they will supplant the conventional four-year track for most students.

Steven B. Abramson, vice dean of NYU's medical school, agrees, but he said he expects three-year programs to multiply over the next five years.

NYU's accelerated program, he said, is best suited for highly qualified students who are typically older, more mature and certain of their choice of specialty. Because three-year students take the same core courses as their classmates, they will be equally well prepared, he said. And Abramson noted the proliferation of dual-degree programs: students who earn an MD along with a graduate degree in science, business administration or public health.

"The core content we deliver is rigorous, comprehensive and very well monitored," he said. To stay in the three-year program, students must remain in the upper half of the class; they retain the option of switching to the four-year track if they find it too taxing. First-year students are also assigned mentors in their intended residency.

While students at NYU can designate a variety of specialties, the three-year Family Medicine Accelerated Track at Texas Tech is limited to those who intend to pursue that specialty.

"There weren't enough primary-care doctors before the Affordable Care Act," said Texas Tech medical school dean Steven Berk, who trained as a family physician. "There are lots of towns in Texas with 25,000 people and no doctor. And it's the primary-care physicians who find the small breast mass or control patients' blood pressure. They are essential to the functioning of the health-care system."

Many students who chose the three-year course have committed to primary care based on their previous work experience. "We have students who have been PAs, EMTs and RNs," he said, referring to physician assistants, emergency medical technicians and registered nurses.

Texas Tech students are awarded a \$15,000 full tuition scholarship to cover the first year. When they graduate, their average debt for tuition and living expenses totals about \$60,000, Berk said. Like the NYU program, students have the option of switching to the four-year track -- none has so far -- and are granted a residency spot when they enter med school.

Fears that they will not perform as well as their four-year counterparts have not been validated, Berk said. Scores on licensing exams are equivalent, and burnout has not been a problem.

Charles Willnauer, 30, a graduate of Texas Tech's first three-year class, said the accelerated program worked well for him. The promise of a residency in family medicine, a specialty that "fits with my values and goals," was enticing, as was the lower price tag.

"A lot of people have to apply to 30 or more residency programs," said Willnauer, now a first-year resident.

"That's a very large cost and a lot of time."

It was also a bonus in other ways. Married and the father of two toddlers born while he was in medical school, Willnauer, age 30, said, "I bought a house and knew I wouldn't have to uproot my family."

<http://www.sciencedaily.com/releases/2014/01/140115143703.htm>

Heart Attack Damage Slashed With Microparticle Therapy

Inflammatory damage is slashed in half when microparticles are injected within 24 hours

After a heart attack, much of the damage to the heart muscle is caused by inflammatory cells that rush to the scene of the oxygen-starved tissue. But that inflammatory damage is slashed in half when microparticles are injected into the blood stream within 24 hours of the attack, according to new preclinical research from Northwestern Medicine® and the University of Sydney in Australia.

When biodegradable microparticles were injected after a heart attack, the size of the heart lesion was reduced by 50 percent and the heart could pump significantly more blood.

"This is the first therapy that specifically targets a key driver of the damage that occurs after a heart attack," said investigator Daniel Getts, a visiting scholar in microbiology-immunology at Northwestern University Feinberg School of Medicine. "There is no other therapy on the horizon that can do this. It has the potential to transform the way heart attacks and cardiovascular disease are treated."

The microparticles work by binding to the damaging cells -- inflammatory monocytes -- and diverting them to a fatal detour. Instead of racing to the heart, the cells head to the spleen and die. The particles are made of poly (lactic-co-glycolic) acid, a biocompatible and biodegradable substance already approved by the Food and Drug Administration for use in re-absorbable sutures. A microparticle is 500 nanometers, which is 1/200th size of a hair. The scientists' study showed the microparticles reduced damage and repaired tissue in many other inflammatory diseases. These include models of West Nile virus, colitis, inflammatory bowel disease, multiple sclerosis, peritonitis and a model that mimics blood flow after a kidney transplant.

"The potential for treating many different diseases is tremendous," said investigator Stephen Miller, the Judy Gugenheim Research Professor at Feinberg. "In all these disease models, the microparticles stop the flood of inflammatory cells at the site of the tissue damage, so the damage is greatly limited and tissues can regenerate." Getts, Miller and Nicholas King, professor of viral immunopathology at the University of Sydney School of Medical Sciences, are corresponding authors on the paper, which will be published January 15 in Science Translational Medicine.

Biotech Startup Aims for FDA Approval and Clinical Trial

The Northwestern and University of Sydney results are so encouraging, the scientists have partnered with a startup biotechnology company, Cour Pharmaceutical Development Co., to produce a refined version of the microparticles in anticipation of what they hope will be a clinical trial in myocardial infarction (heart attack) within two years. The company plans to submit an investigational new drug application to the FDA.

"This discovery has the potential to transform how inflammatory disorders are treated and the use of microparticles derived from biodegradable polymers means that this therapy could be rapidly translated for clinical use," said John Puisis, the chief executive officer of Cour.

How a Fatal Attraction Saves the Heart

The microparticles are designed to have a negative charge on their surface. This makes them irresistible to the inflammatory monocytes, which have a positively charged receptor. It's a fatal attraction. When the inflammatory cell bonds to the microparticle, a signal on the cell is activated that announces it's dying and ready for disposal. The cell then travels to the spleen, the natural path for the removal of dying cells, rather than going to the site of the inflammation. "We're very excited," King said. "The potential for this simple approach is quite extraordinary. Inflammatory cells pick up immune-modifying microparticles and are diverted down a natural pathway used by the body to dispose of old cells. It's amazing that such a simple detour limits major tissue damage in such a wide range of diseases."

D. R. Getts, R. L. Terry, M. T. Getts, C. Deffrasnes, M. Muller, C. van Vreden, T. M. Ashhurst, B. Chami, D. McCarthy, H. Wu, J. Ma, A. Martin, L. D. Shae, P. Witting, G. S. Kansas, J. Kuhn, W. Hafezi, I. L. Campbell, D. Reilly, J. Say, L. Brown, M. Y. White, S. J. Cordwell, S. J. Chadban, E. B. Thorp, S. Bao, S. D. Miller, N. J. C. King. Therapeutic Inflammatory Monocyte Modulation Using Immune-Modifying Microparticles. Science Translational Medicine, 2014; 6 (219): 219ra7 DOI: 10.1126/scitranslmed.3007563

<http://www.sciencedaily.com/releases/2014/01/140115172828.htm>

Head Injuries Triple Long-Term Risk of Early Death

Survivors of traumatic brain injuries (TBI) are three times more likely to die prematurely than the general population, often from suicide or fatal injuries, finds an Oxford University-led study.

A TBI is a blow to the head that leads to a skull fracture, internal bleeding, loss of consciousness for longer than an hour or a combination of these symptoms. Michael Schumacher's recent skiing injury is an example of a TBI. Concussions, sometimes called mild TBIs, do not present with these symptoms and were analyzed separately in this study.

Researchers examined Swedish medical records going back 41 years covering 218,300 TBI survivors, 150,513 siblings of TBI survivors and over two million control cases matched by sex and age from the general population. The work was carried out by researchers at Oxford University and the Karolinska Institute in Stockholm.

'We found that people who survive six months after TBI remain three times more likely to die prematurely than the control population and 2.6 times more likely to die than unaffected siblings,' said study leader Dr Seena Fazel, a Wellcome Trust Senior Research Fellow in Oxford University's Department of Psychiatry. 'Looking at siblings who did not suffer TBIs allows us to control for genetic factors and early upbringing, so it is striking to see that the effect remains strong even after controlling for these.'

The results, published in the journal *JAMA Psychiatry*, show that TBI survivors who also have a history of substance abuse or psychiatric disorders are at highest risk of premature death. Premature deaths were defined as before age 56. The main causes of premature death in TBI survivors are suicide and fatal injuries such as car accidents and falls.

'TBI survivors are more than twice as likely to kill themselves as unaffected siblings, many of whom were diagnosed with psychiatric disorders after their TBI,' said Dr Fazel. 'Current guidelines do not recommend assessments of mental health or suicide risk in TBI patients, instead focusing on short-term survival. Looking at these findings, it may make more sense to treat some TBI patients as suffering from a chronic problem requiring longer term management just like epilepsy or diabetes. TBI survivors should be monitored carefully for signs of depression, substance abuse and other psychiatric disorders, which are all treatable conditions.' The exact reasons for the increased risk of premature death are unknown but may involve damage to the parts of the brain responsible for judgement, decision making and risk taking. TBI survivors are three times more likely to die from fatal injuries which may be a result of impaired judgement or reactions.

'This study highlights the important and as yet unanswered question of why TBI survivors are more likely to die young, but it may be that serious brain trauma has lasting effects on people's judgement,' suggests Dr Fazel. 'People who have survived the acute effects of TBI should be more informed about these risks and how to reduce their impact.'

'When treating traumatic brain injuries focus is placed on immediate treatment and recovery of patients,' says Dr John Williams, Head of Neuroscience and Mental Health at the Wellcome Trust. 'This new finding offers important insight into the longer-term impact of TBIs on the brain and their effect on survival later in life. We hope that further research into understanding which parts of the brain are responsible will help improve future management programmes and reduce the potential for premature death.'

Even relatively minor brain injuries, concussions, had a significant impact on early mortality. People with concussion were found to be twice as likely to die prematurely as the control population, with suicide and fatal injuries as the main causes of death. This raises issues surrounding concussions in a wide range of sports, from American football, rugby and soccer to baseball and cricket.

There were 196,766 head injuries requiring hospital visits in 2012-13 in England alone, of which 125,822 led to TBIs. Approximately 1.7 million people in the United States and one million people in Europe are hospitalised after TBIs each year. Typical causes include vehicle accidents, falls and sporting injuries.

Seena Fazel, Achim Wolf, Demetris Pillas, Paul Lichtenstein, Niklas Långström. Suicide, Fatal Injuries, and Other Causes of Premature Mortality in Patients With Traumatic Brain Injury. JAMA Psychiatry, 2014; DOI: 10.1001/jamapsychiatry.2013.3935

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

Gene therapy restores sight in people with eye disease

"Before the op, I would look at someone and all I could see for their face was blancmange," says Jonathan Wyatt. "Now, I can see people's faces."

00:01 16 January 2014 by Abigail Beall

The 65-year-old is one of six people in the world to receive gene therapy for a rare type of inherited eye disease called choroideremia. The first published results of the trial, released today, suggest that tinkering with people's genes can stop the disease from causing blindness – and restore sight in those whose vision has become impaired.

The results could eventually be relevant to the treatment of a much more common cause of blindness, age-related macular degeneration, which is caused by whole host of faulty genes. Even more broadly, the positive results are part of a recent trend in gene therapy success, following a shaky start more than 20 years ago. Choroideremia is caused by defects in the CHM gene, which produces a protein called REP-1 and affects one in 50,000 people. In those who have the disease, a lack of REP-1 means that cells in the retina stop working and

slowly begin to die off, causing blindness. When he was in his twenties, doctors told Wyatt that he would be blind by the time he was 50 – and that there was no cure.

Neurons for life

Enter gene therapy, which uses a vector – usually a virus – to insert a functioning copy of a gene into cells with a gene defect and could in principle be used to treat many genetic conditions. Robert MacLaren of the University of Oxford and his colleagues decided to see if it could correct choroideremia.

Starting two years ago with Wyatt, they injected a virus carrying a corrective copy of the CHM gene into the retinas of people with choroideremia.

Today the team reports that of the six people who received the treatment six months ago or longer, all have described improvements in their vision. "The very next day I saw a mobile phone and I said 'I can read the digits!' I hadn't been able to read the digits on a mobile phone for five years," says Wyatt.

All the people in this trial had varying levels of degeneration before the treatment. However, MacLaren is hopeful that the therapy could also be used to stop choroideremia before there is any significant loss of vision. It's not the first time gene therapy has been used to improve vision: it has also been used to restore vision in people with the retinal disease Leber's congenital amaurosis, for example. However, in this case the target cells were pigment ones, which eventually die off to be replaced by new ones. By contrast, the MacLaren team's therapy targets photoreceptors that are neurons lasting for life – so in principle patients need only have the treatment once.

Bad start

Still, the long-lasting effects of the treatment remain unknown. Wyatt had the treatment first, so can reveal that the benefits seem to last two years, but he's just one case.

"Given the relatively slow degeneration in this condition, longer-term studies will be required," says James Bainbridge of the Institute of Ophthalmology at University College London.

The treatment also can't replace cells that have been completely destroyed. "We're trying to rescue the cells that are there already, to return the function of those cells to normal," says MacLaren. "What we can't do is bring back the cells that have already gone. That's one of the distinguishing features between stem cell therapy, which is to regenerate lost tissue, and gene therapy, which at the moment is there to sustain cells that would otherwise die."

MacLaren's work is part of a broader trend in the success of gene therapy, which got off to a bad start. The first people to be treated with a gene therapy had ADA-SCID, also called "bubble boy disease", and some later got leukaemia, probably because the virus carrying the new genes also switched on cancer genes.

Specifically, the new results boost knowledge about the effects of the viral vector used, adeno-associated virus, which has been successfully used in gene therapy for the eye since 2008. "The early results of this clinical trial add to the expanding body of experience on the safety of AAV vectors in the eye," says Bainbridge.

Journal reference: The Lancet, DOI: 10.1016/S0140-6736(14)60033-7

http://www.eurekalert.org/pub_releases/2014-01/uoa-pdc011614.php

Prion discovery could help keep deadly brain diseases in check

New research from David Westaway, PhD, of the University of Alberta and Jiri Safar, PhD, Case Western Reserve University School of Medicine has uncovered a quality control mechanism in brain cells that may help keep deadly neurological diseases in check for months or years.

The findings, published in *The Journal of Clinical Investigation*, "present a breakthrough in understanding the secret life of prion molecules in the brain and may offer a new way to treat prion diseases," said Westaway, Director of the Centre for Prions and Protein Folding Diseases and Professor of Neurology in the Faculty of Medicine and Dentistry at the University of Alberta.

Prion diseases lead to incurable neurodegenerative disorders such as Creutzfeldt-Jakob disease in humans, mad cow disease (Bovine Spongiform Encephalopathy) and chronic wasting disease in deer and elk. The diseases are caused by the conversion of normal cellular prion proteins into the diseased form.

For years, scientists have been perplexed by two unexplained characteristics of prion infections: vastly differing asymptomatic periods lasting up to five decades and when symptoms do arise, greatly varying accumulation of the diseased proteins. In striking contrast, test tube prions replicate rapidly, and in a matter of days reach levels found in brains in the final stage of the disease.

"Our study investigated the molecular mechanism of this intriguing puzzle," said Safar, Co-Director of the National Prion Disease Pathology Surveillance Center and Associate Professor in Departments of Pathology and Neurology in Case Western Reserve University School of Medicine.

In probing these mysteries, Westaway, Safar, their teams and other collaborating researchers in the U.S., Italy and the Netherlands studied a molecule called the 'shadow of the prion protein.'

"Dramatic changes in this shadow protein led us to expand our view to include the normal prion protein itself," said Westaway. "This is a crucial molecule in brain cells because it is pirated as the raw material to make diseased prion proteins."

The production and degradation of the normal prion protein had previously received little attention because it was assumed its production pipeline did not vary.

"The puzzle of the long asymptomatic time period required sorting out the different types of prion protein molecules. Our laboratory developed new techniques to tease out these subtle differences in shape," Safar said. The researchers discovered a marked drop in the amount of the normal prion protein in eight different types of prion diseases. Strikingly, this drop occurred months or years before the animal models showed tell-tale clinical symptoms of the brain disease.

"Our belief is that cells under prion attack are smarter than we once thought," Westaway said. "They not only sense the molecular piracy by the diseased proteins, but they also adopt a simple and at least partly effective protective response – they minimize the amount raw material from the pipeline for prion production."

"We believe we can kill two birds with one stone, because the normal prion protein is also a receptor for toxicity. Augmenting this natural protective response may be a preferred route to cure prion infections," Safar added. The study's discovery of a natural protective response can also explain the long latency period in other more common neurodegenerative diseases.

"The pre-clinical phase of the disease—before it shows symptoms—is when you want to set things straight. We may be able to take a slow disease and bring it to a complete standstill," Westaway said. "Since some scientists believe the normal prion protein is an accessory in the brain cell death of Alzheimer's disease, gaining a new understanding of rare yet lethal prion diseases may provoke fresh insights into human dementias."

The study was funded by the Alberta Prion Research Institute, Alberta Innovates-Health Solutions, the Canada Foundation for Innovation, the US National Institutes of Health and Centers for Disease Control and Prevention, the University Health Network, and the Charles S. Britton Fund.

http://www.eurekalert.org/pub_releases/2014-01/tes-tcm011414.php

Traditional Chinese medicines stall progression of diabetes

Clinical trial found herbs comparable to prescriptions for controlling prediabetes

Chevy Chase, MD—Traditional Chinese herbal medicines hold promise for slowing the progression from prediabetes to an official diabetes diagnosis, according to new research accepted for publication in the Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM).

Prediabetes is diagnosed an individual has developed elevated blood sugar levels, but glucose levels have not yet risen to the point of developing type 2 diabetes. People who are prediabetic face a heightened risk of developing type 2 diabetes as well as heart disease and stroke. According to the Centers for Disease Control and Prevention, about 79 million American adults age 20 years or older have prediabetes.

"With diabetes evolving into a serious public health burden worldwide, it is crucial to take steps to stem the flood of cases," said one of the study's authors, Chun-Su Yuan, MD, PhD, of the University of Chicago.

"Patients often struggle to make the necessary lifestyle changes to control blood sugar levels, and current medications have limitations and can have adverse gastrointestinal side effects. Traditional Chinese herbs may offer a new option for managing blood sugar levels, either alone or in combination with other treatments."

During the double-blind, randomized, placebo-controlled trial, 389 participants at 11 research sites in China were randomly assigned to take either a capsule containing a mixture of 10 Chinese herbal medicines or a placebo. For a year, subjects took capsules of either the Chinese herb mixture, called Tianqi, or the placebo three times a day before meals. All participants received a month of lifestyle education at the outset of the trial and met with nutritionists several times during the course of the study. Subjects' glucose tolerance was measured on a quarterly basis.

At the end of the trial, 36 participants in the Tianqi group and 56 in the placebo group had developed diabetes. The analysis found taking Tianqi reduced the risk of diabetes by 32.1 percent compared with the placebo, after adjusting for age and gender. The overall reduction in risk was comparable to that found in studies of diabetes medications acarbose and metformin, and study participants reported few side effects from the Tianqi herbs. Tianqi includes several herbs that have been shown to lower blood glucose levels and improve control of blood glucose levels after meals.

"Few controlled clinical trials have examined traditional Chinese medicine's impact on diabetes, and the findings from our study showed this approach can be very useful in slowing the disease's progression," said one of the study's lead authors, Xiaolin Tong, MD, PhD, of Guang'anmen Hospital in Beijing, China, said. "More research is needed to evaluate the role Chinese herbal medicine can play in preventing and controlling diabetes."

Other authors of the study include: F. Lian, X. Chen, Y. Bai and Z. Zhen of Guang'anmen Hospital; G. Li and Y. An of Fuwai Hospital of Cardiovascular Disease in Beijing; X. Wang of Beijing Pinggu Hospital of Traditional Chinese Medicine in Beijing; C. Piao of the Affiliated Hospital to Changchun University of Chinese Medicine in Changchun, China; J. Wang of Beijing Mentougou Hospital of Traditional Chinese Medicine in Beijing; Y. Hong of Hangzhou Hospital of Traditional Chinese Medicine in Hangzhou, China; Z. Ba of Qinghai Hospital of Traditional Chinese Medicine in Qinghai, China; S. Wu of First Teaching Hospital of Tianjin University of Traditional Chinese Medicine in Tianjin, China; X. Zhou of Guangzhou Tianhe Hospital of Traditional Chinese Medicine in Guangzhou, China; J. Lang of Foshan Hospital of Traditional Chinese Medicine in Foshan, China; Y. Liu of Beijing Huimin Hospital in Beijing; R. Zhang of Yangquan First Municipal People's Hospital in Yangquan, China; J. Hao and Q. Wang of Guangzhou Huangpu Hospital of Traditional Chinese Medicine in Guangzhou; Z. Zhu of First Affiliated Hospital of Guangzhou University of Chinese Medicine in Guangzhou; H. Li of Shenzhen Hospital of Traditional Chinese Medicine in Shenzhen, China; H.F. Liu of Dongzhimen Hospital affiliated to Beijing University of Chinese Medicine in Beijing; A. Cao of Beijing Changping Hospital of Traditional Chinese Medicine in Beijing; Z. Yan of China Academy of Chinese Medical Sciences in Beijing; and C. Yu and C.-Z. Wang of the Tang Center for Herbal Medicine Research at the University of Chicago.

The study, "Chinese Herbal Medicine Tianqi Reduces Progression from Impaired Glucose Tolerance to Diabetes: A Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial," appears in the February issue of JCEM.

http://www.eurekalert.org/pub_releases/2014-01/uocm-gom011314.php

Genomes of modern dogs and wolves provide new insights on domestication

Dogs and wolves evolved from a common ancestor between 9,000 and 34,000 years ago

Dogs and wolves evolved from a common ancestor between 9,000 and 34,000 years ago, before humans transitioned to agricultural societies, according to an analysis of modern dog and wolf genomes from areas of the world thought to be centers of dog domestication.

The study, published in PLoS Genetics on January 16, 2014, also shows that dogs are more closely related to each other than wolves, regardless of geographic origin. This suggests that part of the genetic overlap observed between some modern dogs and wolves is the result of interbreeding after dog domestication, not a direct line of descent from one group of wolves.

This reflects a more complicated history than the popular story that early farmers adopted a few docile, friendly wolves that later became our beloved, modern-day companions. Instead, the earliest dogs may have first lived among hunter-gatherer societies and adapted to agricultural life later.

"Dog domestication is more complex than we originally thought," said John Novembre, associate professor in the Department of Human Genetics at the University of Chicago and a senior author on the study. "In this analysis we didn't see clear evidence in favor of a multi-regional model, or a single origin from one of the living wolves that we sampled. It makes the field of dog domestication very intriguing going forward."

The team generated the highest quality genome sequences to date from three gray wolves: one each from China, Croatia and Israel, representing three regions where dogs are believed to have originated. They also produced genomes for two dog breeds: a basenji, a breed which originates in central Africa, and a dingo from Australia, both areas that have been historically isolated from modern wolf populations. In addition to the wolves and dogs, they sequenced the genome of a golden jackal to serve as an "outgroup" representing earlier divergence. Their analysis of the basenji and dingo genomes, plus a previously published boxer genome from Europe, showed that the dog breeds were most closely related to each other. Likewise, the three wolves from each geographic area were more closely related to each other than any of the dogs.

Novembre said this tells a different story than he and his colleagues anticipated. Instead of all three dogs being closely related to one of the wolf lineages, or each dog being related to its closest geographic counterpart (i.e. the basenji and Israeli wolf, or the dingo and Chinese wolf), they seem to have descended from an older, wolf-like ancestor common to both species.

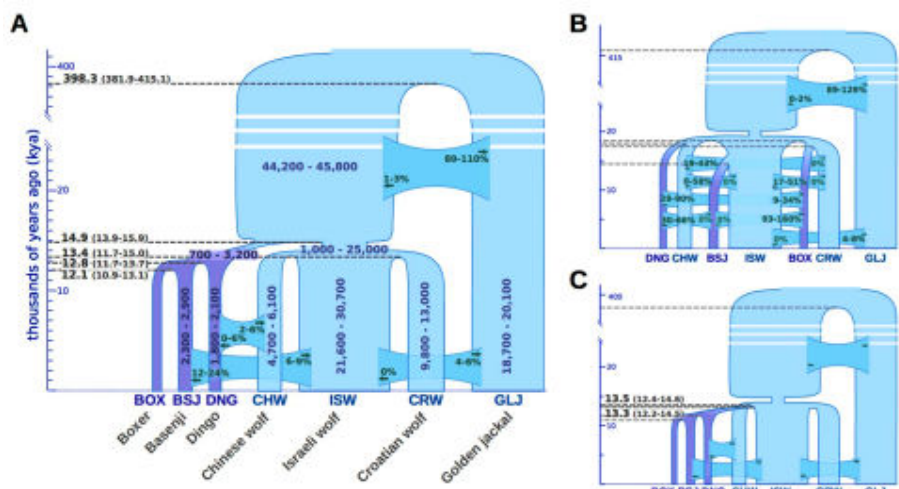


Figure 5 depicts wolf and dog lineages as they diverge over time. Freedma, et al / PLoS Genetics

"One possibility is there may have been other wolf lineages that these dogs diverged from that then went extinct," he said. "So now when you ask which wolves are dogs most closely related to, it's none of these three

because these are wolves that diverged in the recent past. It's something more ancient that isn't well represented by today's wolves."

Accounting for gene flow between dogs and wolves after domestication was a crucial step in the analyses. According to Adam Freedman, a postdoctoral fellow at the University of California, Los Angeles (UCLA) and the lead author on the study, gene flow across canid species appears more pervasive than previously thought. "If you don't explicitly consider such exchanges, these admixture events get confounded with shared ancestry," he said. "We also found evidence for genetic exchange between wolves and jackals. The picture emerging from our analyses is that these exchanges may play an important role in shaping the diversification of canid species." Domestication apparently occurred with significant bottlenecks in the historical population sizes of both early dogs and wolves. Freedman and his colleagues were able to infer historical sizes of dog and wolf populations by analyzing genome-wide patterns of variation, and show that dogs suffered a 16-fold reduction in population size as they diverged from wolves. Wolves also experienced a sharp drop in population size soon after their divergence from dogs, implying that diversity among both animals' common ancestors was larger than represented by modern wolves.

The researchers also found differences across dog breeds and wolves in the number of amylase (AMY2B) genes that help digest starch. Recent studies have suggested that this gene was critical to domestication, allowing early dogs living near humans to adapt to an agricultural diet. But the research team surveyed genetic data from 12 additional dog breeds and saw that while most dog breeds had high numbers of amylase genes, those not associated with agrarian societies, like the Siberian husky and dingo, did not. They also saw evidence of this gene family in wolves, meaning that it didn't develop exclusively in dogs after the two species diverged, and may have expanded more recently after domestication.

Novembre said that overall, the study paints a complex picture of early domestication.

"We're trying to get every thread of evidence we can to reconstruct the past," he said. "We use genetics to reconstruct the history of population sizes, relationships among populations and the gene flow that occurred. So now we have a much more detailed picture than existed before, and it's a somewhat surprising picture."

Robert Wayne, professor in the Department of Ecology and Evolutionary Biology at UCLA, was co-senior author on this study. The National Science Foundation and Life Technologies provided funding and reagents.

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http://www.eurekalert.org/pub_releases/2014-01/m-boa011614.php

Brain on autopilot

How the architecture of the brain shapes its functioning

The structure of the human brain is complex, reminiscent of a circuit diagram with countless connections. But what role does this architecture play in the functioning of the brain? To answer this question, researchers at the Max Planck Institute for Human Development in Berlin, in cooperation with colleagues at the Free University of Berlin and University Hospital Freiburg, have for the first time analysed 1.6 billion connections within the brain simultaneously. They found the highest agreement between structure and information flow in the "default mode network," which is responsible for inward-focused thinking such as daydreaming.

Everybody's been there: You're sitting at your desk, staring out the window, your thoughts wandering. Instead of getting on with what you're supposed to be doing, you start mentally planning your next holiday or find yourself lost in a thought or a memory. It's only later that you realize what has happened: Your brain has simply "changed channels"—and switched to autopilot.

For some time now, experts have been interested in the competition among different networks of the brain, which are able to suppress one another's activity. If one of these approximately 20 networks is active, the others remain more or less silent. So if you're thinking about your next holiday, it is almost impossible to follow the content of a text at the same time.

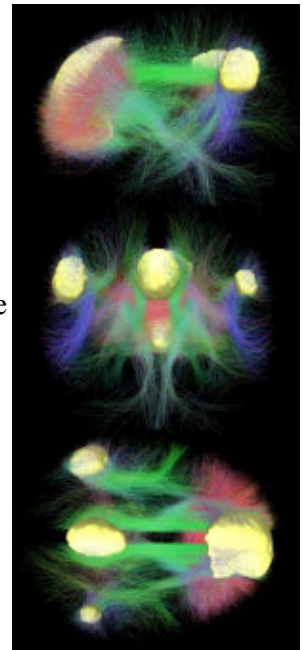
To find out how the anatomical structure of the brain impacts its functional networks, a team of researchers at the Max Planck Institute for Human Development in Berlin, in cooperation with colleagues at the Free University of Berlin and the University Hospital Freiburg, have analysed the connections between a total of 40,000 tiny areas of the brain. Using functional magnetic resonance imaging, they examined a total of 1.6 billion possible anatomical connections between these different regions in 19 participants aged between 21 and

31 years. The research team compared these connections with the brain signals actually generated by the nerve cells.

Their results showed the highest agreement between brain structure and brain function in areas forming part of the "default mode network", which is associated with daydreaming, imagination, and self-referential thought. "In comparison to other networks, the default mode network uses the most direct anatomical connections. We think that neuronal activity is automatically directed to level off at this network whenever there are no external influences on the brain," says Andreas Horn, lead author of the study and researcher in the Center for Adaptive Rationality at the Max Planck Institute for Human Development in Berlin.

Living up to its name, the default mode network seems to become active in the absence of external influences. In other words, the anatomical structure of the brain seems to have a built-in autopilot setting. It should not, however, be confused with an idle state. On the contrary, daydreaming, imagination, and self-referential thought are complex tasks for the brain.

"Our findings suggest that the structural architecture of the brain ensures that it automatically switches to something useful when it is not being used for other activities," says Andreas Horn. "But the brain only stays on autopilot until an external stimulus causes activity in another network, putting an end to the daydreaming. A buzzing fly, a loud bang in the distance, or focused concentration on a text, for example."



A daydreaming brain: the yellow areas depict the default mode network from three different perspectives; the colored fibers show the connections amongst each other and with the remainder of the brain. MPI for Human Development

The researchers hope that their findings will contribute to a better understanding of brain functioning in healthy people, but also of neurodegenerative disorders such as Alzheimer's disease and psychiatric conditions such as schizophrenia. In follow-up studies, the research team will compare the brain structures of patients with neurological disorders with those of healthy controls.

Horn, A., et al. (2013) *The structural-functional connectome and the default mode network of the human brain.* *NeuroImage.* <http://dx.doi.org/10.1016/j.neuroimage.2013.09.069>

http://www.eurekalert.org/pub_releases/2014-01/uop-pmt011614.php

Penn Museum team finds evidence for 3,000+-year-old 'Nordic grog' tradition

Discovery highlights innovative and complex fermented beverages of northernmost Europe in the Bronze and Iron Ages

From northwest Denmark, circa 1500-1300 BC, to the Swedish island of Gotland as late as the first century AD, Nordic peoples were imbibing an alcoholic "grog" or extreme hybrid beverage rich in local ingredients, including honey, bog cranberry, lingonberry, bog myrtle, yarrow, juniper, birch tree resin, and cereals including wheat, barley and/or rye—and sometimes, grape wine imported from southern or central Europe.

Such is the conclusion based on new archaeochemical evidence derived from samples inside pottery and bronze drinking vessels and strainers from four sites in Denmark and Sweden, combined with previous archaeobotanical data.

The research ("A biomolecular archaeological approach to 'Nordic grog'") was recently published online in the Danish Journal of Archaeology (Dec. 23, 2013). Patrick E. McGovern, Scientific Director of the Biomolecular Archaeology Project at the University of Pennsylvania Museum of Archaeology and Anthropology and author of *Uncorking the Past: The Quest for Wine, Beer and Other Alcoholic Beverages* (University of California Press, 2009) is the lead author on the paper, which was researched and written in collaboration with colleagues Gretchen R. Hall (University of Pennsylvania Museum) and Armen Mirzoyan (Scientific Services Division, Alcohol and Tobacco Tax and Trade Bureau [TTB], US Treasury), with key samples and archaeological evidence provided by Scandinavian colleagues.

The new biomolecular archaeological evidence provides concrete evidence for an early, widespread, and long-lived Nordic grog tradition, one with distinctive flavors and probable medicinal purposes—and the first chemically attested evidence for the importation of grape wine from southern or central Europe as early as 1100 BC, demonstrating both the social and cultural prestige attached to wine, and the presence of an active trading network across Europe—more than 3,000 years ago.

"Far from being the barbarians so vividly described by ancient Greeks and Romans, the early Scandinavians, northern inhabitants of so-called Proxima Thule, emerge with this new evidence as a people with an innovative

flair for using available natural products in the making of distinctive fermented beverages," noted Dr. McGovern.

"They were not averse to adopting the accoutrements of southern or central Europeans, drinking their preferred beverages out of imported and often ostentatiously grand vessels. They were also not averse to importing and drinking the southern beverage of preference, grape wine, though sometimes mixed with local ingredients."

Archaeological and Chemical Evidence

To reach their conclusions, the researchers obtained ancient residue samples from four sites in a 150-mile radius of southern Sweden and encompassing Denmark.

The oldest, dated 1500-1300 BC, was from Nandrup in northwestern Denmark, where a warrior prince had been buried in an oak coffin with a massively hafted bronze sword, battle-ax, and pottery jar whose interior was covered with a dark residue that was sampled.

A second Danish sample, dated to a later phase of the Nordic Bronze Age from about 1100-500 BC, came from a pit hoard at Kostræde, southwest of Copenhagen. A brownish residue filling a perforation of a bronze strainer, the earliest strainer yet recovered in the region, was sampled.

A third Danish sample was a dark residue on the interior base of a large bronze bucket from inside a wooden coffin of a 30-year-old woman, dating to the Early Roman Iron Age, about 200 BC, at Juellinge on the island of Lolland, southwest of Kostræde. The bucket was part of a standard, imported Roman wine-set, and the woman held the strainer-cup in her right hand.

A reddish-brown residue filling the holes and interior of a strainer-cup, again part of imported Roman wine-set, provided the fourth sample. Dating to the first century AD, the strainer-cup was excavated from a hoard, which also included a large gold torque or neck ring and a pair of bronze bells, at Havor on the Swedish island of Gotland in the Baltic Sea.

Ancient organic compounds were identified by a combination of chemical techniques: Fourier-transform infrared spectrometry (FT-IR), gas chromatography-mass spectrometry (GC-MS), ultra-high performance liquid chromatography tandem mass spectrometry (LC/MS/MS), and headspace solid phase microextraction (SPME) coupled to GC-MS.

A Tradition and a Revival

According to Dr. McGovern, the importation of southern wine, now proven to have begun, if only as a trickle in the late second millennium BC, grew apace—and eventually eclipsed the grog tradition—but never completely. Many of the ingredients in Nordic grog went on to be consumed in birch beer and as the principal bittering agents (so-called gruit) of medieval beers, before hops gained popularity, and the German purity law (Reinheitsgebot) which limited ingredients of beer to barley, hops and water was enacted in Bavaria in 1516 and eventually became the norm in northern Europe.

"About the closest thing to the grog today is produced on the island of Gotland in the Baltic Sea," the site of the latest residue sample, Dr. McGovern noted. "You can taste Gotlandsdryka in farmhouses. It's made from barley, honey, juniper, and other herbs like those in the ancient version."

"This new evidence of an old tradition resonates with modern inhabitants of Scandinavia, where alcoholic beverages are very much enjoyed and seen as an intrinsic part of Nordic and Viking lore. The story goes that a particularly wise creature named Kvasir was created by two races of gods, the Æsir and the Vanir, by spitting into a large jar. Kvasir was later murdered by two dwarfs, who ran his blood into three huge vessels containing honey. The result was a mixed beverage that conferred the gift of wisdom and poetry to the drinker. Odin himself, the Norse high god, was able to steal the grog back by consuming the beverage, transforming himself into an eagle, and flying back to Valhalla, the Nordic warrior paradise."

New this winter, the Delaware-based Dogfish Head Craft Brewery, in collaboration with Dr. McGovern, re-created their version of the ancient Nordic grog. It is the latest in the celebrated Ancient Ale Series, begun in 2000 with Midas Touch. Appropriately called Kvasir, it is a hybrid barley and winter wheat beer, lingonberry and bog cranberry wine, and honey mead—all rolled into one and seasoned with bog myrtle, yarrow, clover, and birch syrup.

A second version of this extreme hybrid beverage was also collaboratively brewed in Spring 2013 at the Nynäshamns Ångbryggeri on the east coast of Sweden, right across from the island of Gotland. Called Arketyp, it is now available in the state stores (Systembolaget) there.

The Dogfish Head version of the Nordic grog has a somewhat sour, toasty wheat taste profile, comparable to a Belgian lambic and in keeping with the relative scarcity of sugar-rich resources in the far north. Dogfish Head offers details.

"Both versions of the grog will marry nicely with the new Nordic cuisine, with its emphasis on natural ingredients," said Dr. McGovern.

http://www.eurekalert.org/pub_releases/2014-01/e-d0q011614.php

Discovery of quantum vibrations in 'microtubules' corroborates theory of consciousness

Discovery of quantum vibrations in "microtubules" inside brain neurons corroborates theory that consciousness derives from deeper level, finer scale activities inside brain neurons

Amsterdam - A review and update of a controversial 20-year-old theory of consciousness published in *Physics of Life Reviews* claims that consciousness derives from deeper level, finer scale activities inside brain neurons. The recent discovery of quantum vibrations in "microtubules" inside brain neurons corroborates this theory, according to review authors Stuart Hameroff and Sir Roger Penrose. They suggest that EEG rhythms (brain waves) also derive from deeper level microtubule vibrations, and that from a practical standpoint, treating brain microtubule vibrations could benefit a host of mental, neurological, and cognitive conditions.

The theory, called "orchestrated objective reduction" ('Orch OR'), was first put forward in the mid-1990s by eminent mathematical physicist Sir Roger Penrose, FRS, Mathematical Institute and Wadham College, University of Oxford, and prominent anesthesiologist Stuart Hameroff, MD, Anesthesiology, Psychology and Center for Consciousness Studies, The University of Arizona, Tucson. They suggested that quantum vibrational computations in microtubules were "orchestrated" ("Orch") by synaptic inputs and memory stored in microtubules, and terminated by Penrose "objective reduction" ('OR'), hence "Orch OR." Microtubules are major components of the cell structural skeleton.

Orch OR was harshly criticized from its inception, as the brain was considered too "warm, wet, and noisy" for seemingly delicate quantum processes. However, evidence has now shown warm quantum coherence in plant photosynthesis, bird brain navigation, our sense of smell, and brain microtubules. The recent discovery of warm temperature quantum vibrations in microtubules inside brain neurons by the research group led by Anirban Bandyopadhyay, PhD, at the National Institute of Material Sciences in Tsukuba, Japan (and now at MIT), corroborates the pair's theory and suggests that EEG rhythms also derive from deeper level microtubule vibrations. In addition, work from the laboratory of Roderick G. Eckenhoff, MD, at the University of Pennsylvania, suggests that anesthesia, which selectively erases consciousness while sparing non-conscious brain activities, acts via microtubules in brain neurons.

"The origin of consciousness reflects our place in the universe, the nature of our existence. Did consciousness evolve from complex computations among brain neurons, as most scientists assert? Or has consciousness, in some sense, been here all along, as spiritual approaches maintain?" ask Hameroff and Penrose in the current review. "This opens a potential Pandora's Box, but our theory accommodates both these views, suggesting consciousness derives from quantum vibrations in microtubules, protein polymers inside brain neurons, which both govern neuronal and synaptic function, and connect brain processes to self-organizing processes in the fine scale, 'proto-conscious' quantum structure of reality."

After 20 years of skeptical criticism, "the evidence now clearly supports Orch OR," continue Hameroff and Penrose. "Our new paper updates the evidence, clarifies Orch OR quantum bits, or "qubits," as helical pathways in microtubule lattices, rebuts critics, and reviews 20 testable predictions of Orch OR published in 1998 – of these, six are confirmed and none refuted."

An important new facet of the theory is introduced. Microtubule quantum vibrations (e.g. in megahertz) appear to interfere and produce much slower EEG "beat frequencies." Despite a century of clinical use, the underlying origins of EEG rhythms have remained a mystery. Clinical trials of brief brain stimulation aimed at microtubule resonances with megahertz mechanical vibrations using transcranial ultrasound have shown reported improvements in mood, and may prove useful against Alzheimer's disease and brain injury in the future.

Lead author Stuart Hameroff concludes, "Orch OR is the most rigorous, comprehensive and successfully-tested theory of consciousness ever put forth. From a practical standpoint, treating brain microtubule vibrations could benefit a host of mental, neurological, and cognitive conditions."

The review is accompanied by eight commentaries from outside authorities, including an Australian group of Orch OR arch-skeptics. To all, Hameroff and Penrose respond robustly.

Penrose, Hameroff and Bandyopadhyay will explore their theories during a session on "Microtubules and the Big Consciousness Debate" at the Brainstorm Sessions, a public three-day event at the Brakke Grond in Amsterdam, the Netherlands, January 16-18, 2014. They will engage skeptics in a debate on the nature of consciousness, and Bandyopadhyay and his team will couple microtubule vibrations from active neurons to play Indian musical instruments. "Consciousness depends on anharmonic vibrations of microtubules inside neurons, similar to certain kinds of Indian music, but unlike Western music which is harmonic," Hameroff explains.

"Consciousness in the universe: A review of the 'Orch OR' theory," by Stuart Hameroff, MD, and Roger Penrose, FRS. The review is freely available online on ScienceDirect.

Commentaries on the review are:

"Reply to criticism of the 'Orch OR qubit'-'Orchestrated objective reduction' is scientifically justified," by Stuart Hameroff, MD, and Roger Penrose, [FRS](#);

"Reply to seven commentaries on 'Consciousness in the universe: Review of the 'Orch OR' theory,'" by Stuart Hameroff, MD, and Roger Penrose, [FRS](#).

http://www.eurekaalert.org/pub_releases/2014-01/uab-tso011414.php

The symphony of life, revealed

A new imaging technique captures the vibrations of proteins, tiny motions critical to human life

BUFFALO, N.Y. - Like the strings on a violin or the pipes of an organ, the proteins in the human body vibrate in different patterns, scientists have long suspected. Now, a new study provides what researchers say is the first conclusive evidence that this is true. Using a technique they developed based on terahertz near-field microscopy, scientists from the University at Buffalo and Hauptman-Woodward Medical Research Institute (HWI) have for the first time observed in detail the vibrations of lysozyme, an antibacterial protein found in many animals. The team found that the vibrations, which were previously thought to dissipate quickly, actually persist in molecules like the "ringing of a bell," said UB physics professor Andrea Markelz, PhD, who led the study. These tiny motions enable proteins to change shape quickly so they can readily bind to other proteins, a process that is necessary for the body to perform critical biological functions like absorbing oxygen, repairing cells and replicating DNA, Markelz said.

The research opens the door to a whole new way of studying the basic cellular processes that enable life.

"People have been trying to measure these vibrations in proteins for many, many years, since the 1960s,"

Markelz said. "In the past, to look at these large-scale, correlated motions in proteins was a challenge that required extremely dry and cold environments and expensive facilities."

"Our technique is easier and much faster," she said. "You don't need to cool the proteins to below freezing or use a synchrotron light source or a nuclear reactor — all things people have used previously to try and examine these vibrations." The findings will appear in *Nature Communications* on Jan. 16, and publication of information on the research is prohibited until 5 a.m. U.S. Eastern Time on that day.

To observe the protein vibrations, Markelz' team relied on an interesting characteristic of proteins: The fact that they vibrate at the same frequency as the light they absorb. This is analogous to the way wine glasses tremble and shatter when a singer hits exactly the right note. Markelz explained: Wine glasses vibrate because they are absorbing the energy of sound waves, and the shape of a glass determines what pitches of sound it can absorb. Similarly, proteins with different structures will absorb and vibrate in response to light of different frequencies. So, to study vibrations in lysozyme, Markelz and her colleagues exposed a sample to light of different frequencies and polarizations, and measured the types of light the protein absorbed.

This technique, developed with Edward Snell, a senior research scientist at HWI and assistant professor of structural biology at UB, allowed the team to identify which sections of the protein vibrated under normal biological conditions. The researchers were also able to see that the vibrations endured over time, challenging existing assumptions.

"If you tap on a bell, it rings for some time, and with a sound that is specific to the bell. This is how the proteins behave," Markelz said. "Many scientists have previously thought a protein is more like a wet sponge than a bell: If you tap on a wet sponge, you don't get any sustained sound."

Markelz said the team's technique for studying vibrations could be used in the future to document how natural and artificial inhibitors stop proteins from performing vital functions by blocking desired vibrations. "We can now try to understand the actual structural mechanisms behind these biological processes and how they are controlled," Markelz said. "The cellular system is just amazing," she said. "You can think of a cell as a little machine that does lots of different things — it senses, it makes more of itself, it reads and replicates DNA, and for all of these things to occur, proteins have to vibrate and interact with one another."

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

Volcanic mayhem drove major burst of evolution

OUR planet is home to a glorious variety of animals, but it might not have been.

16 January 2014 by Catherine Brahic

Were it not for the birth pangs of a mega-continent, the evolution of animals could have stopped at its earliest stages.

We now have the best evidence yet that an enormous wave of volcanism, caused by several continents crashing together to form the even greater landmass known as Gondwana, was the reason for a sharp rise in global temperature. This change was the driving force for evolutionary explosions that made life more diverse and laid the foundations for all future animal species.

Volcanoes can cause global warming because eruptions often spew huge amounts of the greenhouse gas carbon dioxide. Now a study of volcanic rocks from early in life's evolutionary story shows that such eruptions coincided with a change in the climate from frigid chill to sweltering heat.

This swing, and the way it affected the oceans, caused an explosion of evolutionary diversity, followed by a mass extinction when temperatures got too hot. Then, when Gondwana had formed and the volcanism died down, the planet cooled and life began to bloom again. The findings add to evidence that plate tectonics and living things are linked.

Last year, a study suggested that microbes helped form continents by encouraging volcanic activity (New Scientist, 23 November 2013, p 10). Now Ryan McKenzie of the University of Texas at Austin and colleagues have shown that, in turn, volcanism may have shaped life during the crucial Cambrian period (see illustration). Before the Cambrian, over 600 million years ago, Earth was virtually covered in ice. The first animals arose on this "Snowball Earth", but these "Ediacarans" did not look like modern animals.

Then came the Cambrian explosion. "You had single cell organisms, single cell, single cell, then weird Ediacaran oddballs, and – suddenly – snails and bivalves and sea stars and a whole range of groups that typify the record for the rest of time," says McKenzie's colleague Paul Myrow of Colorado College in Colorado Springs.

The animals that appeared during the Cambrian explosion gave rise to all the major groups alive today, from worms to starfish. But each group only contained a few species, and got no further. The next period is known as the Dead Interval, and was marked by mass extinctions. It was another 50 million years before animal life blossomed once more, during the Ordovician.

We already knew that Earth's temperature changed dramatically over these periods. It thawed in the early Cambrian then became stiflingly hot during the Dead Interval, before cooling again. "These are huge climate swings, from Snowball Earth to one of the warmest intervals of Earth history in the Cambrian," says Lee Kump of Penn State University in University Park.

Volcanic activity during the formation of Gondwana has been suggested as a driver of these violent changes, but Kump says the evidence for increased volcanism was "a house of cards".

McKenzie's new evidence comes from tiny zircon crystals. Zircons are only formed in particular volcanic eruptions that are triggered when continental masses crash into each other, so they act as a record of past continental collisions. McKenzie assembled zircon counts from rocks laid down in the last 3 billion years, from all around the world.

He noticed that zircons were rare from Snowball Earth but common in the Cambrian. It seems a horde of volcanoes began spewing just before the Cambrian, and their activity reached a peak during the Dead Interval (Geology, doi.org/qvp). "We hypothesise that CO₂ outgassing from continental volcanic arcs drove major climate shifts," says McKenzie.

Kump agrees: "This to my knowledge is the first direct and compelling assessment of changes in arc volcanism over this critical interval."

"This is a fundamentally new and radical idea," says Cin-ty Lee of Rice University in Houston, Texas.

Myrow says the formation of Gondwana offers the best explanation for the extra volcanoes. "Throughout the Cambrian two big continental masses were coming together to make Gondwana," he says. The collision generated infernal heat that melted rock and created long chains of volcanoes. "You're making volcanoes like mad," says Myrow. "They produce carbon dioxide and temperatures get very, very hot."

As well as heating the planet, the extra CO₂ acidified the oceans. Many ocean creatures are sensitive to changes in acidity, so this could help explain the Dead Interval. Then the volcanism died off once Gondwana had formed, CO₂ levels fell and a huge diversity of reef-based animals appeared.

"Now we have greater confidence that volcanism and its effect on the greenhouse gas content of the atmosphere drove climate change in deep time," says Kump. "This had direct effects on rates of biotic diversification."

Changes in tectonic activity would go on to affect life on Earth throughout its history, but not always in such a helpful way. For instance, almost all animal and plant life was abruptly wiped out at the end of the Permian period 251 million years ago, a time known as the Great Dying. Rapid climate change triggered by intense volcanic activity could well be to blame. Tectonics may give, but it also takes away.

This article appeared in print under the headline "Volcanic mayhem drove evolution"

Shaky worlds may harbour life

Plate tectonics can affect life through massive volcanic eruptions (see main story). But the links between the two phenomena go much deeper, so much so that those seeking life on other planets are eagerly hunting for signs of tectonic activity.

"Plate tectonics is believed by many to be an element of a planet's potential to support life," says Tilman Spohn of the Institute for Planetary Research in Berlin, Germany.

For one thing, by taking rocks down into Earth's depths and then shoving them back up again, tectonics continually delivers nutrients to the surface. This may help to sustain life, especially in its earliest stages before the evolution of processes like photosynthesis that allow organisms to feed themselves.

What's more, tectonics creates a diversity of environments by deforming the surface of the Earth into mountains and valleys. This fosters evolution by forcing life to adapt to the varying conditions.

Plate tectonics is ultimately driven by the churning of hot rocks deep inside the Earth. This same motion also helps to generate our planet's powerful magnetic field, which protects large life forms like humans from deadly cosmic radiation. These subtle benefits of tectonics suggest that a planet with active geology might also be a living planet, and one without could well be dead.

<http://bit.ly/1dP0FLe>

Japan to 'Drag' Space Junk from Orbit

Japanese space scientists are set to trial a tether they hope will help pull junk out of orbit around Earth, clearing up tonnes of planetary clutter, they said Thursday.

Researchers at The Japan Aerospace Exploration Agency (JAXA) have developed what they called an electrodynamic tether made from thin wires of stainless steel and aluminum.

The idea is that one end of the strip will be attached to one of the thousands of dead satellites or bits of rocket that are jamming up space and endangering working equipment. The electricity generated by the tether as it swings through the Earth's magnetic field is expected to have a slowing effect on the space junk, which should, scientists say, pull it into a lower and lower orbit. Eventually the detritus will enter the Earth's atmosphere, burning up harmlessly long before it has chance to crash to the planet's surface.

"The experiment is specifically designed to contribute to developing a space debris cleaning method," said Masahiro Nohmi, associate professor at Kagawa University, who is working with JAXA on the project, told AFP.

Nohmi said a satellite developed by the university is expected to be launched into space on February 28, with the tether aboard. "We have two main objectives in the trial next month," he said. "First, to extend a 300-meter (1,000-foot) tether in orbit and secondly to observe the transfer of electricity."

The actual reeling in of orbiting rubbish will be the objective of future experiments, he said. A spokesman for JAXA said the agency also plans to conduct its own trial on a tether in 2015.

More than 20,000 bits of cast off equipment, including old satellites, pieces of rocket and other fragments are uselessly orbiting the Earth in a band 800-1,400 kilometers (500-900 miles) from the surface of the planet at terrific speed. Their presence causes problems for space scientists who have to try to prevent them colliding with functioning kit because of the huge damage they can cause.

<http://www.sciencedaily.com/releases/2014/01/140116162019.htm>

Violence, Infectious Disease and Climate Change Contributed to Indus Civilization Collapse

A new study on the human skeletal remains from the ancient Indus city of Harappa provides evidence that inter-personal violence and infectious diseases played a role in the demise of the Indus, or Harappan Civilization around 4,000 years ago.

The Indus Civilization stretched over a million square kilometers of what is now Pakistan and India in the Third Millennium B.C. While contemporaneous civilizations in Egypt and Mesopotamia, are well-known, their Indus trading partners have remained more of a mystery.

Archaeological research has demonstrated that Indus cities grew rapidly from 2200-1900 B.C., when they were largely abandoned. "The collapse of the Indus Civilization and the reorganization of its human population has been controversial for a long time," lead author of the paper published last month in the journal PLOS ONE, Gwen Robbins Schug, explained. Robbins Schug is an associate professor of anthropology at Appalachian State University.

Climate, economic, and social changes all played a role in the process of urbanization and collapse, but little was known about how these changes affected the human population.

Robbins Schug and an international team of researchers examined evidence for trauma and infectious disease in the human skeletal remains from three burial areas at Harappa, one of the largest cities in the Indus Civilization. The results of their analysis counter longstanding claims that the Indus civilization developed as a peaceful,

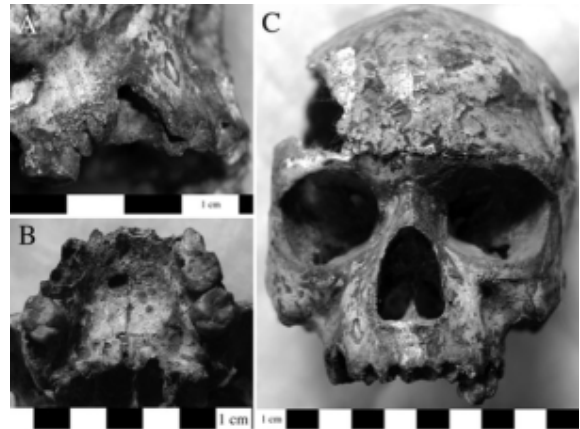
cooperative, and egalitarian state-level society, without social differentiation, hierarchy, or differences in access to basic resources.

The data suggest instead that some communities at Harappa faced more significant impacts than others from climate and socio-economic strains, particularly the socially disadvantaged or marginalized communities who are most vulnerable to violence and disease.

This pattern is expected in strongly socially differentiated, hierarchical but weakly controlled societies facing resource stress.

Robbins Schug's and colleagues' findings add to the growing body of research about the character of Indus society and the nature of its collapse.

"Early research had proposed that ecological factors were the cause of the demise, but there wasn't much paleo-environmental evidence to confirm those theories," Robbins Schug said. "In the past few decades, there have been refinements to the available techniques for reconstructing paleo-environments and burgeoning interest in this field."



Evidence for maxillary infection in individual G.I.S.15. The lesions included porosity, alveolar resorption, abscessing at the right canine and third premolar, and antemortem tooth loss (a = right ventral view). This individual also had inflammatory changes to the palatine process of the maxilla leading to localized bone destruction and perforation (b = inferior view of palate). There is evidence for porosity and inflammation at the inferior margin of the pyriform aperture, porosity and deformation of the infraorbital foramen caused by infection of the left maxillary sinus (c: ventral view). (Credit: Gwen Robbins Schug, K. Elaine Blevins, Brett Cox, Kelsey Gray, V. Mushrif-Tripathy. *Infection, Disease, and Biosocial Processes at the End of the Indus Civilization*. PLoS ONE, 2013; 8 (12): e84814 DOI: 10.1371/journal.pone.0084814)

When paleoclimate, archaeology, and human skeletal biology approaches are combined, scientists can glean important insights from the past, addressing long-standing and socially relevant questions.

"Rapid climate change events have wide-ranging impacts on human communities," Robbins Schug said.

"Scientists cannot make assumptions that climate changes will always equate to violence and disease. However, in this case, it appears that the rapid urbanization process in Indus cities, and the increasingly large amount of culture contact, brought new challenges to the human population. Infectious diseases like leprosy and tuberculosis were probably transmitted across an interaction sphere that spanned Middle and South Asia."

Robbins Schug's research shows that leprosy appeared at Harappa during the urban phase of the Indus Civilization, and its prevalence significantly increased through time. New diseases, such as tuberculosis, also appear in the Late Harappan or post-urban phase burials. Violent injury such as cranial trauma also increases through time, a finding that is remarkable, she said, given that evidence for violence is very rare in prehistoric South Asian sites generally.

"As the environment changed, the exchange network became increasingly incoherent. When you combine that with social changes and this particular cultural context, it all worked together to create a situation that became untenable," she said.

The results of the study are striking, according to Robbins Schug, because violence and disease increased through time, with the highest rates found as the human population was abandoning the cities.

However, an even more interesting result is that individuals who were excluded from the city's formal cemeteries had the highest rates of violence and disease. In a small ossuary southeast of the city, men, women, and children were interred in a small pit. The rate of violence in this sample was 50 percent for the 10 crania preserved, and more than 20 percent of these individuals demonstrated evidence of infection with leprosy.

Robbins Schug said lessons from the Indus Civilization are applicable to modern societies.

"Human populations in semi-arid regions of the world, including South Asia, currently face disproportionate impacts from global climate change," the researchers wrote. "The evidence from Harappa offers insights into how social and biological challenges impacted past societies facing rapid population growth, climate change and environmental degradation. Unfortunately, in this case, increasing levels of violence and disease accompanied massive levels of migration and resource stress and disproportionate impacts were felt by the most vulnerable members of society."

Gwen Robbins Schug, K. Elaine Blevins, Brett Cox, Kelsey Gray, V. Mushrif-Tripathy. *Infection, Disease, and Biosocial Processes at the End of the Indus Civilization*. PLoS ONE, 2013; 8 (12): e84814 DOI: 10.1371/journal.pone.0084814

<http://bit.ly/1f27Vmu>

Natural ball lightning probed for the first time

Goodness gracious, a great ball of lightning seen in China offers the first evidence in nature that the elusive glowing orbs form thanks to vaporised dirt.

21:31 16 January 2014 by Michael Slezak

Anecdotes about ball lightning stretch back for centuries, but the phenomenon has been hard to study as the balls are unpredictable – and when they do materialise, they last for mere seconds. Lacking detailed observations, explanations have ranged from electrically charged meteorites to hallucinations induced by magnetism during storms.

In 2012, Jianyong Cen and his colleagues at Northwestern Normal University in Lanzhou, China, were observing a thunderstorm in Qinghai, China with video cameras and spectrographs. Purely by chance, they recorded a ball lightning event. When a bolt struck the ground, a glowing ball about 5 metres wide rose up and travelled about 15 metres, disappearing after 1.6 seconds.

The spectrograph revealed that the main elements in the ball were the same as those found in the soil: silicon, iron and calcium. The observations support a theory for making ball lightning put forth in 2000 by John Abrahamson at the University of Canterbury in New Zealand.

Gold dust

Abrahamson surmised that when lightning hits the ground, the sudden, intense heat can vaporise silicon oxide in the dirt, and a shockwave blows the gas up into the air. If there's also carbon in the soil, perhaps from dead leaves or tree roots, it will steal oxygen from the silicon oxide, leaving a bundle of pure silicon vapour. But the planet's oxygen-rich atmosphere rapidly re-oxidises the hot ball of gas, and this reaction makes the orb glow briefly.

The theory garnered support in 2006, when scientists at Tel Aviv University in Israel were able to create ball lightning in the lab by firing mock lightning at sheets of silicon oxide. The event in China marks the first time such an orb has been captured in nature with scientific instruments.

The study authors say that other mechanisms could also explain their observations. But Abrahamson thinks the findings are a perfect fit for the soil hypothesis. "Here's an observation which has all the hallmarks of our theory. This is gold dust as far as confirmation goes," he says.

Journal reference: [Physical Review Letters](#) (accepted for publication)

http://www.eurekalert.org/pub_releases/2014-01/gsu-sfc011714.php

Study finds chimps can use gestures to communicate in hunt for food

Chimpanzees are capable of using gestures to communicate as they pursue specific goals, such as finding a hidden piece of food, according to a new Georgia State University research study.

Researchers at Georgia State University's Language Research Center examined how two language-trained chimpanzees communicated with a human experimenter to find food. Their results are the most compelling evidence to date that primates can use gestures to coordinate actions in pursuit of a specific goal.

The team devised a task that demanded coordination among the chimps and a human to find a piece of food that had been hidden in a large outdoor area. The human experimenter did not know where the food was hidden, and the chimpanzees used gestures such as pointing to guide the experimenter to the food.

Dr. Charles Menzel, a senior research scientist at the Language Research Center, said the design of the experiment with the "chimpanzee-as-director" created new ways to study the primate.

"It allows the chimpanzees to communicate information in the manner of their choosing, but also requires them to initiate and to persist in communication," Menzel said. "The chimpanzees used gestures to recruit the assistance of an otherwise uninformed person and to direct the person to hidden objects 10 or more meters away. Because of the openness of this paradigm, the findings illustrate the high level of intentionality chimpanzees are capable of, including their use of directional gestures. This study adds to our understanding of how well chimpanzees can remember and communicate about their environment."

The paper, "Chimpanzees Modify Intentional Gestures to Co-ordinate a Search for Hidden Food," has been published in *Nature Communications*. Academics at the University of Chester and University of Stirling collaborated on the research project.

Dr. Anna Roberts of the University of Chester said the findings are important. "The use of gestures to coordinate joint activities such as finding food may have been an important building block in the evolution of language," she said.

Dr. Sarah-Jane Vick of the University of Stirling added, "Previous findings in both wild and captive chimpanzees have indicated flexibility in their gestural production, but the more complex coordination task used here demonstrates the considerable cognitive abilities that underpin chimpanzee communication."

Dr. Sam Roberts, also from the University of Chester, pointed out the analogy to childhood games. "This flexible use of pointing, taking into account both the location of the food and the actions of the experimenter, has not been observed in chimpanzees before," Roberts said.

The project was supported by Leakey Foundation, the Wenner-Gren Foundation, National Institutes of Health, the Economic and Social Research Council, the British Academy, the Carnegie Trust for the Universities of Scotland and the University of Stirling.

<http://phys.org/news/2014-01-lichen-mars.html>

Lichen on Mars

Astrobiology's study of life in the universe has much to say about how humans live sustainably on Earth. Humans cannot hope to survive life on Mars without plenty of protection from the surface radiation, freezing night temperatures and dust storms on the red planet. So they could be excused for marveling at humble Antarctic lichen that has shown itself capable of going beyond survival and adapting to life in simulated Martian conditions.

The mere feat of surviving temperatures as low as -51 degrees C and enduring a radiation bombardment during a 34-day experiment might seem like an accomplishment by itself. But the lichen, a symbiotic mass of fungi and algae, also proved it could adapt physiologically to living a normal life in such harsh Martian conditions—as long as the lichen lived under "protected" conditions shielded from much of the radiation within "micro-niches" such as cracks in the Martian soil or rocks.

"There were no studies on adaptation to Martian conditions before," said Jean-Pierre de Vera, a scientist at the German Aerospace Center's Institute of Planetary Research in Berlin, Germany. "Adaptation is very important to be investigated, because it tells you more about the interactions of life in relation to its environment." Previous Mars simulation experiments focused on simply measuring the survival of organisms at the end of a given time period. By contrast, de Vera and his group of German and U.S. colleagues measured the lichen's activities throughout the experiment that was detailed in the Sept. issue of the journal *Planetary and Space Science*. They wanted to see whether the lichen had continued its normal activities rather than simply clinging to life in a dormant state.

Two groups of lichen samples were placed inside a Mars simulation chamber about the size of a big pressure cooker, which itself sat within a fridge about the size of an armoire. That allowed researchers to simulate almost everything about Martian conditions such as atmospheric chemistry, pressure, temperatures, humidity and solar radiation—the lone exceptions being Martian gravity and the added contribution of galactic radiation.

One of the lichen samples in the Mars chamber was exposed to the full brunt of radiation expected on the Martian surface, while the second set of samples received a radiation dose almost 24 times lower to simulate life in the "protected" condition. A third group of lichen samples sat outside the chamber as a control.

Both lichen sample groups survived their month-long period under Martian conditions. But the heavier dose of radiation from a Xenon lamp simulating the surface radiation conditions kept the unprotected sample group from doing much beyond clinging to survival.

Only the "protected" lichen carried on normal activities such as using photosynthesis to turn sunlight into chemical energy for itself. The protected lichen recovered quickly after an initial "shock" period by adapting well enough to steadily ramp up its photosynthetic activities all the way until the end of the experiment.

"We have shown the first time, that in particular photosynthesis is possible in micro-niches on the surface of Mars," de Vera explained.

The lichen chosen for the experiment, called *P. chlorophanum*, has proven itself a survival champion even before the Mars simulation. Researchers removed lichen samples for testing from its home atop the rocky Black Ridge in Antarctica's North Victoria Land—a frozen, dry landscape not unlike that of many places on Mars. Similar lichens have shown they can survive exposure to the vacuum of space as well as space radiation. The past experiments conducted by the European Space Agency aboard Russian FOTON satellites and the International Space Station included de Vera as a co-investigator.

The latest Mars simulation experiment did not try to simulate the Martian dust storms that can blanket the entire planet for a month. But de Vera points out that lichen can survive in a resting state for thousands of years on Earth while covered with dust, snow or ice.

Lichen don't exist alone as possible Earth survivors on Mars. Other studies conducted by de Vera have suggested that methane-producing bacteria, known as methanogens, could also manage a Martian existence.

"There are important indices that Earth life can survive, to be metabolically active and adapt physiologically to live on Mars during the time periods which have been investigated," de Vera said.

The experiment's results have huge implications for ongoing robotic missions searching for evidence of life on Mars. First, they confirm that such missions would do well to focus on searching for possible Martian life

within the "micro-niche" environments beneath the soil or within rocks protected from surface radiation. Second, they lend hope to the idea that Martian life—if at all similar to Earth life—could have indeed survived up until today.

The lichen's remarkable adaptation to Martian conditions suggests a third, equally important lesson—it justifies the ongoing caution of NASA and other space agencies in ensuring that Earth organisms don't accidentally hitchhike a ride to Mars. Such planetary protection measures seem likely to continue until the possible day that humanity decides to colonize Mars and perhaps change the planet's landscape in the process.

Provided by Astrobio.net

<http://www.sciencedaily.com/releases/2014/01/140116130822.htm>

How Vision Captures Sound Now Somewhat Uncertain

New research challenges previous understanding of how the brain links sights and sounds

When listening to someone speak, we also rely on lip-reading and gestures to help us understand what the person is saying. To link these sights and sounds, the brain has to know where each stimulus is located so it can coordinate processing of related visual and auditory aspects of the scene. That's how we can single out a conversation when it's one of many going on in a room.

While past research has shown that the brain creates a similar code for vision and hearing to integrate this information, Duke University researchers have found the opposite: neurons in a particular brain region respond differently, not similarly, based on whether the stimuli is visual or auditory. The finding, which posted Jan. 15 in the journal PLOS ONE, provides insight into how vision captures the location of perceived sound.

The idea among brain researchers has been that the neurons in a brain area known as the superior colliculus employ a "zone defense" when signaling where stimuli are located. That is, each neuron monitors a particular region of an external scene and responds whenever a stimulus -- either visual or auditory -- appears in that location. Through teamwork, the ensemble of neurons provides coverage of the entire scene.

But the study by Duke researchers found that auditory neurons don't behave that way. When the target was a sound, the neurons responded as if playing a game of tug-of-war, said lead author Jennifer Groh, a professor of psychology and neuroscience at Duke.

"The neurons responded to nearly all sound locations. But how vigorously they responded depended on where the sound was," Groh said. "It's still teamwork, but a different kind. It's pretty cool that the neurons can use two different strategies, play two different games, at the same time."

Groh said the finding opens up a mystery: if neurons respond differently to visual and auditory stimuli at similar locations in space, then the underlying mechanism of how vision captures sound is now somewhat uncertain. "Which neurons are 'on' tells you where a visual stimulus is located, but how strongly they're 'on' tells you where an auditory stimulus is located," said Groh, who conducted the study with co-author Jung Ah Lee, a postdoctoral fellow at Duke. "Both of these kinds of signals can be used to control behavior, like eye movements, but it is trickier to envision how one type of signal might directly influence the other."

The study involved assessing the responses of neurons, located in the rostral superior colliculus of the midbrain, as two rhesus monkeys moved their eyes to visual and auditory targets.

The sensory targets -- light-emitting diodes attached to the front of nine speakers -- were placed 58 inches in front of the animals. The speakers were located from 24 degrees left to 24 degrees right of the monkey in 6-degree increments. The researchers then measured the monkey's responses to bursts of white noise and the illuminating of the lights.

Groh said how the brain takes raw input of one form and converts it into something else "may be broadly useful for more cognitive processes." "As we develop a better understanding of how those computations unfold it may help us understand a little bit more about how we think," she said.

Jungah Lee, Jennifer M. Groh. Different Stimuli, Different Spatial Codes: A Visual Map and an Auditory Rate Code for Oculomotor Space in the Primate Superior Colliculus. PLoS ONE, 2014; 9 (1): e85017 DOI: 10.1371/journal.pone.0085017

<http://www.sciencedaily.com/releases/2014/01/140116162010.htm>

Diet Beverages Not the Solution for Weight Loss

Overweight and obese adults who drink diet beverages consume more calories from food than obese or overweight adults who drink regular soda

Heavy adults who believe drinking diet soda will help them lose or keep weight off should think again. Researchers at the Johns Hopkins Bloomberg School of Public Health who examined national patterns in adult diet beverage consumption and calorie intake found that overweight and obese adults who drink diet beverages consume more calories from food than obese or overweight adults who drink regular soda or other sugary beverages. The results are featured in the January 16 issue of the American Journal of Public Health.

"Although overweight and obese adults who drink diet soda eat a comparable amount of total calories as heavier adults who drink sugary beverages, they consume significantly more calories from solid food at both meals and snacks," said Sara Bleich, PhD, associate professor with the Bloomberg School's Department of Health Policy and Management and lead author of the paper.

Using data from the 1999-2010 National Health and Nutrition Examination Survey (NHANES), researchers looked at national patterns in adult diet beverage consumption and caloric intake by body-weight status. The NHANES is a population-based survey designed to collect information on the health and nutrition of the US population.

Consumption of diet soda has increased considerably in the past few decades from 3% in 1965 to 20% today. Individuals who drink diet soda typically have a higher BMI (Body Mass Index) and consume more snack food than those who drink sugary beverages.

Earlier research may explain why the investigators found higher consumption of solid food among heavy adults who drink diet beverages. Artificial sweeteners, which are present in high doses in diet soda, are associated with a greater activation of reward centers in the brain, thus altering the reward a person experiences from sweet tastes. In other words, among people who drink diet soda, the brain's sweet sensors may no longer provide a reliable gauge of energy consumption because the artificial sweetener disrupts appetite control. As a result, consumption of diet drinks may result in increased food intake overall.

"The results of our study suggest that overweight and obese adults looking to lose or maintain their weight--who have already made the switch from sugary to diet beverages--may need to look carefully at other components of their solid-food diet, particularly sweet snacks, to potentially identify areas for modification," said Bleich.

Sara N. Bleich, Julia A. Wolfson, Sienna Vine and Y. Claire Wang. Diet Beverage Consumption and Caloric Intake Among US Adults Overall and by Body Weight. American Journal of Public Health, January 2014

<http://www.sciencedaily.com/releases/2014/01/140117103923.htm>

Searching for Magic Bullet Against Cancer Caused by Asbestos: One Step Closer?

Two separate studies aiming to address the urgent need to identify possible new methods for mesothelioma treatment

Mesothelioma is a very aggressive cancer associated with asbestos exposure, which is usually diagnosed in an advanced stage. So far no therapeutic strategy has proven effective against this deadly cancer and the prognosis remains very poor with only few exceptions.

In December, the research team of Antonio Giordano, a pathologist, Director and Founder of the Sbarro Health Research Organization in Philadelphia, PA, and Professor of Pathology and Oncology at the University of Siena, Italy, published two separate studies aiming to address the urgent need to identify possible new methods for mesothelioma treatment.

In the first study, published in the scientific journal *Cell Cycle*, Giordano's researchers tested on mesothelioma cells the effect of two drugs designed to reactivate the p53 protein, one of the most important 'tumor suppressors', which is turned off in most human cancers. "In mesothelioma, although p53 is rarely mutated, it is inactivated by alterations in its pathway," says Francesca Pentimalli of the National Cancer Institute of Naples, Italy, lead author of the study. Both of the drugs used in the study target p53, but with different mechanisms of action. One in particular, called RITA, proved to be very toxic. Specifically, RITA caused mesothelioma cells, and not 'healthy' cells, to undergo apoptosis -- a type of programmed cell death that occurs through the activation of a specific 'cascade' of events.

"The ability of RITA to induce apoptosis is remarkable considering that mesothelioma is very refractory to this process. In fact the most aggressive and rare variant, sarcomatoid mesothelioma, did not respond to the treatment probably because of its intrinsically high levels of molecules acting as inhibitors of this process" says Alfredo Budillon, Head of the Experimental Pharmacology Unit of the National Cancer Institute of Naples and coauthor of the study. "It remains to be seen whether the combination of RITA with other activators of apoptosis can achieve efficacy also against the more aggressive cases."

Furthermore, challenging mesothelioma cells with RITA worked in synergy with the chemotherapy drug cisplatin, which is the mainstay of treatment for this disease, suggesting that its use in a clinical setting could possibly help to reduce the required doses and the side effects of chemotherapy, thereby improving patients' quality of life.

The second study, published online in *Cancer Biology and Therapy* and led by Paola Indovina of the University of Siena and the Sbarro Institute for Cancer Research and Molecular Medicine, Temple University in Philadelphia, was designed along the same lines as the first study. In the second study, the authors tested, for the first time in mesothelioma, a new drug called MK-1775 in combination with cisplatin. MK-1775 is a

selective inhibitor of WEE1, a protein that is crucial in activating a 'checkpoint' for the repair of damaged DNA before the cell starts its division process.

The rationale for this strategy is based on the fact that many cancer cells, especially those with non-functional p53, rely on WEE1 to stall cell division and allow cells to repair the damage induced by genotoxic agents, such as many chemotherapeutic drugs, including cisplatin.

WEE1 inhibition limits the time available for repair and, therefore, sensitizes cancer cells to DNA-damaging agents. Indeed, inhibiting WEE1 with MK-1775 selectively sensitized mesothelioma cells to the genotoxic action of cisplatin by preventing checkpoint activation and forcing the cells to divide despite the damage, thus triggering apoptosis.

"Overall our studies are aimed at identifying promising new molecular therapies against mesothelioma that hold the potential for clinical use in the near future. MK-1775, for example, is already being utilized in clinical trials for other types of tumors in the United States," Giordano concludes.

Domenico Di Marzo, Iris Maria Forte, Paola Indovina, Elena Di Gennaro, Valeria Rizzo, Francesca Giorgi, Eliseo Mattioli, Carmelina Antonella Iannuzzi, Alfredo Budillon, Antonio Giordano, Francesca Pentimalli. Pharmacological targeting of p53 through RITA is an effective antitumoral strategy for malignant pleural mesothelioma. Cell Cycle, December 2013

<http://www.sciencedaily.com/releases/2014/01/140117104027.htm>

New Insights Into Facial Transplantation

T cells, involved in the rejection process are significantly of donor origin

In 2009, the first face transplant was performed at Brigham and Women's Hospital (BWH), and lead surgeon, Dr. Bohdan Pomahac has been pioneering the procedure since. However, understanding the technical challenges, particularly around how the recipient accepts or rejects the donated face, is just beginning.

Following any transplant, including facial transplant, T cells in the recipient mount an immune response to the donated tissue, threatening rejection. This process is successfully managed through immunosuppression medication so that the recipient is able to tolerate the transplanted face.

Now, researchers at BWH have made a discovery that provides new insight into the body's rejection process. Researchers have demonstrated that immune cells, or T cells, involved in the rejection process are significantly of donor origin. These findings are published in *Modern Pathology* on January 17, 2014.

"The conventional belief about face transplant was that rejection is directly related to the recipient T cells attacking the donor T cells of the face, which are perceived as foreign to the recipient's immune system," explained Christine Lian, MD, a skin pathologist at BWH and lead author of this study. "We now need to rethink this process. Based on our findings, it is clear that the donor T cells, which are transferred as part of the new face, play a significant role in the rejection process as well."

The researchers examined 131 face transplant biopsy specimens from a total of five patients who received a face transplant between 2009 and 2013 at BWH.

The samples were examined by conventional microscopy for categorizing the level of rejection and guiding immunosuppressant therapy, and additional antibody based biomarkers were also applied.

The use of biomarkers allowed the researchers to differentiate between the donor and recipient cells under the microscope. Researchers found that during active rejection episodes, many to most of the immune cells in the face specimens that were involved in the rejection were of donor origin.

"The participation of these donor immune cells in face transplant rejection represents a paradigm shift in the understanding of the rejection process," explained George F. Murphy, MD, director of Dermatopathology at BWH and a senior author of this study. "One intriguing possibility that now exists is that the transplanted faces are not simply passive targets vulnerable to rejection, but carry along with them their own army of immune cells that may defend the face against attacking recipient cells in order to thwart the rejection process," says Murphy.

Researchers note that more studies need to be done to better understand these complex immune cell interactions, but these new findings will help to develop the best diagnostic and therapeutic strategies that, for the first time, will consider include immune cells from the donor as well as the recipient.

Christine Guo Lian, Ericka M Bueno, Scott R Granter, Alvaro C Laga, Arturo P Saavedra, William M Lin, Joseph S Susa, Qian Zhan, Anil K Chandraker, Stefan G Tullius, Bohdan Pomahac, George F Murphy. Biomarker evaluation of face transplant rejection: association of donor T cells with target cell injury. Modern Pathology, 2014; DOI: 10.1038/modpathol.2013.249

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

Rise in Bird Flu Cases in China Stokes Worry Before Peak Travel Time

Concerns among health experts that bird flu may be spreading and could pose a further threat as the world's largest annual human migration begins

By KEITH BRADSHERJAN. 17, 2014

HONG KONG - China is disclosing a steadily growing number of cases of H7N9 bird flu, including four more cases announced on Friday, reviving concerns among health experts that the disease may be spreading and could pose a further threat as the world's largest annual human migration begins ahead of Chinese New Year. Mainland China has confirmed 14 cases this week alone, including the four announced on Friday, and seven on Thursday.

Human cases of the H7N9 avian influenza virus began to emerge in late March near Shanghai, infecting 131 people, including 26 who died, by early May. The virus then seemed to fade away, as influenza viruses often do over the summer. The virus then re-emerged much earlier in the season last October with a trickle of cases, and that trickle has now accelerated in January.

The increased tempo of cases comes just before people across China begin their traditional trips to family reunions for celebrations of the Chinese New Year, which falls on Jan. 31 this year. The official travel season in China began Thursday, with the government estimating that 3.62 billion trips would be taken in the next 40 days by road, train, airplane and other modes of transportation.

Many of those trips are to hometowns in rural areas. A large majority of today's Chinese grew up in the countryside, even though the country as a whole became more than 50 percent urban in 2011 because of heavy migration to factories, construction sites and universities in cities.

Contact with poultry, common in rural areas, is still the main route of infection for the virus. Heavy travel in densely packed vehicles offers the virus more chances to pass from person to person, and possibly evolve into new forms that may be more readily transmissible.

In a sign that governments around the region are starting to take precautions as well, Hong Kong announced late Friday that it would begin conducting blood tests on Jan. 24 on local and imported poultry to determine if they have the virus. Any birds with confirmed infections will be killed, as will any birds that have been kept with the infected birds, said Dr. Ko Wing-man, the secretary for food and health.

Health experts are watching closely for two warning signs of greater human-to-human transmission that have not yet occurred on a large scale.

One sign would be a spate of cases among people who have had no apparent contact with poultry or environments contaminated by the feces, uncooked blood or other fluids of poultry. The other would be a series of cases in which several members of the same family fall ill in quick succession and appear to have transmitted the disease to one another.

Helen Yu, a spokeswoman for the Beijing office of the World Health Organization, wrote in an email that the proportion of cases among people who had no contact with poultry had stayed low since the disease emerged nearly a year ago and showed no sign of increasing this winter.

Similarly, there has been only one family cluster of cases this winter, compared with four clusters last spring.

"It is possible that limited human-to-human transmission may occur, but there is no evidence of sustained or widespread human-to-human transmission," she wrote. "We continue to expect sporadic human cases."

Extensive testing for bird flu may also result in more cases being detected even if the actual rate of infections is not increasing as rapidly as the data on confirmed infections might suggest.

Yet the H7N9 virus remains a particular concern for two reasons.

It has a series of genetic mutations that have been associated in other viruses with greater adaptation to human-to-human transmission. And the H7N9 virus has proved itself to be "much, much better than other avian influenza viruses" at growing in human lung tissue samples in a laboratory at Hong Kong University, said Dr. Malik Peiris, a prominent avian influenza researcher at the university.

The laboratory uses lung tissue that was removed from people during lung cancer surgery or other procedures. The tissue would normally be discarded after such surgeries but is sent to the laboratory for tests instead, Dr. Peiris said.

The Center for Infectious Disease Research and Policy at the University of Minnesota noted in a short report on Thursday that the pace of new cases in China in recent days has already matched the busiest pace reached last spring.

According to the W.H.O., 183 cases have been reported from mainland China since last March. Hong Kong has also reported three cases, and Taiwan has reported two, all of them involving people apparently infected in mainland China.

The W.H.O. is not currently recommending any restrictions on travel to China. But the Geneva-based organization is suggesting that visitors to China avoid live bird markets or if they must visit them, that they avoid live animals and surfaces in contact with live animals or with the blood or feces of poultry. The organization is also recommending that poultry be cooked thoroughly, that poultry-cooking implements be cleaned thoroughly, and that visitors wash their hands regularly and cover their mouths and noses when coughing or sneezing.

<http://www.bbc.co.uk/news/science-environment-25743806>

Is our Sun falling silent?

"I've been a solar physicist for 30 years, and I've never seen anything quite like this," says Richard Harrison, head of space physics at the Rutherford Appleton Laboratory in Oxfordshire.

Rebecca Morelle By Rebecca Morelle Science reporter, BBC World Service

"I've been a solar physicist for 30 years, and I've never seen anything quite like this," says Richard Harrison, head of space physics at the Rutherford Appleton Laboratory in Oxfordshire. He shows me recent footage captured by spacecraft that have their sights trained on our star. The Sun is revealed in exquisite detail, but its face is strangely featureless. "If you want to go back to see when the Sun was this inactive... you've got to go back about 100 years," he says.

This solar lull is baffling scientists, because right now the Sun should be awash with activity. It has reached its solar maximum, the point in its 11-year cycle where activity is at a peak.

This giant ball of plasma should be peppered with sunspots, exploding with flares and spewing out huge clouds of charged particles into space in the form of coronal mass ejections. But apart from the odd event, like some recent solar flares, it has been very quiet. And this damp squib of a maximum follows a solar minimum - the period when the Sun's activity troughs - that was longer and lower than scientists expected.

"It's completely taken me and many other solar scientists by surprise," says Dr Lucie Green, from University College London's Mullard Space Science Laboratory.

The drop off in activity is happening surprisingly quickly, and scientists are now watching closely to see if it will continue to plummet. "It could mean a very, very inactive star, it would feel like the Sun is asleep... a very dormant ball of gas at the centre of our Solar System," explains Dr Green.

This, though, would certainly not be the first time this has happened. During the latter half of the 17th Century, the Sun went through an extremely quiet phase - a period called the Maunder Minimum. Historical records reveal that sunspots virtually disappeared during this time. Dr Green says: "There is a very strong hint that the Sun is acting in the same way now as it did in the run-up to the Maunder Minimum."

Mike Lockwood, professor of space environment physics, from the University of Reading, thinks there is a significant chance that the Sun could become increasingly quiet.

An analysis of ice-cores, which hold a long-term record of solar activity, suggests the decline in activity is the fastest that has been seen in 10,000 years. "It's an unusually rapid decline," explains Prof Lockwood. "We estimate that within about 40 years or so there is a 10% to 20% - nearer 20% - probability that we'll be back in Maunder Minimum conditions."

The era of solar inactivity in the 17th Century coincided with a period of bitterly cold winters in Europe.

Londoners enjoyed frost fairs on the Thames after it froze over, snow cover across the continent increased, the Baltic Sea iced over - the conditions were so harsh, some describe it as a mini-Ice Age.

And Prof Lockwood believes that this regional effect could have been in part driven by the dearth of activity on the Sun, and may happen again if our star continues to wane. "It's a very active research topic at the present time, but we do think there is a mechanism in Europe where we should expect more cold winters when solar activity is low," he says. He believes this local effect happens because the amount of ultraviolet light radiating from the Sun dips when solar activity is low.

This means that less UV radiation hits the stratosphere - the layer of air that sits high above the Earth. And this in turn feeds into the jet stream - the fast-flowing air current in the upper atmosphere that can drive the weather. The results of this are dominantly felt above Europe, says Prof Lockwood.

"These are large meanders in the jet stream, and they're called blocking events because they block off the normal moist, mild winds we get from the Atlantic, and instead we get cold air being dragged down from the Arctic and from Russia," he says. "These are what we call a cold snap... a series of three or four cold snaps in a row adds up to a cold winter. And that's quite likely what we'll see as solar activity declines."

So could this regional change in Europe have a knock-on effect on for the rest of the world's climate? And what are the implications for global warming?

In a recent report by the UN's climate panel, scientists concluded that they were 95% certain that humans were the "dominant cause" of global warming since the 1950s, and if greenhouse gases continue to rise at their current rate, then the global mean temperature could rise by as much as 4.8C.

And while some have argued that ebbs and flows in the Sun's activity are driving the climate - overriding the effect of greenhouse gas emissions, the Intergovernmental Panel on Climate Change concludes that solar variation only makes a small contribution to the Earth's climate.

Prof Lockwood says that while UV light varies with solar activity, other forms of radiation from the Sun that penetrate the troposphere (the lower layer of air that sits above the Earth) do not change that much.

He explains: "If we take all the science that we know relating to how the Sun emits heat and light and how that heat and light powers our climate system, and we look at the climate system globally, the difference that it makes even going back into Maunder Minimum conditions is very small.

"I've done a number of studies that show at the very most it might buy you about five years before you reach a certain global average temperature level. But that's not to say, on a more regional basis there aren't changes to the patterns of our weather that we'll have to get used to."

But this weather would not be the only consequence of a drawn out period of inactivity, says Dr Green.

"If the Sun were to get very quiet, one of the few things that would happen is that we'd have very few displays of the northern lights. They are driven by solar activity, and we'd miss out on this beautiful natural phenomenon," she explains.

However, there could be positive effects too.

"Solar activity drives a whole range of space weather, and these are ultimately effects on the electricity networks, on satellites, on radio communications and GPS on your sat-nav," she explains.

And while scientists cannot discount that the random bursts of activity may still occur, calmer periods of space weather would help to maintain the technological infrastructure that we rely so heavily on.

While the full consequences of a quietening Sun are not fully understood, one thing scientists are certain about is that our star is unpredictable, and anything could happen next.

"This feels like a period where it's very strange... but also it stresses that we don't really understand the star that we live with." says Prof Harrison. "Because it's complicated - it's a complex beast."

http://www.eurekaalert.org/pub_releases/2014-01/uoea-icc011714.php

Ingredients in chocolate, tea and berries could guard against diabetes

Eating high levels of flavonoids including anthocyanins and other compounds could offer protection from type 2 diabetes

Eating high levels of flavonoids including anthocyanins and other compounds (found in berries, tea, and chocolate) could offer protection from type 2 diabetes - according to research from the University of East Anglia (UEA) and King's College London.

Findings published today in the Journal of Nutrition reveal that high intakes of these dietary compounds are associated with lower insulin resistance and better blood glucose regulation.

A study of almost 2,000 people also found that these food groups lower inflammation which, when chronic, is associated with diabetes, obesity, cardiovascular disease, and cancer.

Prof Aedin Cassidy from UEA's Norwich Medical School led the research. She said: "Our research looked at the benefits of eating certain sub-groups of flavanoids. We focused on flavones, which are found in herbs and vegetables such as parsley, thyme, and celery, and anthocyanins, found in berries, red grapes, wine and other red or blue-coloured fruits and vegetables.

"This is one of the first large-scale human studies to look at how these powerful bioactive compounds might reduce the risk of diabetes. Laboratory studies have shown these types of foods might modulate blood glucose regulation – affecting the risk of type 2 diabetes. But until now little has been known about how habitual intakes might affect insulin resistance, blood glucose regulation and inflammation in humans."

Researchers studied almost 2,000 healthy women volunteers from TwinsUK who had completed a food questionnaire designed to estimate total dietary flavonoid intake as well as intakes from six flavonoid subclasses. Blood samples were analysed for evidence of both glucose regulation and inflammation. Insulin resistance, a hallmark of type 2 diabetes, was assessed using an equation that considered both fasting insulin and glucose levels.

"We found that those who consumed plenty of anthocyanins and flavones had lower insulin resistance. High insulin resistance is associated with Type 2 diabetes, so what we are seeing is that people who eat foods rich in these two compounds – such as berries, herbs, red grapes, wine– are less likely to develop the disease.

"We also found that those who ate the most anthocyanins were least likely to suffer chronic inflammation – which is associated with many of today's most pressing health concerns including diabetes, obesity, cardiovascular disease, and cancer.

"And those who consumed the most flavone compounds had improved levels of a protein (adiponectin) which helps regulate a number of metabolic processes including glucose levels.

"What we don't yet know is exactly how much of these compounds are necessary to potentially reduce the risk of type 2 diabetes," she added.

Prof Tim Spector, research collaborator and director of the TwinsUK study from King's College London, said: "This is an exciting finding that shows that some components of foods that we consider unhealthy like chocolate or wine may contain some beneficial substances. If we can start to identify and separate these substances we can potentially improve healthy eating. There are many reasons including genetics why people prefer certain foods so we should be cautious until we test them properly in randomised trials and in people developing early diabetes."

'Intakes of Anthocyanins and Flavones Are Associated with Biomarkers of Insulin Resistance and Inflammation in Women' by Jennings A, Welch AA, Spector T, Macgregor A, and Cassidy A, is published in the Journal of Nutrition on Monday, January 20, 2014.

http://www.eurekalert.org/pub_releases/2014-01/uoe-icc011714.php

Island channel could power about half of Scotland, studies show

Renewable tidal energy sufficient to power about half of Scotland could be harnessed from a single stretch of water off the north coast of the country, engineers say

Renewable tidal energy sufficient to power about half of Scotland could be harnessed from a single stretch of water off the north coast of the country, engineers say.

Researchers have completed the most detailed study yet of how much tidal power could be generated by turbines placed in the Pentland Firth, between mainland Scotland and Orkney, and estimate 1.9 gigawatts (GW) could be available.

The in-depth assessment by engineers at the Universities of Oxford and Edinburgh offers valuable insights into how to develop and regulate this clean energy resource effectively.

The Pentland Firth is a prime candidate to house marine power projects because of its tidal currents, which are among the fastest in the British Isles.

Engineers say that their study improves on previous estimates of the generating capacity of turbines embedded in the Firth – ranging from 1 to 18 GW – which were too simplistic or based on inappropriate models.

Researchers calculated that as much as 4.2 GW could be captured, but because tidal turbines are not 100 per cent efficient, they say that 1.9 GW is a more realistic target.

To exploit the Firth's full potential, turbines would need to be located across the entire width of the channel. In order to minimise the impacts on sea life and shipping trade, a number of individual sites have been identified for development by the UK Crown Estate, which will lease these sites to tidal energy firms.

Researchers have pinpointed locations where turbines would need to be positioned for the Firth to meet its full energy production potential.

The research was commissioned and funded as part of the Energy Technologies Institute's Performance Assessment of Wave and Tidal Array Systems project (PerAWAT).

Professor Alistair Borthwick, of the School of Engineering at the University of Edinburgh, who worked on the research, said: "Our research builds on earlier studies by analysing the interactions between turbines and the tides more closely. This is a more accurate approach than was used in the early days of tidal stream power assessment, and should be useful in calculating how much power might realistically be recoverable from the Pentland Firth."

Professor Guy Houlby of the Department of Engineering Science, University of Oxford, said: "The UK enjoys potentially some of the best tidal resources worldwide, and if we exploit them wisely they could make an important contribution to our energy supply. These studies should move us closer towards the successful exploitation of the tides."