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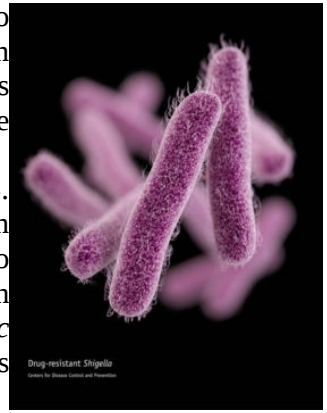
Highly Contagious, Antibiotic-Resistant Food Poisoning Establishes U.S. Presence [Infographic]

A Scientific American investigation explores the growing threat from multidrug-resistant shigella in the U.S.

By Rebecca Harrington | May 18, 2015 | Véalo en español

The kinds of bacteria that can cause food poisoning lurk all around us. These germs can be especially easy to pick up when traveling internationally as well as in places, such as children's day cares, which are hard to keep clean. The infections usually clear up on their own but sometimes require hospitalizations and hefty doses of antibiotics to expunge. Unfortunately, the bacteria are becoming increasingly resistant to treatment.



The latest bad news came in April when the U.S. Centers for Disease Control and Prevention reported an outbreak of *Shigella sonnei* that has become resistant to ciprofloxacin - one of the last remaining medications in pill form that can kill the germ. Since then a *Scientific American* investigation shows the worrisome strain is still circulating in the U.S. a year after it first emerged.

Shigella sonnei is a rod-shaped bacterium that causes 500,000 cases of diarrheal illness and 40 deaths in the United States every year. **Centers for Disease Control and Prevention**

Shigella bacteria typically cause about 500,000 diarrheal illnesses and 40 deaths in the U.S. every year. Children who are malnourished and people with compromised immune systems are particularly at risk of developing severe cases. Symptoms include diarrhea that is sometimes bloody, fever and abdominal pain, and typically last about a week.

The bacteria occur naturally in the U.S. but, heretofore, people typically caught ciprofloxacin-resistant strains while traveling internationally. In the current outbreak, however, many people who became sick had not recently been out of the country, which proves that the multidrug-resistant bug has now established a firm domestic presence.

The CDC has confirmed 275 cases of ciprofloxacin-resistant shigella across the country from May 2014 to May 2015, according to data obtained exclusively by *Scientific American* (see chart below).

Although these figures appear small, they almost certainly represent but a tiny fraction of the true number of ciprofloxacin-resistant cases. Shigella infections are supposed to be reported to the CDC but a lot of people who get sick do not go to the doctor. And those who do are sometimes not tested for the presence of shigella, let alone drug resistance. Vulnerable populations are some of the hardest hit in this outbreak, including cases linked to a day care center, homeless people in San Francisco and HIV-positive individuals in Philadelphia. As few as 10 shigella germs can cause an infection - making the bacteria virtually undetectable as it quickly spreads in contaminated food and water or from person to person.

Other drugs that the pathogen has overcome in the past include ampicillin, streptomycin and tetracycline. Anna Bowen, a medical officer in the CDC's Waterborne Diseases Prevention Branch and lead author of the April study, says the CDC has identified some cases in this outbreak that were resistant to all of the oral treatment options currently available. The next line of defense is a broader-spectrum, more expensive antibiotic that must be administered via injection or an intravenous line.

Whereas labs can test for ciprofloxacin resistance, there are currently no standardized tests to identify if a shigella infection is resistant to azithromycin, which is the go-to drug for children. (The U.S. Food and Drug Administration has approved ciprofloxacin only for adults.) "Almost no clinical labs are doing this sort of testing," Bowen says, "and so patients are being treated kind of blindly since the providers don't know if azithromycin is an appropriate choice or not."

Lag time in reporting is another issue. San Francisco, for example, is tracking nearly two times the number of cases that the CDC counts as confirmed for the city - 228 cases versus 119.

Cora Hoover, director of Communicable Disease Control and Prevention for the San Francisco Department of Public Health, says they have slightly different case definitions because as the city agency on the ground investigating this outbreak they want assurance all possible patients are identified; also it takes so long to confirm a case. Public health officials normally follow up with each patient, and lab tests can take weeks.

It can take around a month to confirm a case of shigellosis is both antibiotic-resistant and part of the same outbreak, though it varies. Generally, once a doctor identifies a shigella infection, he or she reports it to the city or state public health agency and sends a stool sample to the lab to confirm the diagnosis.

The lab grows or "cultures" the bacteria and reports its findings back to the doctor and agency in about a week. The health agency then reports the case to the CDC, which tests a selection of cases for antibiotic resistance via the National Antimicrobial Resistance Monitoring System and its national laboratory network, PulseNet. Results from PulseNet's genetic testing of sample cases can be complete within a couple of weeks. By the time the full picture of a single case is confirmed, the patient is usually better.

Caroline Johnson, director of the Division of Disease Control at Public Health for the City of Philadelphia, says her division usually suspects that a case is part of an outbreak but does not know for sure until the full results are in. Peter Gerner-Smidt, chief of the CDC's Enteric Diseases Laboratory Branch and PulseNet, says labs will gradually move away from having to culture bacteria to identify them.

As genetic testing becomes cheaper and more accessible, state labs will eventually be able to get that information by determining the whole DNA sequence of each sample. This approach will hopefully reveal antibiotic-resistance more quickly, he says, but it will likely take years before these tests are widely used.

Because of the increasing threat of multidrug-resistant shigella, the CDC and other health agencies recommend doctors only prescribe antibiotics for severe cases. Shigellosis can actually clear up on its own with proper hydration and rest. Prevention is therefore the best weapon for controlling resistant shigella, Bowen says, particularly because the U.S. cannot regulate antibiotic overuse in other countries, but it still affects patients here.

"Problems with antibiotic resistance anywhere are problems with antibiotic resistance everywhere," she says. "There are no borders when it comes to antibiotic resistance, and we have all got to be vigilant."

http://www.eurekalert.org/pub_releases/2015-05/uomh-tah051815.php

Temper, anxiety, homework trouble are medical issues? Many parents don't realize it

Just half of parents of school-aged children would discuss anxiety or temper tantrums that seemed worse than peers

VIDEO: Sarah J. Clark, M.P.H., associate director of the National Poll on Children's Health, discusses findings on the latest Mott poll regarding behavioral health.

University of Michigan C.S. Mott Children's Hospital National Poll on Children's Health

ANN ARBOR, Mich. - Parents often bring their school-aged children to check-ups or sick visits armed with questions. What should he put on that rash? What about her cough that won't go away?

But when children's temper tantrums or mood swings are beyond the norm, or they are overwhelmed by homework organization, do parents speak up?

Today's University of Michigan C.S. Mott Children's Hospital National Poll on Children's Health finds that many parents of children age 5-17 wouldn't discuss behavioral or emotional issues that could be signs of potential health problems with their doctors. While more than 60 percent of parents definitely would talk to the doctor if their child was extremely sad for more than a month, only half would discuss temper tantrums that seemed worse than peers or if their child seemed more worried or anxious than normal. Just 37 percent would tell the doctor if their child had trouble organizing homework.

The most common reason for not sharing these details with their children's doctors?

Nearly half of parents believed that these simply were not medical problems. Another 40 percent of parents say they would rather handle it themselves and about 30 percent would rather speak to someone other than a doctor.

"Behavioral health and emotional health are closely tied to a child's physical health, well-being and development, but our findings suggest that we are often missing the boat in catching issues early," says Sarah J. Clark, M.P.H., associate director of the National Poll on Children's Health and associate research scientist in the University of Michigan Department of Pediatrics.

"Many children experience challenges with behavior, emotions or learning. The key is for parents to recognize their children's behavior patterns and share that information with the doctor. Unfortunately, our findings suggest that parents don't understand their role in supporting their children's behavioral health."

The findings come just as the nation recognizes mental health awareness month in May. Behavioral health problems, sometimes called mental health problems, affect boys and girls of all ages, impacting their learning, social interactions and physical health. While some behavior and emotional issues are mild and short-lived, others are signs of longer-term problems like depression, attention deficit-hyperactivity disorder, anxiety, mood and behavior disorders, or substance abuse.

"Some behavioral and emotional changes are just part of a child's natural growth and development and just part of growing up," Clark says.

"However, health care providers rely on parents to describe how children act in their regular, day-to-day lives outside of the doctor's office in order to identify situations or behaviors that may be signs of larger problems.

This conversation between doctors and parents is an essential step that allows providers to assess the severity of the problem, offer parents guidance on strategies to deal with certain behaviors and help families get treatment if needed."

Full report: C.S. Mott Children's Hospital National Poll on Children's Health *http://mottnpch.org/reports-surveys/many-parents-missing-link-between-child-behavior-and-health*

http://www.eurekalert.org/pub_releases/2015-05/uomh-uti051815.php

Urine-based test improves on PSA for detecting prostate cancer

Use of Mi-Prostate Score would reduce unneeded biopsies

ANN ARBOR, Mich. - A new urine-based test improved prostate cancer detection - including detecting more aggressive forms of prostate cancer - compared to traditional models based on prostate serum antigen, or PSA, levels, a new study finds.

The test, developed at the University of Michigan Comprehensive Cancer Center, is called Mi-Prostate Score, or MiPS. It combines PSA with two markers for prostate cancer, T2:ERG and PCA3, both of which can be detected through a urine sample. The test has been available clinically since September 2013.

"Around 50 percent of men who undergo a prostate biopsy will not have cancer. We need better ways to manage elevated PSA and determine who really needs to have a biopsy. MiPS gives men and their doctors better information to help make those decisions," says lead study author Scott A. Tomlins, M.D., Ph.D., assistant professor of pathology and urology at the University of Michigan Medical School.

The study looked at a total of 1,977 men who were undergoing prostate biopsy because of elevated PSA levels. Using urine samples, the researchers conducted MiPS testing and compared results to various combinations of PSA, PCA3, T2:ERG and other PSA-based risk calculators. They assessed how well the individual biomarkers and combinations of biomarkers predicted the likelihood of cancer and the likelihood of high-risk cancer - the aggressive type that needs immediate treatment.

The test reports individual risk estimates for prostate cancer and high grade cancer. Each patient's personal threshold for choosing to undergo biopsy may vary, so there is no single cutoff for a "positive" result. However, using one MiPS cutoff score to decide whether to biopsy patients would reduce the number of biopsies by one-third, while delaying the diagnosis of only about 1 percent of high-risk prostate cancers."MiPS gives men a more individualized risk assessment for prostate cancer, so that men concerned about their serum PSA levels can have a more informed conversation with their doctor about next steps in their care," Tomlins says. A cost/benefit analysis of MiPS is being conducted.

PCA3 is approved by the U.S. Food and Drug Administration for prostate cancer risk assessment in men with a previous negative biopsy. Most of the men involved in this study were undergoing initial biopsy, suggesting MiPS can be useful earlier in the process.

The test is part of broader efforts at the University of Michigan to improve prostate cancer diagnosis, particularly detecting the type of cancer that requires immediate and aggressive treatment.

Mi-Prostate Score is available to anyone but requires a request from a doctor. For further information, call the University of Michigan's MLabs at 800-862-7284. Patients with questions about prostate cancer detection or treatment may call the U-M Cancer AnswerLine at 800-865-1125.

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Disclosure: The University of Michigan has been issued a patent on the detection of ETS gene fusions in prostate cancer on which Chinnaiyan and Tomlins are listed as co-inventors. The University of Michigan licensed the diagnostic field of use to Hologic/Gen-Probe Inc., which sublicensed some rights to Ventana Medical Systems. Chinnaiyan has served as consultant to Gen-Probe and Ventana. Tomlins has received Honoria from and served as a consultant to Ventana.

Reference: European Urology, "Urine TMPRSS2:ERG Plus PCA3 for Individualized Prostate Cancer Risk Assessment," http://dx.doi.org/10.1016/j.eururo.2015.04.039

http://www.eurekalert.org/pub_releases/2015-05/nyu-gmw051815.php

Going my way? We think so, if we really want to get there, NYU study finds

The more committed we are to achieving that goal, the more likely we are to assume others have exactly the same objective

Whether we're buying a ticket to a movie, catching a train, or shopping for groceries, the more committed we are to achieving that goal, the more likely we are to assume others have exactly the same objective, a study by New York University psychology researcher Janet Ahn shows.

The findings, which appear in the European Journal of Social Psychology, point to the types of assumptions we make about others' behavior, which may have an impact on social interaction. It may be downloaded here: http://bit.ly/1bZJf1D.

"If we're fixated on seeing that blockbuster film or purchasing those fresh strawberries, we're more likely to see others wanting to do the same," explains Ahn, an NYU doctoral candidate. "These assumptions may unnecessarily spur a competitive spirit and, with it, more aggressive behavior."

The study, co-authored with NYU psychology professors Gabriele Oettingen and Peter Gollwitzer, centers on a well-established psychological phenomenon, "goal projection," which is an egocentric way of understanding other people's goals by projecting your goals onto them - or, put another way, assuming that others share the same goal as you. To determine how goal projection applies in certain real-life situations, Ahn conducted surveys in three different New York City environments: a multiplex movie theater near Union Square, Penn Station, and outside a Whole Foods Market.

In the movie-theater study, Ahn and her colleagues randomly approached people preparing to buy tickets, asking them to identify both the movie they came to see and then, to gauge their goal commitment, "How badly do you want to watch this movie?" Responses were on a 1- (not at all) to 5-point (extremely) scale. The

researchers then pointed out the first person waiting in line to purchase a ticket at the multiplex and asked the test subjects which movie they thought the individual was going to see.

The researchers controlled for the frequency at which the subjects attended the movies and the popularity of the movies playing the multiplex - two variables that may increase the likelihood of making informed guesses rather than ones driven by goal projection. The results showed that among these subjects, the stronger participants' goal commitment, the higher the probability of inferring that the target person had the goal to watch the same movie.

In the second study - of commuters at Penn Station from which dozens of trains depart every hour - the researchers approached people waiting for the track number of their train to appear. Test subjects were asked their destination; their goal commitment was ascertained through two questions: "How frustrated would you be if you missed your train?" and "How rushed are you to get to your destination?"

At this point, experimenters singled out a target person who was waiting in closest vicinity to them and was easily observable. Here, they also wanted to determine if perceived similarity to the target could influence goal projection, so the researchers asked test subjects how similar to themselves they perceived the target person. The study measured goal projection by asking subjects how likely the target was headed to the same destination they were.

The results showed that participants with strong goal commitment were more likely to believe the target person would go to the same destination the more that person was perceived to be similar - but this was not true of participants with weak goal commitment. In other words, perceived similarity can dampen goal projection.

In the final study, conducted outside a Whole Foods Market, the researchers examined whether differences in goal attainment affect the relationship between goal commitment and the perceived similarity of the target person.

The researchers studied two types of individuals: those surveyed before shopping, and who had yet to attain their goal, and those surveyed after shopping and had reached their goal. Participants were asked to name the main item they came to purchase, or just purchased, then indicated their goal commitment to purchase that item: 1 (not at all) to 7 (extremely).

The researchers then chose a target person who was just about to enter the supermarket at that given moment for both types of shoppers - those who were going to shop and shoppers who just shopped. Participants indicated how similar to themselves they viewed the target person using a 7-point scale: "How similar do you think that person is to you?" Then, as an indication of goal projection, participants answered the following item: "Please indicate the probability (from 1-100%) that the other shopper is committed to purchasing the same item."

The study's subjects projected their goal onto another shopper when goal commitment was strong and the target person was viewed to be similar, as long as the goal had not been attained yet - a finding consistent with the train study.

However, when the subjects had already achieved their goals - that is, they'd completed their shopping - there was no relationship between goal commitment and perceived similarity with another.

"After purchasing their groceries, these shoppers, compared to those who were about to shop, were less likely to think others wanted the same products," explains Ahn. "This suggests there is a competitive aspect to goal projection - we think others are after the same things if we have yet to obtain them."

http://www.eurekalert.org/pub_releases/2015-05/osu-pao051815.php

Pactamycin analogs offer new, gentler approach to cancer treatment

Two promising "analogs" of an old compound that was once studied as a potent anti-tumor agent, but long ago abandoned because it was too toxic

CORVALLIS, Ore. - Researchers at Oregon State University are pursuing a new concept in treatment of epithelial cancer, especially head and neck cancer, by using two promising "analogs" of an old compound that was once studied as a potent anti-tumor agent, but long ago abandoned because it was too toxic.

The analogs are more highly selective than the parent compound, pactamycin, which originally was found to kill all cells, from bacteria to mammals, by inhibiting their protein synthesis.

The pactamycin analogs, which were developed with biosynthetic engineering, also offer a different approach toward cancer therapy - an effort to essentially put cancer cells to sleep, instead of killing them. If successful, this trend may herald a new future in "kinder and gentler" cancer treatments.

Findings on this promising approach to cancer were just published in PLOS One, in work supported by the National Institute of Health and other agencies.

The effects of the pactamycin analogs, called TM-025 and TM-026, were characterized in head and neck cancer cell lines, which cause the eighth most common cancer in the world. But they may have applications to a wider range of cancers, the researchers said, particularly melanoma.

"A traditional view of chemotherapy is that you try to completely kill cancer cells and destroy tumors," said Arup Indra, an associate professor in the OSU College of Pharmacy and one of the lead authors on the study. "Sometimes this is effective, sometimes not as much. An alternative approach is to cause rapid cell aging and

induce premature senescence, which we believe could become a new frontier in cancer drug development."

A senescent cancer cell, Indra said, doesn't usually die, but the growth of it and the larger tumor is slowed or stops, and it continues to live in a vegetative state, almost like being asleep. Such an approach can be an alternative way to control cancer without completely killing it, which may help reduce problems with resistance that can quickly develop to chemotherapeutic drugs. And it also avoids some of the most toxic and debilitating side effects of cancer chemotherapies, which are often caused by cell death.

The new findings showed that these analogs of pactamycin largely stopped cancer cell proliferation and growth, causing cells to age and lose their ability to divide and grow. These effects are partly mediated by tumor suppressor p53, which is frequently mutated in human cancers. They do not yet form the basis for a therapy, researchers said, because methods must still be perfected to get them more selectively into the cancer cells.

"With further research we hope to create a nontoxic nanocarrier that could provide targeted delivery of the TM-025 and TM-026 analogs specifically to cancer cells," said Gitali Indra, an OSU assistant professor and also a lead and corresponding author on the study. "In some cases, such as oral cancer, it may also be possible to use topical treatments. But this approach should have significant promise if we can develop techniques to adequately target the cancer cells."

The OSU researchers are continuing work to more fully understand the mode of action of these pactamycin analogs. Collaborators on this study include Taifo Mahmud, an OSU professor in the College of Pharmacy, and researchers from the Oregon Health & Science University. The study this story is based on is available online: http://bit.ly/1PlJvdS

http://www.eurekalert.org/pub_releases/2015-05/mali-btt051815.php

Blood test to detect traumatic brain injury could reduce unnecessary CT scans

Simple blood test to measure brain-specific proteins released after traumatic brain injury reliably predicts both evidence of TBI on radiographic imaging and injury severity

New Rochelle, NY - New study results show that a simple blood test to measure brain-specific proteins released after a person suffers a traumatic brain injury (TBI) can reliably predict both evidence of TBI on radiographic imaging and injury severity.

The potential benefit of adding detection of glial fibrillary acidic protein breakdown products (GFAP-BDP) to clinical screening with computed tomography (CT) and magnetic resonance imaging (MRI) is described in an article published in Journal of Neurotrauma, a peer-reviewed journal from Mary Ann Liebert, Inc., publishers (http://www.liebertpub.com/).

The article is available free on the Journal of Neurotrauma (http://online.liebertpub.com/doi/full/10.1089/neu.2014.3635) website until June 18, 2015.

Paul McMahon, University of Pittsburgh Medical Center, and a team of international researchers, including TRACK-TBI investigators, analyzed blood levels of GFAP-BDP from patients ages 16-93 years treated at multiple trauma centers for suspected TBI. They evaluated the ability of the blood-based biomarker to predict intracranial injury as compared to the findings on an admission CT and a delayed MRI scan.

The authors reported a net benefit for the use of GFAP-BDP above imaging-based screening alone and a net reduction in unnecessary scans by 12-30% in the article "Measurement of the Glial Fibrillary Acidic Protein and Its Breakdown Products GFAP-BDP Biomarker for the Detection of Traumatic Brain Injury Compared to Computed Tomography and Magnetic Resonance Imaging (http://online.liebertpub.com/doi/full/10.1089/neu.2014.3635)."

John T. Povlishock, PhD, Editor-in-Chief of Journal of Neurotrauma and Professor, Medical College of Virginia Campus of Virginia Commonwealth University, Richmond, notes that "this impressive multi-center study joins with other streams of emerging evidence supporting the use of biomarkers as an important tool in the clinical decision making and prediction process."

"Importantly, this study significantly expands upon other studies that speak to the usefulness of GFAP and, specifically, serum-derived GFAP-BDP in identifying those traumatically brain injured patients whose clinical course is complicated by intracranial injury, demonstrating that GFAP-BDP offers good predictive ability, significant discrimination of injury severity, and net benefit in reducing the need for unnecessary scans, all of which have significant implications for the brain injured patient," says Dr. Povlishock.

http://www.eurekalert.org/pub_releases/2015-05/uota-mpb051815.php

Mobile phone bans lead to rise in student test scores

Banning cellphones in schools reaps the same benefits as extending the school year by five days, according to a study co-authored by an economist at The University of Texas at Austin.

"New technologies are typically thought of as improving productivity, however this is not always the case," said Richard Murphy, an assistant professor of economics.

"When technology is multipurpose, such as cellphones, it can be both distracting and disruptive."

Murphy and Louis-Philippe Beland, an assistant professor of economics at Louisiana State University, measured the impact of mobile phones on student performance by surveying 91 schools in four English cities (Birmingham, London, Leicester and Manchester) before and after strict cellphone policies were implemented.

By comparing student exam records and mobile phone policies from 2001 to 2013, researchers noted a significant growth in student achievement in classrooms that banned cellphones, with student test scores improving by 6.41 percent points of a standard deviation.

This made them 2 percentage points more likely to pass the required exams at the end of high school, researchers explained.

"We found the impact of banning phones for these students equivalent to an additional hour a week in school, or to increasing the school year by five days," Murphy said.

Low-achieving students benefited most from the ban, with test scores increasing by 14.23 percent points of a standard deviation - a gain that was double compared with that of average students - making them 4 percentage points more likely to pass the exams.

Likewise, the ban greatly benefitted special education needs students and those eligible for free school meals, improving exam scores 10 and 12 percent points of a standard deviation respectively.

However, researchers found that strict cellphone policies had little effect on both high-achieving students and 14-year-olds, suggesting that high achievers are less distracted by mobile phones and younger teens own and use phones less often.

"This means allowing phones into schools would be the most damaging to low-achieving and low-income students, exacerbating any existing learning inequalities," Murphy said.

"Whilst we cannot test the reason why directly, it is indicative that these students are distracted by the presence of phones, and high-ability students are able to concentrate."

Though phone ownership among English teens is high - 90.3 percent owned a mobile phone by 2012 - results are likely to be significant in U.S. schools where 73 percent of teenagers own a mobile phone, Murphy said.

"Banning cell phones in schools would be a low-cost way for schools to reduce educational inequality," Murphy said.

"However, these findings do not discount the possibility that mobile phones could be a useful learning tool if their use is properly structured.

Regardless, these results show that the presence of cellphones in schools cannot be ignored."

http://www.eurekalert.org/pub_releases/2015-05/tuhs-amc051815.php

Academic medical centers at risk of a 'Kodak moment' if they fail to adapt

Today's academic medical centers (AMCs) need to embrace the changing healthcare marketplace or run the risk of becoming the next Kodak

Philadelphia, PA- Today's academic medical centers (AMCs) need to embrace the changing healthcare marketplace or run the risk of becoming the next Kodak - a former industrial giant that became obsolete when it failed to adapt to a shifting technological landscape.

That is the premise of a commentary published this month electronically ahead of the print edition of Academic Medicine, the journal of the Association of American Medical Colleges. The commentary is authored by Verdi DiSesa, MD, MBA, Chief Operating Officer of the Temple University Health System (TUHS) and Vice Dean for Clinical Affairs and Professor of Surgery at Temple University School of Medicine (TUSM), and Larry Kaiser, MD, President and CEO of TUHS, Senior Executive Vice President for Health Affairs at Temple University, and Dean and Professor of Surgery at TUSM.

"AMCs and those who lead them need to recognize that they are in a business that is transitioning from a system of 'sickness' care to one of 'health' care, accountable for the health of defined populations and for the value of the services provided," says Dr. DiSesa.

According to the authors, a failure to recognize the importance of this transition may impair AMCs irrevocably. They argue that leaders of academic medicine need to understand, respond to and ultimately lead the transformation toward a population health paradigm which demands the best combination of preventive and therapeutic services to deliver the best outcomes at the lowest overall cost.

"Historically, payments have been based on volume - do more for more patients and get paid more," says Dr. Kaiser. "The system fostered incentives to increase the number of services. We are now groping our way to an era in which 'value' will replace 'volume' as the measure driving payment for service. Payers, regulators and patients are demanding a shift from a system of intervention for episodes of illness - 'sickness care' - to one which maximizes the health of the population served - 'health care.'"n

In their commentary, the authors review the pressures driving healthcare changes, including value-based purchasing, "observation" status, denial of payments for re-admission, "risk" contracts, "tiering" based on historical costs, accountable care, and payer-mandated medical management. They also offer potential responses to these challenges, including:

Redesign the delivery mechanisms for specialty referral services by reorganizing them into multi-disciplinary systems of care, usually focused on an organ system (e.g., Heart Institute) or disease process (e.g., Cancer Center), and which engage patients in lifetime health management through a combination of hospital-based and outpatient services

Position AMCs as the tertiary/quaternary hub in a networked system of lower cost-basis community hospitals and outpatient resources

Create new fields of medical specialization such as "observation medicine" or "low-cost hospital medicine," which also incorporate telemedicine and "virtual" outpatient visits into their practice

Accelerate the growth of population health and accountable care as academic disciplines.

"To survive, AMCs will need to become an integral part of a system in which enhancement of population health is the explicit mission," says Dr. DiSesa. "This transformation presumably must be accomplished while the AMCs still fulfill their traditional missions of advanced patient care, teaching and research. It's likely that some AMCs will need to redefine their mission and not try to be everything for everyone."

http://www.eurekalert.org/pub_releases/2015-05/uoc - unr051815.php

UCI neurobiologists restore youthful vigor to adult brains

Reactivated plasticity points to new treatments for developmental disorders

Irvine, Calif, - They say you can't teach an old dog new tricks. The same can be said of the adult brain. Its connections are hard to change, while in children, novel experiences rapidly mold new connections during critical periods of brain development.

UC Irvine neurobiologist Sunil Gandhi and colleagues wanted to know whether the flexibility of the juvenile brain could be restored to the adult brain. Apparently, it can: They've successfully re-created a critical juvenile period in the brains of adult mice. In other words, the researchers have reactivated brain plasticity - the rapid and robust changes in neural pathways and synapses as a result of learning and experience.

And in doing so, they've cleared a trail for further study that may lead to new treatments for developmental brain disorders such as autism and schizophrenia. Results of their study appear online in Neuron. (Link to study: http://www.sciencedirect.com/science/article/pii/S089662731500286X)

The scientists achieved this by transplanting a certain type of embryonic neuron into the brains of adult mice. The transplanted neurons express GABA, a chief inhibitory neurotransmitter that aids in motor control, vision and many other cortical functions.

Much like older muscles lose their youthful flexibility, older brains lose plasticity. But in the Gandhi study, the transplanted GABA neurons created a new period of heightened plasticity that allowed for vigorous rewiring of the adult brain. In a sense, old brain processes became young again.

In early life, normal visual experience is crucial to properly wire connections in the visual system. Impaired vision during this time leads to a long-lasting visual deficit called amblyopia. In an attempt to restore normal sight, the researchers transplanted GABA neurons into the visual cortex of adult amblyopic mice.

"Several weeks after transplantation, when the donor animal's visual system would be going through its critical period, the amblyopic mice started to see with normal visual acuity," said Melissa Davis, a postdoctoral fellow and lead author of the study. These results raise hopes that GABA neuron transplantation might have future clinical applications. This line of research is also likely to shed light on the basic brain mechanisms that create critical periods.

"These experiments make clear that developmental mechanisms located within these GABA cells control the timing of the critical period," said Gandhi, an assistant professor of neurobiology & behavior. He added that the findings point to the use of GABA cell transplantation to enhance retraining of the adult brain after injury. Furthermore, this work sparks new questions as to how these transplanted GABA neurons reactivate plasticity, the answers to which might lead to therapies for currently incurable brain disorders.

http://nyti.ms/1F1xrTO

A Way to Brew Morphine Raises Concerns Over Regulation

Very soon the poppy will no longer be the only way to produce heroin's raw ingredient.

By DONALD G. McNEIL Jr.MAY 18, 2015

All over the world, the heavy heads of opium poppies are nodding gracefully in the wind - long stalks dressed in orange or white petals topped by a fright wig of stamens. They fill millions of acres in Afghanistan, Myanmar, Laos and elsewhere. Their payload - the milky opium juice carefully scraped off the seed pods - yields morphine, an excellent painkiller easily refined into heroin.

But very soon, perhaps within a year, the poppy will no longer be the only way to produce heroin's raw ingredient. It will be possible for drug companies, or drug traffickers, to brew it in yeast genetically modified to turn sugar into morphine.

Almost all the essential steps had been worked out in the last seven years; a final missing one was published Monday in the journal Nature Chemical Biology.

"All the elements are in place, but the whole pathway needs to be integrated before a one-pot glucose-to-morphine stream is ready to roll," said Kenneth A. Oye, a professor of engineering and political science at M.I.T.

This rapid progress in synthetic biology has set off a debate about how - and whether - to regulate it. Dr. Oye and other experts said this week in a commentary in the journal Nature that drug-regulatory authorities were ill prepared to control a process that would benefit the heroin trade much more than the prescription painkiller industry. The world should take steps to head that off, they argue, by locking up the bioengineered yeast strains and restricting access to the DNA that would let drug cartels reproduce them.

Other biotech experts counter that raising the specter of fermenting heroin like beer, jokingly known among insiders as "Brewing Bad," is alarmist and that Dr. Oye's proposed solutions are overkill. Although making small amounts of morphine will soon be feasible, they say, the yeasts are so fragile and the fermentation process so delicate that it is not close to producing salable quantities of heroin. Restricting DNA stifles all research, they argue, and is destined to fail just as restrictions on precursor chemicals have failed to curb America's crystal meth epidemic.

A spokesman for the Drug Enforcement Administration said his agency "does not perceive an imminent threat" because no modified yeast strain is commonly available yet. If that happens, he said, D.E.A. laboratories would be able to identify heroin made from it. An F.B.I. agent who has been following the yeast strains since 2009 said he was glad that the debate was beginning before the technology was ready and before lawmakers moved to restrict it.

"We've learned that the top-down approach doesn't work," said Supervisory Special Agent Edward You, who said he coined the "Brewing Bad" term and had held workshops for biotech students and companies. "We want the people in the field to be the sentinels, to recognize when someone is trying to abuse or exploit their work and call the F.B.I."

No scientific team has yet admitted having one strain capable of the entire sugar-to-morphine pathway, but several are trying, and the Stanford lab of Christina D. Smolke is a leader. She said she expected one to be published by next year.

No one in the field thought there should be no regulation, she said, but suggestions that home brewers would soon make heroin were "inflammatory" because fermenting manipulated yeasts "is a really special skill." Implications of research like hers should be calmly discussed by experts, she said, and Dr. Oye's commentary "was getting people to react in a very freaked-out way."

Robert H. Carlson, the author of "Biology Is Technology," said restrictions were doomed to fail just as Prohibition failed to stop the home brewing of alcohol.

"DNA synthesis is already a democratic, low-cost technology," he said. "If you restrict access, you create a black market."

What is considered one of the last important missing steps, a way to efficiently grow a morphine precursor, (S)-reticuline, in brewer's yeast, Saccharomyces cerevisiae, was published in Nature Chemical Biology on Monday by scientists from the University of California, Berkeley, and Canada's Concordia University.

The leader of the Berkeley team, John E. Dueber, said it was not trying to make morphine but 2,500 other alkaloids for which reticuline is a precursor, some of which might become antibiotics or cancer drugs.

Nonetheless, he said, since he realized his research has implications for the making of morphine, he sent his draft paper to Dr. Oye, suggesting the debate become more public. One crucial question is whether the technology is of more use to the pharmaceutical industry or drug cartels. Dr. Oye argues it is the latter.

Companies are always seeking painkillers that create less addictive euphorias or do not paralyze breathing muscles, and having a predictable process they could tweak would be useful, but they already have a cheap, steady supply of opium from India, Turkey and Australia, where poppies are grown legally by licensed farmers.

That chain will be hard to disrupt. Since the 1960s, when it was created to convince Turkey to crack down on heroin, the International Narcotics Control Board has set quotas. Thousands of small farmers, their bankers and equipment suppliers depend on the sales, and they have local political clout just as American corn farmers do. Also, pharmaceutical companies can already synthesize opiates in their labs. Fentanyl, a painkiller 100 times as powerful as morphine, is synthetic, as is loperamide (Imodium), an antidiarrheal opiate.

Heroin sellers, by contrast, must smuggle raw materials out of lawless Afghanistan, Laos, Myanmar and Mexico. Their supply lines are disrupted when any local power - from the Taliban to the United States Army - cracks down. Brewing near their customers would save them many costs: farmers, guards, guns, planes, bribes and so on.

One frightening prospect Dr. Oye raised was how viciously drug cartels might react if Americans with bioengineering know-how started competing with them. Gunmen from Mexican drug gangs have taken control of many secret marijuana fields in American forests.

His commentary suggested several possible steps to prevent misuse of the technology. The yeasts could be locked in secure laboratories, worked on by screened employees. Sharing them with other scientists without government permission could be outlawed.

Their DNA could be put on a watch list, as sequences for anthrax and smallpox are, so any attempt to buy them from DNA supply houses would raise flags. Chemically silent DNA "watermarks" could be inserted so stolen yeasts could be

traced. Or the strains could be made “wimpier and harder to grow,” Dr. Oye said, perhaps by making them require nutrients that were kept secret.

Agent You said he did not want to comment on Dr. Oye’s suggestions, but was glad a threat had been identified by scientists before it was a reality, adding, “If this occurred across the board, it would make the F.B.I.’s life a heck of a lot easier.”

http://bit.ly/1PAMPC3

This 1,500-Year-Old Skeleton May Belong to the Man That Brought Leprosy to Britain

Modern techniques show that the young man was in his 20s and likely Scandinavian

By Marissa Fessenden

In the early 1950’s workers digging for gravel uncovered skeletons of people interred in an Anglo-Saxon cemetery a century and a half before. At the time, the team noted that the bones of one man in particular had joint damage and the narrow toe bones typically caused by leprosy. When researchers recently reanalyzed those same bones using modern techniques they realized the man may have had the first case of the disease in Britain. On top of that, other tests show that he was probably from Scandinavia, not Britain.

This 1,500 year old skeleton from the Anglo-Saxon town of Great Chesterford was a young man who had leprosy **University of Southampton**

The researchers were able to gather some bacterial DNA from the bones and sequence it, reports Maev Kennedy for *The Guardian*. They genetic fingerprint they found was that of a leprosy strain belonging to the lineage 3I, which has been found at other burial sites in Scandinavia and southern Britain but at later dates. The man likely died in the 5th or 6th century.

“The radiocarbon date confirms this is one of the earliest cases in the UK to have been successfully studied with modern biomolecular methods," says Sonia Zakrzewski, of the University of Southampton in a press release. "This is exciting both for archaeologists and for microbiologists. It helps us understand the spread of disease in the past, and also the evolution of different strains of disease, which might help us fight them in the future.”

The research team also analyzed elements in the man’s teeth. Specifically, they looked at several isotopes - element can different numbers of neutrons, each of variation is a different isotope. They measured the ratio oxygen isotopes, which reflect those found in the water he drank, and strontium isotopes found in his enamel, which reflect the geology of his homeland, explains Maddie Stone for Vice. This analysis told the researchers that the man likely came from Scandinavia. He may have carried the disease to Britain from there. When he died, he was in his 20s, the researchers report. They published their findings in *PLOS One*.

The 3I leprosy strain is one of five strains found around the world. It not only gave rise to the leprosy of the British Isles, but that in the southern U.S. (where it’s often carried by armadillos) and in the U.K. even today. However, the leprosy epidemic didn’t peak in Europe until the 13th century. If the man had seen a physician in his new country, they wouldn’t have recognized the deformations and scaly skin of a leprosy infection. Perhaps he would have escaped the social stigma that later arose around the disease too.

This man isn't the first person in the world to get leprosy, explains Stone. "There are a handful of cases worldwide that predate this young man, including several from second century BC Egypt, first century AD Israel, and 1st through 4th century AD Uzbekistan," she writes. But he is the first known case in Britain.

The team’s project leader, Sarah Inskip of Leiden University told Stone: “We plan to carry out similar studies on skeletons from different locations to build up a more complete picture of the origins and early spread of this disease.”

http://www.eurekalert.org/pub_releases/2015-05/osu-iss051915.php

In study, skipping meals is linked to abdominal weight gain

Research in animals shows spikes, drops in insulin affect liver

COLUMBUS, Ohio - A new study in animals suggests that skipping meals sets off a series of metabolic miscues that can result in abdominal weight gain.

In the study, mice that ate all of their food as a single meal and fasted the rest of the day developed insulin resistance in their livers - which scientists consider a telltale sign of prediabetes. When the liver doesn't respond to insulin signals telling it to stop producing glucose, that extra sugar in the blood is stored as fat.

These mice initially were put on a restricted diet and lost weight compared to controls that had unlimited access to food. The restricted-diet mice regained weight as calories were added back into their diets and nearly caught up to controls by the study's end.

But fat around their middles - the equivalent to human belly fat - weighed more in the restricted-diet mice than in mice that were free to nibble all day long. An excess of that kind of fat is associated with insulin resistance and risk for type 2 diabetes and heart disease.

"This does support the notion that small meals throughout the day can be helpful for weight loss, though that may not be practical for many people," said Martha

Belury, professor of human nutrition at The Ohio State University and senior author of the study. "But you definitely don't want to skip meals to save calories because it sets your body up for larger fluctuations in insulin and glucose and could be setting you up for more fat gain instead of fat loss."

The research is published online in the Journal of Nutritional Biochemistry.

Belury and colleagues were able to tie these findings to the human tendency to skip meals because of the behavior they expected to see - based on previous work - in the mice on restricted diets. For three days, these mice received half of the calories that were consumed daily by control mice. Food was gradually added so that by day six, all mice received the same amount of food each day.

But the mice that had been on restricted diets developed gorging behavior that persisted throughout the study, meaning they finished their day's worth of food in about four hours and then ended up fasting for the next 20 hours.

"With the mice, this is basically bingeing and then fasting," Belury said. "People don't necessarily do that over a 24-hour period, but some people do eat just one large meal a day."

The gorging and fasting in these mice affected a host of metabolic measures that the researchers attributed to a spike and then severe drop in insulin production. In mice that gorged and then fasted, the researchers saw elevations in inflammation, higher activation of genes that promote storage of fatty molecules and plumper fat cells - especially in the abdominal area - compared to the mice that nibbled all day.

To check for insulin resistance, the scientists used a sophisticated technique to assess glucose production. The liver pumps out glucose when it receives signals that insulin levels are low - for example, while people sleep, the liver supplies glucose to the brain. But that production stops after a meal, when insulin is released by the pancreas and performs its main task of removing sugar from the blood and shepherding the glucose to multiple types of cells that absorb it for energy.

With this research technique, Belury and colleagues found that glucose lingered in the blood of mice that gorged and fasted - meaning the liver wasn't getting the insulin message.

"Under conditions when the liver is not stimulated by insulin, increased glucose output from the liver means the liver isn't responding to signals telling it to shut down glucose production," Belury said. "These mice don't have type 2 diabetes yet, but they're not responding to insulin anymore and that state of insulin resistance is referred to as prediabetes."

Insulin resistance is also a risk for gaining abdominal fat known as white adipose tissue, which stores energy.

"Even though the gorging and fasting mice had about the same body weights as control mice, their adipose depots were heavier. If you're pumping out more sugar into the blood, adipose is happy to pick up glucose and store it. That makes for a happy fat cell - but it's not the one you want to have. We want to shrink these cells to reduce fat tissue," Belury said.

This work was supported by the Carol S. Kennedy endowment, the Ohio Agricultural Research and Development Center, a Pelotonia graduate fellowship and grants from the National Institutes of Health.

Co-authors include Kara Kliewer, Jia-Yu Ke, Hui-Young Lee, Michael Stout and Rachel Cole of the Department of Human Sciences at Ohio State; and Varman Samuel and Gerald Shulman of Yale University.

http://www.eurekalert.org/pub_releases/2015-05/uom-cdm051915.php

Cancer drugs may hold key to treating Down syndrome and other brain disorders

A class of FDA-approved cancer drugs may be able to prevent problems with brain cell development associated with disorders including Down syndrome and Fragile X syndrome

ANN ARBOR - -A class of FDA-approved cancer drugs may be able to prevent problems with brain cell development associated with disorders including Down syndrome and Fragile X syndrome, researchers at the University of Michigan Life Sciences Institute have found.

The researchers' proof-of-concept study using fruit fly models of brain dysfunction was published today in the journal eLife. They show that giving the leukemia drugs nilotinib or bafetinib to fly larvae with the equivalent of Fragile X prevented the wild overgrowth of neuron endings associated with the disorder. Meanwhile, the drugs - both tyrosine-kinase inhibitors - did not adversely affect the development or neuronal growth in healthy flies.

"This study proposes a potential therapeutic approach for treating brain disorders associated with dysregulated expression of the Dscam protein, which is seen in both Down syndrome and Fragile X syndrome," said senior study author Bing Ye, whose lab is in the LSI. Graduate student Gabriella Sterne and postdoctoral fellow Jung Hwan Kim are co-first authors of the paper.

Down syndrome and Fragile X are the two most prevalent genetic causes of intellectual disabilities. Down syndrome is caused by an extra copy of chromosome 21, while Fragile X is caused by a mutation in a single gene. Recent studies by the Ye lab and by researchers at other institutions have pointed to a possible link between the two conditions.

During early development, neurons produce high levels of the proteins encoded by a gene called DSCAM as they undergo an intense period of extending and

branching to connect with other neurons. (DSCAM stands for Down Syndrome Cell-Adhesion Molecule.) But problems can occur when Dscam levels don't go back down.

In flies, when Dscam levels stay high, branches off of the ends of their neurons grow too long and make faulty connections with neighboring neurons. In humans, whose nervous systems and brains are far more complicated, the downstream impacts of Dscam dysregulation have not been fully identified.

In a series of experiments outlined in the study, the researchers showed that the Dscam protein activates another protein known as Abelson tyrosine kinase (Abl). The scientists then took genetically modified flies that produced high levels of Dscam and gave them the cancer drug, which acts by blocking the action of Abl.

In one experiment, directly overexpressing Dscam led to flies with neuron endings (called presynaptic terminals) more than 50 percent longer than normal. But flies treated with the cancer drug showed only a 15 percent increase.

In another experiment using a genetic model of Fragile X, the flies had presynaptic terminals almost a third longer than normal, but those that received the drug saw only 3 percent more terminal growth than the control group.

"Although there's an amazing amount of similarity between flies and humans, more study is needed before we'll know if this could be a safe and effective treatment for human patients," said Ye, who is also an assistant professor in the Department of Cell and Developmental Biology at the U-M Medical School.

The next step would be to test the approach in mouse models of these brain disorders. Collaborations with oncologists and pharmaceutical companies will also be essential to ensure Abl inhibitors are safe to use in this context, Ye said.

"This study is also an example of the utility of model organisms," Ye said. "Fruit flies grow and develop rapidly - and although the behaviors of flies and humans are very different, our neurons grow in much the same way, and the genes controlling this process are usually the same or very similar."

This work was supported by grants from the National Institutes of Health, the Protein Folding Disease Initiative of the University of Michigan and the Pew Scholars Program in the Biological Sciences. U-M has a patent application based on this discovery and is looking for a commercial partner to develop it into treatments.

http://bit.ly/1ekKR85

Pacific Trade Pact Would Mean Higher Drug Prices, Says Report

Trans Pacific Partnership, now being negotiated by U.S., will keep low-cost generics off the market, says the Foundation for AIDS Research

By Rebecca Trager and ChemistryWorld | May 18, 2015

A leaked draft of a trade agreement under negotiation among 12 Pacific rim countries, including the US and Japan, contains language that could delay the entrance of generic competition for much-needed medicines and keep pharmaceutical prices high, according to the Foundation for Aids Research (amfAR), an international non-profit headquartered in New York. The organisation is lending its voice to those expressing similar concerns, like humanitarian organisation Doctors Without Borders.

Although details of the proposed Trans-Pacific Partnership (TPP) have been kept confidential, leaked texts of the treaty have offered some clues, such as its embrace of intellectual property protections that go further than previous free trade agreements and expand existing intellectual property (IP) protections on pharmaceutical products, amfAR says in a new report released on May 8.

Overall, amfAR argues that access to affordable generic medicines for diseases like HIV–Aids, cancer and tuberculosis would be compromised by these new avenues for pharmaceutical companies to extend IP protection beyond current international requirements. This would especially affect low- and middle-income countries where these drugs are especially needed and brand-named pharmaceuticals are prohibitively expensive, the group says.

For example, amfAR points to a provision on patent term extensions that would make it easier for pharmaceutical companies to demand longer patent extensions and further delay generic competitors from entering the market.

In addition, the report refers to ‘data exclusivity’ language prohibiting drug safety regulators from using existing clinical trial data to give market approval to generic or biosimilar versions of drugs. While generic companies would have to develop their own clinical safety data, amfAR says they might be unable to do so because of ethical concerns about carrying out medical research on patients when existing clinical trials have demonstrated the benefits of a new treatment.

Dangerous global precedent

‘If the TPP moves forward, it will set a dangerous global precedent,’ warns amfAR’s chief executive, Kevin Frost. Doctors Without Borders agrees that the TPP, if approved in its current form, would lower the standard for which medicines deserve a patent and would delay the availability of affordable versions of biologics.

‘We rely on affordable medicines for all of our programmes,’ says Doctors Without Borders spokesperson Sandra Murillo. ‘We have serious concerns about access to medicines and the repercussions for that in the TTP.’

But Mark Grayson, a spokesperson for the Pharmaceutical Research and Manufacturers of America, says amfAR’s report includes lots of ‘supposition.’ He calls the TPP ‘a forward-looking agreement’ that contains provisions to protect the ‘climate of innovation’ across the globe.

'In the US, there are very strong IP laws, but we have the largest generic penetration in the world,' Grayson states. 'We believe that these [TPP] provisions will continue to encourage the research that is necessary to fight HIV and other major diseases all around the world,' he adds.

http://nyti.ms/1AqsKXT

Antibiotics Resurface as Alternative to Removing Appendix

Every year, 300,000 Americans with appendicitis are rushed into emergency surgery.

By GINA KOLATAMAY 18, 2015

Most think that if the appendix is not immediately removed, it will burst — with potentially fatal consequences. But now some doctors say there may another option: antibiotics.

Five small studies from Europe, involving a total of 1,000 patients, indicate that antibiotics can cure some patients with appendicitis; about 70 percent of those who took the pills did not require surgery. Patients who wound up having an appendectomy after trying antibiotics first did not face any more complications that those who had surgery immediately.

"These studies seem to indicate that antibiotics can cure appendicitis in many patients," said Dr. David Talan, a specialist in emergency medicine and infectious diseases at the University of California, Los Angeles. "You at least have the chance of avoiding surgery altogether."

Dr. Talan and other researchers are planning a large clinical trial to compare people with appendicitis who receive antibiotics or surgery.

In preparation, Dr. Talan and his colleague Dr. David Flum, a surgeon at the University of Washington, spent much of the past year asking patients if they would be interested in participating. Nearly half said yes. In another survey, nearly three-quarters of those who had already had an appendectomy said they would have preferred to try antibiotics first. By suggesting an antibiotic alternative, the researchers are bucking longstanding medical tradition.

Surgical treatment for appendicitis began in the 1880s, when surgery itself was something of a new idea. Doctors struggled to figure out which patients to operate on, because the procedure was dangerous and they knew some patients would get better without it.

As surgery and anesthesia improved, however, the appendectomy became the treatment of choice. According to the medical thinking of the day, it made sense.

For years, doctors thought the appendix — a tiny worm-shaped tube that hangs off the right side of the colon — became inflamed because it was blocked by a small piece of hardened feces. As it turns out, though, the vast majority of people with appendicitis do not have such a blockage.

"No one knows what causes appendicitis," said Dr. James Barone, a retired chairman of surgery at Stamford Hospital in Connecticut and Lincoln Hospital in the Bronx.

And an inflamed appendix is not, as most people think, a ticking time bomb. While perforation occurs in 15 percent to 25 percent of patients, researchers hypothesize that those who get perforations may have a predisposing immune response or infection with certain kinds of bacteria. In others, appendicitis goes away on its own. Nor is the length of time that an appendix is inflamed necessarily linked to the risk of perforation. Most people with a ruptured appendix already have it when they show up in the emergency room.

But surprising as antibiotics might seem, this is not the first time they have emerged as a possible alternative to an appendectomy.

When antibiotics became available in the 1940s and '50s, doctors in England began giving them to patients with appendicitis, reporting excellent results. During the Cold War, when American sailors spent six months or more on nuclear submarines prohibited from surfacing, those who developed appendicitis were given antibiotics. "Those submariners did great, and no deaths or complications were reported," Dr. Flum said.

But that did not put a dint in the perception that surgery was the treatment of choice. In 1961 a Russian doctor stationed in Antarctica, Leonid Rogozov, went so far as to cut out his own appendix when it became inflamed. "I work mainly by touch. The bleeding is quite heavy, but I take my time," he wrote in his journal. "I grow weaker and weaker, my head starts to spin …Finally, here it is, the accursed appendix."

The planned clinical trial pitting antibiotics against surgery will attempt to answer important questions. Are antibiotics as good as surgery in curing appendicitis? Could they do so at less cost, avoiding a hospitalization afterward? How often does appendicitis recur after a person is treated with antibiotics? Will patients successfully treated with antibiotics later rush to the emergency room every time they feel abdominal pain? It's even not clear how the drugs should be administered.

In the European trials, patients had a day or two of intravenous infusions at a hospital, then went home to take a week of pills. But, Dr. Talan said, there are now long-acting intravenous antibiotics that may permit some patients to simply visit a doctor for a couple of days, and then take pills — while avoiding hospitalization.

There is already a debate in the medical field over whether to tell patients about the antibiotic option, and if so, which patients to tell.

Dr. Giana Davidson, a general surgeon at the University of Washington, will discuss antibiotics with appendicitis patients who ask, but has qualms about drugs as a treatment option. “We don’t have the answers to questions that matter to patients,” Dr. Davidson said. “What are the chances of it coming back? When I get belly pain, what should make me come back to the hospital?” “I just have a lot of hesitation on my side to go away from a 30-minute operation that cures them for the rest of their lives,” she added.

Dr. Philip S. Barie, the editor in chief of the journal Surgical Infections and a professor of surgery at Weill Cornell Medical College, does not routinely mention antibiotics, saying he would like to see results of a national clinical trial. For now, he says, “I would not include it as part of informed consent as an equivalent option.” But patients are beginning to find out on their own.

Richard Redelfs, a 40-year-old manager of condominiums and homeowner associations in Edmonds, Wash., woke up with abdominal pain a few years ago. An emergency room doctor told Mr. Redelfs he needed immediate surgery for appendicitis. But Mr. Redelfs was uninsured, and he told the surgeon that he had read online that antibiotics might be a viable alternative.

“Once he found out I didn’t have insurance, it was easy to talk him into prescribing me antibiotics,” Mr. Redelfs said. He felt better almost immediately. But six months later, Mr. Redelfs felt a twinge in his abdomen and returned to the hospital. This time, he had insurance. Told he had appendicitis again, he opted for surgery. “I wanted the peace of mind,” he said.

http://www.eurekalert.org/pub_releases/2015-05/e-e2a051815.php

EuroPCR 2015: Advances in mechanical thrombectomy warrant call to action in acute stroke

Experts believe new technologies may significantly reduce the number of people who die or are severely disabled by stroke

PARIS, FRANCE - Experts speaking at EuroPCR 2015 say the explosion of positive results for new-generation endovascular devices for the treatment of acute stroke warrant a call to action to ensure swifter implementation of this technology. Known as "stent-retrievers," mechanical thrombectomy devices use catheters introduced into a blocked cerebral artery to suck out or lyse a clot that is cutting off circulation to part of the brain.

On Tuesday, EuroPCR 2015 featured a special breaking news session devoted to this rapidly evolving field to review the recent evidence and discuss the rationale for boosting use of the therapy.

Seven clinical trials in the past six months have demonstrated that intracranial thrombus retrieval or lysis is feasible and safe, and yields significant improvements in neurological functional on top of best medical therapy (including IV thrombolysis whenever indicated), as compared to best medical therapy alone.*

"Acute ischaemic stroke is as common as acute coronary syndrome, but the prognosis is still very grave," Dr. Petr Widimsky, head of the Cardiocenter and Chair of the Cardiology Department at the Third Faculty of Medicine, Charles University & University Hospital "Royal Vineyards," Prague, Czech Republic observed. With conservative treatment following a moderate or severe stroke, only 10% will recover to the state of functional independence, he noted. "So 90% patients who are not treated die or are severely disabled. Thrombolysis increases the rate of people who return to functional independence from 10% to 20-25%, but that still leaves 75% disabled or dead."

According to Widimsky, the accumulated evidence from the various clot retrieval trials published or presented in the past few months suggests that the number of moderate/severe stroke patients who regain full or near-full neurological function rises to 40-50% with this novel therapy. "And with good patient selection, that may increase to 60%. Sometimes we face something that looks close to a miracle when we are treating a patient with a severe stroke, who is profoundly disabled, and he makes a full recovery before your eyes. It's really dramatic."

A range of clot retrieval systems already hold regulatory approval in both Europe and North America, but implementation into practice will require concentrated effort of many parties, Widimsky said.

"It is a difficult technique routinely used so far only in a few comprehensive stroke centres and physicians need the appropriate training, but these data have only been out for a few months. If you remember the story of myocardial infarction, the fact that MI should be treated with coronary angioplasty was known in 1993, but it took 10 years before it was widely used."

There are risks to the procedure, Widimsky acknowledged, with an adverse event rate in the range of 5%. The most important risks are intracranial bleeding, or new stroke in another territory, caused by a clot fragment embolising during removal. So far, most of the procedures in Europe are being done by radiologists and in the US, primarily neurosurgeons, but Widimsky predicts there will be wider uptake in the coming years by angiologists, neurologists, vascular surgeons, and cardiologists depending on the local situation.

"We are highlighting these new data here at EuroPCR in order to spread the message that this therapy shows great promise. We need to build health care systems and train physicians to be able to offer this effective method to as many patients with acute ischaemic stroke as possible."

http://bit.ly/1F2w5Z1

Iron levels in brain predict when people will get Alzheimer's

Does this qualify as irony? Our bodies need iron to be healthy – but too much could harm our brains by bringing on Alzheimer's disease.

16:56 19 May 2015 by Clare Wilson

If that's the case, measuring people's brain iron levels could help identify those at risk of developing the disease. And since we already have drugs that lower iron, we may be able to put the brakes on.

Despite intense efforts, the mechanisms behind this form of dementia are still poorly understood. For a long time the main suspect has been a protein called beta-amyloid, which forms distinctive plaques in the brain, but drugs that dissolve it don't result in people improving.

Not so good ferrous

Studies have suggested that people with Alzheimer's also have higher iron levels in their brains. Now it seems that high iron may hasten the disease's onset.

Researchers at the University of Melbourne in Australia followed 144 older people who had mild cognitive impairment for seven years. To gauge how much iron was in their brains, they measured ferritin, a protein that binds to the metal, in their cerebrospinal fluid. For every nanogram per millilitre people had at the start of the study, they were diagnosed with Alzheimer's on average three months earlier.

The team also found that the biggest risk gene for Alzheimer's, ApoE4, was strongly linked with higher iron, suggesting this is why carrying the gene makes you more vulnerable. Iron is highly reactive, so it probably subjects neurons to chemical stress, says team member Scott Ayton.

Anti-iron drugs

The finding by itself doesn't prove that reducing iron levels would cut people's risk of Alzheimer's but a trial of a drug that rids the body of some of its iron, carried out 24 years ago, suggests it's a hypothesis worth investigating.

The drug halved the rate of Alzheimer's cognitive decline but was overlooked when the beta-amyloid theory of the disease became dominant, says Ayton. "Perhaps it's time to refocus the field on looking at iron as a target," he says.

One easy way of reducing iron levels - having regular blood donations - would not be a good idea for older people as it can bring on anaemia. Also, says Ayton, "there is only a modest correlation between iron levels in the blood and in the brain."

However, there is an iron-binding drug called deferiprone which gets into the brain and reduces levels of the metal there without disturbing blood levels too much. It is used to treat cases of iron poisoning and has also been found to slow the progression of Parkinson's disease, another condition in which high iron levels have been implicated.

Journal reference: Nature Communications, DOI: 10.1038/ncomms7760

http://www.eurekalert.org/pub_releases/2015-05/uob-tds051515.php

The dark side of the 'love hormone'; similarities with the effects of alcohol

Researchers at the University of Birmingham have highlighted significant similarities between the behavioural effects of oxytocin and alcohol.

The research, published today in Neuroscience and Biobehavioral Reviews, draws on existing studies into the two compounds and details the similarities between the effects of alcohol and the 'love hormone', oxytocin, on our actions. The team warn that the oft-used nickname hides the darker side of oxytocin, and claim that it bears more semblances with the effects of alcohol than previously thought.

Oxytocin is a neuropeptide hormone produced in the hypothalamus and secreted by the posterior pituitary gland. It has long been established as playing a significant role in childbirth and maternal bonding. More recently it has been identified as a brain chemical with a key role in determining our social interactions and our reactions to romantic partners - hence its nickname of 'the love hormone'.

Oxytocin increases prosocial behaviours such as altruism, generosity and empathy; while making us more willing to trust others. The socio-cognitive effects come about by suppressing the action of prefrontal and limbic cortical circuits - removing the brakes on social inhibitors such as fear, anxiety and stress.

Dr Ian Mitchell, from the School of Psychology at the University of Birmingham, explained, "We thought it was an area worth exploring, so we pooled existing research into the effects of both oxytocin and alcohol and were struck by the incredible similarities between the two compounds."

"They appear to target different receptors within the brain, but cause common actions on GABA transmission in the prefrontal cortex and the limbic structures. These neural circuits control how we perceive stress or anxiety, especially in social situations such as interviews, or perhaps even plucking up the courage to ask somebody on a date. Taking compounds such as oxytocin and alcohol can make these situations seem less daunting."

The team acknowledge that the ability to inhibit anxieties could explain the temptation to summon a little 'Dutch courage' - particularly in the context of social situations such a first date. Dr Steven Gillespie said, "The idea of 'Dutch courage' - having a drink to overcome nerves - is used to battle those immediate obstacles of fear and anxiety. Oxytocin appears to mirror these effects in the lab."

When administered nasally, oxytocin appears to closely mirror the well-established effects of alcohol consumption. However the researchers warn against self-medicating with either the hormone or a swift drink to provide a little more confidence in difficult moments.

Alongside the health concerns that accompany frequent alcohol consumption, there are less desirable socio-cognitive effects that both alcohol and oxytocin can facilitate. People can become more aggressive, more boastful, envious of those they consider to be their competitors, and favour their in-group at the expense of others. The compounds can affect our sense of fear which normally acts to protect us from getting into trouble and we often hear of people taking risks that they otherwise wouldn't.

A dose of either compound can further influence how we deal with others by enhancing our perception of trustworthiness, which would further increase the danger of taking unnecessary risks.

Dr Gillespie added, "I don't think we'll see a time when oxytocin is used socially as an alternative to alcohol. But it is a fascinating neurochemical and, away from matters of the heart, has a possible use in treatment of psychological and psychiatric conditions. Understanding exactly how it suppresses certain modes of action and alters our behaviour could provide real benefits for a lot of people. Hopefully this research might shed some new light on it and open up avenues we hadn't yet considered."

http://nyti.ms/1PDdmi2

Stone Tools From Kenya Are Oldest Yet Discovered

Our hominin ancestors were making stone tools 3.3 million years ago, some 700,000 years earlier than previously thought.

By JOHN NOBLE WILFORD MAY 20, 2015

One morning in July 2011, while exploring arid badlands near the western shore of Lake Turkana in Kenya, a team of archaeologists took a wrong turn and made a big discovery about early human technology: Our hominin ancestors were making stone tools 3.3 million years ago, some 700,000 years earlier than previously thought.

The findings promise to extend knowledge of the first toolmakers even deeper in time, probably before the emergence of the genus Homo, once considered the first to gain an evolutionary edge through stone technology.

“Immediately, I knew that we had found something very special,” said Sonia Harmand, a research associate professor at Stony Brook University in New York, in a telephone interview from Nairobi, Kenya.

Within an hour, Dr. Harmand and Jason E. Lewis, co-leaders of the project, traced the source of the artifacts scattered in a dry riverbed to datable volcanic sediments at the top of a nearby hill. The stones showed that at least some ancient hominins — the group that includes humans and their extinct ancestors — had started intentionally knapping stones, breaking off pieces with quick, hard strikes from another stone to make sharp tools sooner than other findings suggested.

After further field research and laboratory analysis, the findings at the site known as Lomekwi 3 were described Wednesday in the journal Nature.

What the sharp blades were used for is not yet known. Nor is the identity of the toolmakers.

No bone fossils have been found at the discovery site. But in all likelihood, Dr. Harmand and Dr. Lewis said, the tools were produced by a more primitive member of the human family well before the appearance of the genus Homo. The earliest known Homo specimen, announced more than two months ago, lived 2.8 million years ago in what is now Ethiopia. The earliest previous evidence of toolmaking, also from Ethiopia, was dated 2.6 million years ago.

“These tools shed light on an unexpected and previously unknown period of hominin behavior, and can tell us a lot about cognitive development in our ancestors that we can’t understand from fossils alone,” said Dr. Harmand, who is also affiliated with France’s National Center for Scientific Research. “Our finding disproved the longstanding assumption that Homo habilis was the first toolmaker.”

Alison Brooks, an anthropology professor at George Washington University and a research associate at the Smithsonian Institution, who was independent of the discovery team, pronounced the finding “truly pathbreaking.” She said it “reaffirms the argument that the repeated and competent manufacture of useful sharp edges, on which we came to depend, may have been a driving factor in the evolution of our genus, both anatomically and cognitively.”

In a sense, the deeper record of stone technology was no surprise to paleoanthropologists. Previous examples, especially the 2.5-million-year-old artifacts collected at Olduvai Gorge in Tanzania, were thought to be too well made to have been a recent innovation. How far back the evidence for this stone technology extends is anyone’s guess, the experts say.

In a commentary in the journal, Erella Hovers, an archaeologist at the Hebrew University of Jerusalem, wrote that some form of toolmaking may have extended back to the last common ancestor of chimpanzees and hominins, as much as seven million years ago.

Dr. Hovers and other scientists not involved in the new research said that the dating of the material appeared solid and that the objects were deliberately produced tools, not scraps of rock broken by accident or natural causes.

“Because the sediments in these layers are fine-grained, and a flake found by the authors could be fitted back onto the core from which it had been detached,” Dr.

Hovers said, “it is unlikely that the tools accumulated through stream activity or that substantial disturbance of the sediments occurred after the tools had been discarded.”

Eric Delson, a paleoanthropologist at Lehman College of the City University of New York and a researcher at the American Museum of Natural History, noted that once in a generation, the age of humanity’s first known use of tools increases significantly. “Harmand’s find is the longest jump back in time,” he said, “nearly three quarters of a million years, to a period when the only known hominin fossils belong to Australopithecus,” the genus most famously represented by the “Lucy” skeleton and found throughout East Africa.

Another possibility is a hominin known as Kenyanthropus platyops, whose fossils were found in the region of Lake Turkana. But Dr. Delson cautioned that fossils of this genus are “poorly known and still questionably distinct” as a separate hominin entity.

Dr. Delson said the discovery of what Dr. Harmand and her colleagues are calling the Lomekwian industry raises several questions: namely, are these really tools, and what were these hominins, whoever they were, doing with implements far larger and heavier than the small and simple flakes and cores that characterized the more recent 2.6-million-year-old technologies?

Even now, researchers doubt that they have reached the earliest origins of stone tool technology. As Dr. Hovers said, “Why not dig deeper in time?” The Lomekwi 3 site, she added, “may not be the final — or rather, the first — word on the roots of human technology.”

Dr. Harmand and Dr. Lewis will return to Lake Turkana this summer to search for more clues to the identities of the toolmakers. “Now we have a better idea of what we should look for,” Dr. Harmand said.

http://www.eurekalert.org/pub_releases/2015-05/uoth-cia051915.php

Caffeine intake associated with reduced levels of erectile dysfunction

Men drinking two to three cups of coffee a day are less likely to have erectile dysfunction

HOUSTON - Men who drink the equivalent caffeine level of two to three cups of coffee a day are less likely to have erectile dysfunction (ED), according to researchers from The University of Texas Health Science Center at Houston (UTHealth).

The results of a study published recently in PLOS ONE found that men who consumed between 85 and 170 milligrams of caffeine a day were 42 percent less likely to report ED, while those who drank between 171 and 303 milligrams of caffeine a day were 39 percent less likely to report ED compared to those who drank zero to seven milligrams a day. This trend was also true among overweight, obese and hypertensive men.

"Even though we saw a reduction in the prevalence of ED with men who were obese, overweight and hypertensive, that was not true of men with diabetes. Diabetes is one of the strongest risk factors for ED, so this was not surprising," said David S. Lopez, Dr.P.H., M.P.H., lead author and assistant professor at UTHealth School of Public Health.

According to the journal article, the suggested biological mechanism is that caffeine triggers a series of pharmacological effects that lead to the relaxation of the penile helicine arteries and the cavernous smooth muscle that lines cavernosal spaces, thus increasing penile blood flow.

In the United States, 18.4 percent of men 20 years and older have ED, suggesting that more than 18 million men are affected. Caffeine is consumed by more than 85 percent of adults, according to previous research.

Data for the study came from the National Health and Nutrition Examination Survey and ED was assessed by a single question during a computer-assisted interview. Caffeine sources in the study included coffee, tea, soda and sports drinks.

Co-authors include Run Wang, M.D.; Steven Canfield, M.D., from UTHealth Medical School and Arup Sinhafrom the School of Public Health.

http://www.eurekalert.org/pub_releases/2015-05/uhn-nms052015.php

New music strategy shows 70 percent increase in exercise adherence

use of personalized music playlists with tempo-pace synchronization increases adherence to cardiac rehab by almost 70 %

TORONTO - The use of personalized music playlists with tempo-pace synchronization increases adherence to cardiac rehab by almost 70 per cent--according to a study published in Sports Medicine -Open.

"Cardiac rehab has been proven to improve long-term survival for someone who's had a heart event by 20 per cent," said Dr. David Alter, Senior Scientist, Toronto Rehab, University Health Network, and Institute for Clinical Evaluative Sciences. "Our challenge is there is a high drop-out rate for these programs and suboptimal adherence to the self-management of physical activity."

In Dr. Alter's study, each research subject's personalized playlist was the music genre they enjoyed with tempos that matched their pre-determined walking or running pace.

"The music tempo-pace synchronization helps cue the person to take their next step or stride and helps regulate, maintain and reinforce their prescribed exercise

pace," explained Dr. Alter, who is also Research Chair in Cardiovascular Prevention and Metabolic Rehabilitation at Toronto Rehab, UHN.

Thirty-four cardiac rehabilitation patients from Toronto Rehab participated in the study: one third of the patients didn't have any music during their cardiac rehab exercises; and the other two-thirds had audio devices with personalized music playlists during their cardiac rehab exercises. Among those who had music, half received tempo-pace synchronized audio devices, which means their music playlists were sonically modified by embedding extra rhythmic beats--called rhythmic auditory stimulation (RAS)--to further enhance tempo-pace synchronization. Patients receiving RAS were unaware that their music playlists had been modified.

The patients who used the personalized music playlists with tempo-pace synchronization did an average of 105.4 minutes more exercise than patients who did not use music. Patients who received RAS had the greatest increase in their total physical activity, achieving 261.1 minutes or more of weekly physical activity than their music or non-music playlist counterparts--corresponding to a 70 per cent increase in weekly exercise.

"If this average increase of exercise was sustained for an average 65-year-old male patient, it would correlate with a projected life-expectancy increase of two and a half years," said Dr. Alter.

Future clinical trials will be designed to further test the clinical application of tempo-pace synchronized music playlists with and without RAS in cardiac rehab patients.

This study was supported by a grant from the Ontario Centres of Excellence. Dr. Alter's work is supported by a Research Chair in Cardiovascular Prevention and Metabolic Rehabilitation at Toronto Rehab, UHN and a career-investigator award with the Heart and Stroke Foundation, Ontario Provincial Office.

http://www.eurekalert.org/pub_releases/2015-05/uoc--tba052015.php

The Bronze Age Egtved Girl was not from Denmark

The Bronze Age Egtved Girl came from far away, as revealed by strontium isotope analyses of the girl's teeth.

The analyses show that she was born and raised outside Denmark's current borders, and strontium isotope analyses of the girl's hair and a thumb nail also show that she travelled great distances the last two years of her life.

The wool from the Egtved Girl's clothing, the blanket she was covered with, and the oxhide she was laid to rest on in the oak coffin all originate from a location outside present-day Denmark. The combination of the different provenance analyses indicates that the Egtved Girl, her clothing, and the oxhide come from Schwarzwald ("the Black Forest") in South West Germany - as do the cremated remains of a six-year-old child who was buried with the Egtved Girl. The girl's coffin dates the burial to a summer day in the year 1370 BC.

It is senior researcher Karin Margarita Frei, from the National Museum of Denmark and Centre for Textile Research at the University of Copenhagen, who has analysed the Egtved Girl's strontium isotope signatures. The analyses have been carried out in collaboration with Kristian Kristiansen from the University of Gothenburg and the Department of Geosciences and Natural Resource Management and the Centre for GeoGenetics, both University of Copenhagen.

The research has been possible through the support of The Danish National Research Foundation, European Research Council, the Carlsberg Foundation and L'Oréal Denmark-UNESCO For Women in Science Award.

The results have just been published in Scientific Reports.

The girl's movements mapped month by month

Strontium is an element which exists in the earth's crust, but its prevalence is subject to geological variation. Humans, animals, and plants absorb strontium through water and food. By measuring the strontium isotopic signatures in archaeological remains, researchers can determine where humans and animals lived, and where plants grew because of their strontium isotope signatures. In that sense, strontium serves as a kind of GPS for scientists.

"I have analysed the strontium isotopic signatures of the enamel from one of the Egtved Girl's first molars, which was fully formed/crystallized when she was three or four years old, and the analysis tells us that she was born and lived her first years in a region that is geologically older than and different from the peninsula of Jutland in Denmark," Karin Margarita Frei says.

Karin Margarita Frei has also traced the last two years of the Egtved Girl's life by examining the strontium isotopic signatures in the girl's 23-centimetre-long hair. The analysis shows that she had been on a long journey shortly before she died, and this is the first time that researchers have been able to so accurately track a prehistoric person's movements.

"If we consider the last two years of the girl's life, we can see that, 13 to 15 months before her death, she stayed in a place with a strontium isotope signature very similar to the one that characterizes the area where she was born. Then she moved to an area that may well have been Jutland. After a period of c. 9 to 10 months there, she went back to the region she originally came from and stayed there for four to six months before she travelled to her final resting place, Egtved. Neither her hair nor her thumb nail contains a strontium isotopic signatures which indicates that she returned to Scandinavia until very shortly before she died. As an area's strontium isotopic signature is only detectable in human hair and nails after

a month, she must have come to "Denmark" and "Egtved" about a month before she passed away," Karin Margarita Frei explains.

The Black Forest Girl

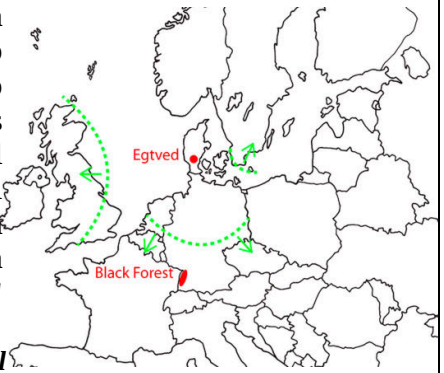
If the Egtved Girl was not born in Jutland, then where did she come from? Karin Margarita Frei suggests that she came from South West Germany, more specifically the Black Forest, which is located 500 miles south of Egtved.

Considered in isolation, the Egtved Girl's strontium isotope signature could indicate that she came from Sweden, Norway or Western or Southern Europe. She could also come from the island Bornholm in the Baltic Sea. But when Karin Margarita Frei combines the girl's strontium isotopic signatures with that of her clothing, she can pinpoint the girl's place of origin relatively accurately.

"The wool that her clothing was made from did not come from Denmark and the strontium isotope values vary greatly from wool thread to wool thread. This proves that the wool was made from sheep that either grazed in different geographical areas or that they grazed in one vast area with very complex geology, and Black Forest's bedrock is characterized by a similarly heterogeneous strontium isotopic range," Karin Margarita Frei says.

That the Egtved Girl in all probability came from the Black Forest region in Germany comes as no surprise to professor Kristian Kristiansen from the University of Gothenburg; the archaeological finds confirm that there were close relations between Denmark and Southern Germany in the Bronze Age.

"In Bronze Age Western Europe, Southern Germany and Denmark were the two dominant centres of power, very similar to kingdoms. We find many direct connections between the two in the archaeological evidence, and my guess is that the Egtved Girl was a Southern German girl who was given in marriage to a man in Jutland so as to forge an alliance between two powerful families," Kristian Kristiansen says.



Map showing the location of the Egtved burial site (red dot). Borders of the nearest areas with bioavailable $^{87}Sr/^{86}Sr$ values that potentially fit the tooth enamel, the child's bone, wool garments and oxhide belonging to the Egtved find are marked with green lines and arrows. Of these regions the Black Forest area (red ellipse) appears to be the most plausible place of origin as constrained by the multiple strontium isotope codes contained in materials from the Egtved find combined with the archaeological artefact record patterns. **Drawing by Marie Louise Andersson, with kind permission of the National Museum of Denmark.**

According to him, Denmark was rich in amber and traded amber for bronze. In Mycenaean Greece and in the Middle East, Baltic amber was as coveted as gold, and, through middlemen in Southern Germany, large quantities of amber were transported to the Mediterranean, and large quantities of bronze came to Denmark as payment. In the Bronze Age, bronze was as valuable a raw material as oil is today so Denmark became one of the richest areas of Northern Europe.

"Amber was the engine of Bronze Age economy, and in order to keep the trade routes going, powerful families would forge alliances by giving their daughters in marriage to each other and letting their sons be raised by each other as a kind of security," Kristian Kristiansen says.

A great number of Danish Bronze Age graves contain human remains that are as well-preserved as those found the Egtved Girl's grave. Karin Margarita Frei and Kristian Kristiansen plan to examine these remains with a view to analysing their strontium isotope signatures.

http://bit.ly/1LxNkXE

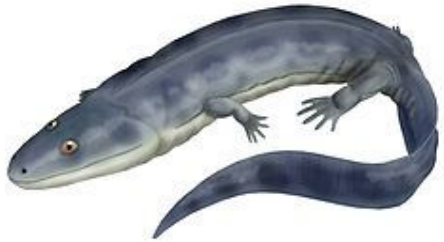
Oldest broken bone reveals our ancestors' switch to life on land

IT WAS one small fall for a tetrapod, but it signals one giant leap for tetrapod kind.

20 May 2015 by Colin Barras

A broken leg bone pushes back the emergence of our four-legged ancestors from water on to land by at least 2 million years.

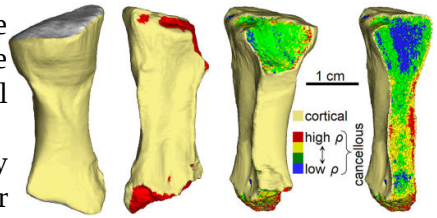
A gap in the tetrapod fossil record means we know little about what happened between the time when limbs evolved from fish fins some 360 million years ago and the first land-adapted tetrapods appeared 330 million years ago.



Life restoration of Ossinodus pueri. **Based on figure 11 of "New data on Ossinodus pueri, a stem tetrapod from the Early Carboniferous of Australia" by A. Warren Journal of Vertebrate Paleontology 27(4):850-862.**

To find out, Peter Bishop at the Queensland Museum in Hendra, Australia, and his colleagues analysed a rare tetrapod fossil from that gap, a 1.5-metre-long Ossinodus which lived some 333 million years ago in what is now Australia. They found that Ossinodus's forearm bones were strong enough to support the animal's body on land.

It also has what Bishop believes is the world's oldest known broken tetrapod bone. When the team used computer software to reconstruct the forces required to cause the break, they found the magnitude of the force was so large relative to the size of the animal that the accident must have occurred on land.



"Those kinds of impact forces are very difficult to achieve in water, because water acts like a cushion," says Bishop.

Models were used to assess the fracture mechanics **2015 Bishop et al**

The team concludes that the break happened when the animal dropped 85 centimetres, perhaps by falling off a rock or a log in the temperate forests that covered parts of Australia at the time (PLoS One, doi.org/4qg).

Together, the evidence suggests Ossinodus must have spent some time on land, making it the oldest known tetrapod to be adapted to land life – although earlier footprints exist.

Dominique Adriaens at Ghent University, Belgium, agrees the fracture probably occurred on land, but says the height of the fall would depend on unknowable factors including the surface the animal hit.

"This is a quirky but convincing study," says Ted Daeschler at the Academy of Natural Sciences in Philadelphia. "Rarely does the fossil record offer up a moment in time like this injury." Even though we still haven't found the exact origins of land animals, this brings us closer to a more robust understanding of the transition from aquatic to terrestrial lifestyles, says Daeschler.

http://bit.ly/1F3wtqc

When People Want an Upgrade They Tend to Break and Lose Their Old Gadgets

Researchers call it the "Must-Have Effect"

By Marissa Fessenden

Anyone who loses their iPhone can check an online database to see if their phone has been found. But when a new model is about to be released, fewer people check for their lost phones, researchers report in a new study. Cracked phones were also deemed more seriously broken during new release times. The scientists call this phenomenon"The Must-Have Effect."

At *Scientific American,* researcher Francesca Gino explains the results of his investigations into why humans find the old dispensable when the new comes ***along:***

As human beings, we are wonderful storytellers. We want others to believe we are responsible, fair, and logical, and it's also important for us to view ourselves this way. For this reason, when we behave in ways that are not consistent with the rosy image we hold of ourselves, we come up with all sorts of justifications to rationalize our behavior. In fact, we go as far as treating our possessions—and even our romantic partners—carelessly when an "upgrade" is on the market.

Gino and her colleagues tested this careless behavior with some less expensive goods. In the lab, they told researcher participants to play Jenga — a game where wooden blocks are removed from a tower one by one until the precarious structure tumbles down. In the experiment, the participants earned money for each block they removed. But the catch was a coffee mug balanced on top of the tower. Earlier, the researchers gave the participants this mug and told them it was worth about $1. If it fell and broke, they didn't get to keep it.

Half the participants were also told that they had the opportunity to purchase a nicer-looking mug (with a given value of $10) for a special price at the end of the experiment. Those participants offered the upgrade option were more cavalier with the $1 mug: 61 percent dropped the mug, compared to the 37 percent who did when they didn't have an option to get a better mug. "Careless behavior allowed participants to justify buying an upgrade without having to consciously admit to themselves or others that they had been intentionally wasteful," Gino writes.

The researchers published their findings, along with the results from the iPhone data, online at the *Social Science Research Network*. Gino also quotes Benjamin Franklin: "So convenient a thing it is to be a reasonable creature, since it enables one to find or make a reason for everything one has a mind to do."

http://www.bbc.com/news/science-environment-32837201

Antarctic Peninsula in 'dramatic' ice loss

Satellites have seen a sudden dramatic change in the behaviour of glaciers on the Antarctica Peninsula, according to a Bristol University-led study.

By Jonathan Amos BBC Science Correspondent

The ice streams were broadly stable up until 2009, since when they have been losing on the order of 56 billion tonnes of ice a year to the ocean. Warm waters from the deep sea may be driving the changes, the UK-based team says.

The details of the satellite research are published in Science Magazine.

They include more than 10 years of space observations of a broad swathe of coastline roughly 750km in length, on the south-western sector of the peninsula.

Here there is a multitude of glaciers slipping down mountainous terrain and terminating in the Bellingshausen Sea.

"Around 2009/2010, the surface in this part of the southern Antarctic Peninsula started to lower at a really quite dramatic rate, of 4m per year in some places. That's a pretty big signal," said Bristol's Prof Jonathan Bamber.

"The total loss of ice per year is about 60 cubic km. Just to put that into some kind of context: 4 cubic km is roughly equivalent to the domestic water supply of the UK every year."

Antarctica's contribution to sea level rise from melting ice, although growing, is still less than 0.5mm per year. The reported behaviour, however, would mean the south-western peninsula sector now has the second biggest input to that contribution behind the large glaciers that drain into the Amundsen Sea even further to the south and west.

One of the key elements of the new study was the use of the European Space Agency's Cryosat platform, which circles the Earth at a height of over 700km.

This satellite has a remarkable radar altimeter that measures the shape of the ice surface below, and this instrument can be tuned to see rugged regions like the peninsula with a previously unobtainable resolution.

For a check on its work, the Bristol team also used a completely different type of measurement from the US space agency's Grace satellites. This pair of platforms senses the Earth's gravity field and can, in a coarse way, calculate how much ice mass has been lost from a particular region of the continent. These observations are said to be in good agreement with the altimetry data.

The scientists say the Antarctic climate models indicate no significant changes in snowfall or air temperature over the study period, which leads them to think the rapid ice loss is the result of warmer ocean waters.

"The westerly winds flowing around Antarctica have increased in strength in recent decades, probably as a result of global warming and changes in the ozone hole," explained lead author Dr Bert Wouters.

"Now, because these winds have become much stronger, they are pushing more water from the deep ocean on to the continental shelf of Antarctica. This water is relatively warm. It's not warm like in Majorca, for example, but it has a temperature of 1-2 degrees centigrade, which is above the freezing temperature of ice, so it carries enough heat to melt the glaciers and their ice shelves from below."

Some other glaciologists who have seen the Science paper are concerned the numbers reported by Wouters and colleagues may be too high. Certainly, they are out of step with recent studies that could find losses that were only a third to a half as big.

Last year, Veit Helm and colleagues reported annual losses of about 35 cubic km from the entire peninsula. Malcolm McMillan and colleagues, also in 2014, calculated the deficit to be about 25 cubic km per annum, again from the whole peninsula.

Cryosat's principal scientific adviser, Prof Andy Shepherd, said: "Cryosat first spotted this pattern of thinning last year, and although the basic measurements in this new study do seem to be consistent with the older estimates, I think the extremely high rates of ice loss that have been computed are incredible.

"For this much ice to have been lost so quickly, the glaciers would need to have speeded up dramatically, but all the evidence suggests that just hasn't happened. So I will treat these huge ice losses with caution for the time being," the Leeds University researcher told BBC News.

At issue will be the models that describe snow conditions on the ice. The top snow is much less dense than the underlying ice, and if the elevation changes observed by the satellites are attributed to the wrong fraction then the calculation of any mass loss will go awry.

But the Bristol team is adamant that it has captured the situation properly.

"We've done a very thorough and careful analysis of all the various processes, to separate out the impact of each of those processes - and the dynamic signal is so strong it's pretty unequivocal," said Prof Bamber.

"The other thing to say about the other papers is that they were looking at the whole continent whereas we really drilled down into this area."

The way the south-western sector of the peninsula behaves is being closely monitored. Much of the coastal ice actually sits below sea level, with the bedrock under the glaciers sloping back towards the land interior. It is a geometry that the theorists say is potentially unstable, and makes the region's ice streams particularly sensitive to any changes in the temperature of ocean water.

http://bit.ly/1Ks99tY

Sir Arthur Conan Doyle Once Helped Clear an Innocent Man of Murder

On his birthday, revist the mystery author's most famous case

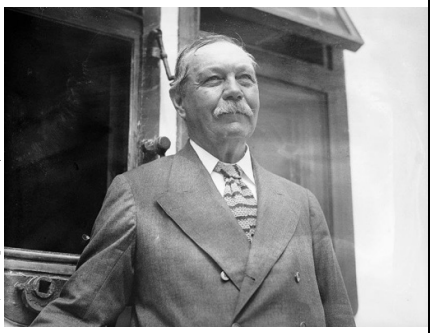
By Helen Thompson

Today, marks the birth of one of the world's most renowned authors, Sir Arthur Conan Doyle, best known as the writer behind Sherlock Holmes. But, Conan Doyle didn't just pen detective stories, he also dabbled in detective work himself.

As many writers do, Conan Doyle had some interesting hobbies, including applying Holmes' techniques to contemporary cases. This caused many in his own time to blur the lines between novelist and character. One well-known instance of this was the murder of an elderly woman named Marion Gilchrist.

At 82 years old and unmarried, Gilchrist lived in the wealthy neighborhood of West Princes Street in Glasgow. On the evening of December 21, 1908, just after 7pm, someone attacked Gilchrist and beat her to death in her own home. When the housemaid Helen Lambie returned from errands, she found find her employer

dead on the dining room floor, papers ransacked and a diamond broach mysteriously missing.



There was no sign of forced entry, so police assumed that she had known her attacker, who had absconded with the broach. Within five days, the police had a suspect: A petty crook named Oscar Slater had recently tried to sell a pawn ticket for a diamond broach before hopping on a ship to the United States. Slater lived near Gilchrist, and Lambie had identified him as a man she had seen running from Gilchrist's house that night.

Sir Arthur Conan Doyle, pictured here in 1923, enjoyed using the methods of Sherlock Holmes on real cases. **(Corbis)**

Perhaps thinking their evidence was lacking, Slater waived extradition and returned to Scotland where he stood trial. The Scottish court convicted and sentenced him to death in 1909. The verdict generated quite the public outcry. Though scheduled for execution, Slater's lawyer gathered signatures for a petition and successfully got his client's sentence commuted. Slater appeared destined to spend his life in jail instead.

By then, the publicity surrounding the case had garnered the interest of Conan Doyle, who began a reexamination of the facts by Sherlockian methods. Despite the sentence, the prosecution had left some glaring holes in their case. The broach he said he had pawned actually belonged to a lady friend, and rumors surfaced that witnesses, including Lambie, had been coached.

Conan Doyle interviewed new witnesses, searched for additional evidence and even covered some of Slater's legal fees. In 1912, he published his findings in *The Case of Oscar Slater*. But, it wasn't enough to induce a retrial, and Conan Doyle lost interest in the case.

Seven years later, the widow of a Glasgow police officer contacted him. Her husband, John Thompson Trench, had kept documents revealing that other officers withheld evidence about suspects among Gilchrist's family — suspects with powerful friends. Conan Doyle also received at plea from Slater in prison around the same time, and a journalist published a piece on the case that highlighted Conan Doyle's work. Suddenly, he was on the case again.

Eventually, thanks in part to Conan Doyle's influence, Slater was released in 1927. Once authorities reopened and retried the case, Slater's name was cleared. As for Marion Gilchrist's actual murderer, his identity remains unknown.

http://bit.ly/1Hq3H4F

Mummy Madness In The Anatomical Record - All Open Access

If you like mummies (and who doesn't like mummies?) you are in luck: The Anatomical Record has a special issue with 26 articles devoted to them, all open access. You may not leave the house this weekend.

By Hank Campbell

The issue takes an "integrative anatomy" approach, looking at mummies from the inside and outside using methodologies from physiology, molecular biology, and cell biology along with the more traditional dissection, histology, or histochemistry. One article mummifies modern tissue using ancient techniques, for example, while others deals with mummies from various regions. They are not just from Egypt. Mummies have been studied in-depth for a century and one article delves into issues related to discovery and preservation.

Investigators even take on the thorny issue of ethics as it applies to human remains in general and in the specific case of mummy research.

In the United States, environmentalists have learned they can block science of all kinds by getting native Americans to invoke "sacred lands" and the political proclivities of the social sciences won't allow them to violate their own self-identification and object. Such maneuvering has worked most recently in Hawaii, where astronomy 13,000 feet in the air is supposedly violating sacred land, and they just drove out biological science too.

But archeology was first to the cultural party in wondering why some things were sacred so they have had a lot of time to think about it. Unfortunately since the archaeologists involved are often not natives themselves, they get accused of microaggression for even discussing it. So forget cultural drama for a few days and learn about the orthopedic diseases of ancient Egypt.

Scoliosis seemed to be rather common, at least in 52 mummies in one study. Why elite Egyptians had so many painful orthopedic conditions is an intriguing topic.

http://bit.ly/1BjykXq

EARTH: Flames fan lasting fallout from Chernobyl

In the years following the 1986 Chernobyl nuclear disaster, forest fires billowed plumes of contaminated smoke, carrying radioactive particles throughout Europe on the wind.

Alexandria, VA - Now, researchers fear that a shift to a hotter, drier climate in Eastern Europe could increase the frequency of these fires.

Researchers from the University of South Carolina in Columbia used satellite imagery of fires in the 2000s and field measurements of radioisotope levels to model changes in the distribution of radiation over the region. The researchers found that fires likely spread radiation across much of Eastern Europe, with

Ukraine, Belarus and Russia receiving the highest doses. Traces of radioactive cesium-137 may have even traveled to Turkey, Italy and Scandinavia.

Previously, the same researchers had found that reduced microbial activity in the area leads to slower than expected rates of decomposition of dead plant matter, leading to a build-up of leaf litter and plant debris on the forest floor -- providing more fuel for forest fires.

Under climate models that predict a hotter, drier Eastern Europe in the future, such forest fires could become more frequent, the researchers concluded. Read more about it in EARTH Magazine: http://www.earthmagazine.org/article/flames-fan-lasting-fallout-chernobyl.

The June issue of EARTH Magazine, now available on the digital newsstand at http://www.earthmagazine.org, looks at how solar winds are mapped, and how tiny plant fossils offer scientists insight about ancient ecosystems, as well exclusive features on how geologists are potrayed on the silver screen and how new collaborations in paleoanthropology are bringing our ancestors to life.

http://www.eurekalert.org/pub_releases/2015-05/mc-mcp052115.php

Mayo Clinic, Phoenix Children's Hospital study highlighted during Dog Bite Prevention Week

Prior studies have shown that most dog bite injuries result from family dogs.

PHOENIX -- A new study conducted by Mayo Clinic and Phoenix Children's Hospital shed some further light on the nature of these injuries.

The American Veterinary association has designated this week as Dog Bite Prevention Week.

The study, published last month in the Journal of Pediatric Surgery, demonstrated that more than 50 percent of the dog bites injuries treated at Phoenix Children's Hospital came from dogs belonging to an immediate family member.

The retrospective study looked at a 74-month period between 2007 and 2013 in which there were 670 dog bite injuries treated at Phoenix Children's Hospital. Of those, 282 were severe enough to require evaluation by the trauma team or transportation by ambulance. Characteristics of the most common injuries included:

Both genders were affected (55 percent male)

The most common patient age was 5 years, but spanned from 2 months to 17 years

28 dog breeds were identified and the most common dog was pit bull

More than 50 percent of the dogs belonged to the patient's immediate family

The most common injuries were lacerations (often to the face) but there were also a number of fractures and critical injuries such as severe neck and genital trauma

"More than 60 percent of the injuries we studied required an operation," said lead author Erin Garvey, MD, a surgical resident at Mayo Clinic "While the majority of patients were able to go home the next day, the psychological effects of being bitten by a dog also need to be taken into account."

"The biggest warning from this study is that familiarity with a dog may confer a false sense of safety," said Ramin Jamshidi, MD, senior author on the study and a pediatric surgeon at Phoenix Children's Hospital and Medical Director of Pediatric Trauma at Maricopa Medical Center.

"The next step is to find out what type of education is needed and for whom - the parents, owners of the dogs and even the kids themselves," explains Dr. Garvey.

"Above all, we are interested in the health of children, so we hope to educate families on the importance of following safety tips and guidelines when dealing with dogs, even the well-known family pet at home," echoes Dr. Jamshidi.

The Injury Prevention Center at Phoenix Children's Hospital works to educate patients and families in areas of safety - whether it is water safety, car seat safety or home safety - their goal is to make sure families have the tools they need to keep their children safe. When there is a family dog in the home, the Injury Prevention Center recommends families follow some of the below tips:

Never leave infants or young children alone with a dog, including the family dog

Make sure all dogs in the home are neutered or spayed

Take time to train and socialize your dogs

Keep dogs mentally stimulated by walking and exercising them

Teach children appropriate ways to interact with animals

For more information, please visit http://www.phoenixchildrens.org/health-information/children/29973/30008/30010/1,2739.

http://www.eurekalert.org/pub_releases/2015-05/iocr-sup052015.php

Scientists unveil prostate cancer's 'Rosetta Stone'

Landmark study hails new era of personalized treatment for cancers that have spread round the body

Almost 90 per cent of men with advanced prostate cancer carry genetic mutations in their tumours that could be targeted by either existing or new cancer drugs, a landmark new study reveals.

Scientists in the UK and the US have created a comprehensive map of the genetic mutations within lethal prostate cancers that have spread around the body, in a paper being hailed as the disease's 'Rosetta Stone'.

Researchers say that doctors could now start testing for these 'clinically actionable' mutations and give patients with advanced prostate cancer existing drugs or drug combinations targeted at these specific genomic aberrations in their cancers. The study was led in the UK by scientists at The Institute of Cancer Research, London, in collaboration with researchers from eight academic clinical trials centres around the world.

Uniquely, doctors at The Royal Marsden NHS Foundation Trust and at hospitals in the US were able to collect large numbers of samples of metastatic cancers - cancers that had spread from the original tumour to other parts of the body.

Normally these samples are extremely hard to access, and this is the first study in the world to carry out in-depth analysis of metastatic prostate cancers that are resistant to standard treatments.

The research is published today (Thursday) in the major scientific journal Cell, and is funded by Stand up to Cancer and the Prostate Cancer Foundation.

Researchers analysed the genetic codes of metastatic tumours from the bone, soft tissues, lymph nodes and liver of 150 patients with advanced prostate cancer.

Nearly two thirds of the men in the study had mutations in a molecule that interacts with the male hormone androgen which is targeted by current standard treatments - potentially opening up new avenues for hormone therapy.

Mutations in the BRCA1 and BRCA2 genes - most famous for their roles in breast cancer - were found in nearly 20 per cent of patients. Recent work at The Institute of Cancer Research (ICR) and The Royal Marsden has shown that these patients can be treated effectively by drugs called PARP inhibitors.

Researchers also discovered new mutations, never detected before in prostate cancer, but which do occur in other cancers. These include mutations in the PI3K and RAF gene families which can also be targeted by existing drugs, either currently in trials or approved for use in the clinic.

The researchers also took blood tests to analyse patients' own genomes, and found that 8 per cent were born with DNA errors that predisposed them to prostate cancer. They said this could strengthen the case for genetic screening for people with a family history of the disease.

Previous genetic studies on prostate cancers had mostly analysed tissue from the primary tumours, which tend to carry fewer mutations than metastatic sites.

Studies of metastatic sites had been small and mostly used tissue taken during post mortems - whereas in this study doctors took needle biopsies taken from patients during the course of their treatment.

Professor Johann de Bono, Professor of Experimental Cancer Medicine at The Institute of Cancer Research, London, and Consultant at The Royal Marsden NHS Foundation Trust, said: "We have for the first time produced a comprehensive genetic map of the mutations in prostate cancers that have spread round the body. This map will guide our future treatment and trials for this group of different lethal diseases. We're describing this study as prostate cancer's Rosetta Stone - because of the ability it gives us to decode the complexity of the disease, and to translate the results into personalised treatment plans for patients.

"Our study shines new light on the genetic complexity of prostate cancer as it develops and spreads - revealing it to be not a single disease, but many diseases each driven by their own set of mutations. What's hugely encouraging is that many of the key mutations we have identified are ones targeted by existing cancer drugs - meaning that we could be entering a new era of personalised cancer treatment."

Professor Paul Workman, Chief Executive and President of The Institute of Cancer Research, London, said: "Cancer becomes lethal at the stage when it spreads round the body and stops responding to treatment - but until now it has been incredibly difficult to find out exactly what is going on genetically at that critical point.

"This major new study opens up the black box of metastatic cancer, and has found inside a wealth of genetic information that I believe will change the way we think about and treat advanced disease. The study found that almost 90 per cent of metastatic tumours had actionable mutations, which means that these findings could make a real difference to large numbers of patients."

http://www.eurekalert.org/pub_releases/2015-05/uoc--hsc052115.php

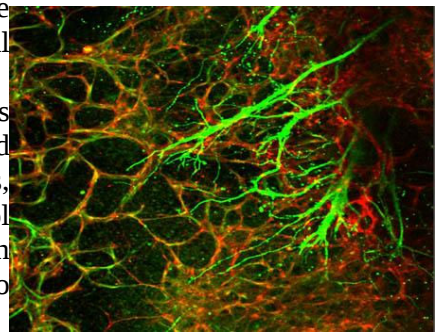
Human stem cell model reveals molecular cues critical to neurovascular unit formation

Real-time tracking of cellular behavior during human development provides new insights

Crucial bodily functions we depend on but don't consciously think about -- things like heart rate, blood flow, breathing and digestion -- are regulated by the neurovascular unit. The neurovascular unit is made up of blood vessels and smooth muscles under the control of autonomic neurons. Yet how the nervous and vascular systems come together during development to coordinate these functions is not well understood. Using human embryonic stem cells, researchers at University of California, San Diego School of Medicine and Moores Cancer Center and Sanford-Burnham Medical Research Institute created a model that allows them to track cellular behavior during the earliest stages of human development in real-time. The model reveals, for the first time, how autonomic neurons and blood vessels come together to form the neurovascular unit. The study is published May 21 by Stem Cell Reports.

"This new model allows us to follow the fate of distinct cell types during development, as they work cooperatively, in a way that we can't in intact embryos, individual cell lines or mouse models," said co-senior author of the study David Cheresh, PhD, Distinguished Professor of Pathology, vice-chair for research and development and associate director for translational research at UC San Diego.

"And if we're ever going to use stem cells to develop new organ systems, we need to know how different cell types come together to form complex and functional structures such as the neurovascular unit."



There are autonomic neurons (green) co-patterning with blood vessels (red). **Credit: UC San Diego School of Medicine**

The neurovascular unit comprises three cells types: endothelial cells, which form the blood vessel (vascular) tube; smooth muscle cells, which cover the endothelial tube and control vascular tone; and autonomic neurons, which influence the smooth muscle's ability to contract and maintain vascular tone.

The study revealed that separate signals produced by endothelial cells and smooth muscle cells are required for embryonic cells to differentiate into autonomic neurons. The researchers discovered that endothelial cells secrete nitric oxide, while smooth muscle cells use the protein T-cadherin to interact with the neural crest, specialized embryonic cells that give rise to portions of the nervous system and other organs. The combination of endothelial cell nitric oxide and the T-cadherin interaction is sufficient to coax neural crest cells into becoming autonomic neurons, where they can then co-align with developing blood vessels.

In addition to answering long-standing questions about human development and improving the odds that scientists will one day be able to generate artificial organs from stem cells, this new insight on the autonomic nervous system also has implications for rare inherited conditions such as neurofibromatosis, tuberous sclerosis and Hirschsprung's disease.

"These observations may help to explain certain human disease syndromes in which abnormalities of the nervous system appear to be associated, for previously unclear reasons, with vascular abnormalities," said co-senior author Evan Snyder, MD, PhD, professor and director of the Center for Stem Cells and Regenerative Medicine at Sanford-Burnham. "Furthermore, we demonstrate here that modeling human development and disease in the lab must take into account multiple cell types in order to reflect the actual human condition. We can no longer rely on merely examining pure populations of one cell type or another."

Co-authors include Lisette M. Acevedo, Jeffrey N. Lindquist, UC San Diego and Sanford-Burnham; Breda M. Walsh, Peik Sia, UC San Diego; Flavio Cimadamore, Connie Chen, Martin Denzel, Cameron D. Pernia, Barbara Ranscht, and Alexey Terskikh, Sanford-Burnham.

This research was funded, in part, by the National Institutes of Health (grants K01CA148897 and P20GM075059) and California Institute for Regenerative Medicine (grants CIRM-CL1-00511-1 and CIRM-RB3-02098).

http://www.eurekalert.org/pub_releases/2015-05/mu-btf051915.php

Blood to feeling: McMaster scientists turn blood into neural cells

Adult sensory neurons made from human patients blood sample

Hamilton, ON - Scientists at McMaster University have discovered how to make adult sensory neurons from human patients simply by having them roll up their sleeve and providing a blood sample.

Specifically, stem cell scientists at McMaster can now directly convert adult human blood cells to both central nervous system (brain and spinal cord) neurons as well as neurons in the peripheral nervous system (rest of the body) that are responsible for pain, temperature and itch perception. This means that how a person's nervous system cells react and respond to stimuli, can be determined from his blood.

The breakthrough, published online today and featured on the cover of the journal Cell Reports, was led by Mick Bhatia, director of the McMaster Stem Cell and Cancer Research Institute. He holds the Canada Research Chair in Human Stem Cell Biology and is a professor in the Department of Biochemistry and Biomedical Sciences of the Michael G. DeGroote School of Medicine. Also playing a key role was Karun Singh, a co-author in the study and holder of the David Braley Chair in Human Stem Cell Research.

Currently, scientists and physicians have a limited understanding of the complex issue of pain and how to treat it. The peripheral nervous system is made up of different types of nerves - some are mechanical (feel pressure) and others detect temperature (heat). In extreme conditions, pain or numbness is perceived by the brain using signals sent by these peripheral nerves.

"The problem is that unlike blood, a skin sample or even a tissue biopsy, you can't take a piece of a patient's neural system. It runs like complex wiring throughout the body and portions cannot be sampled for study," said Bhatia.

"Now we can take easy to obtain blood samples, and make the main cell types of neurological systems - the central nervous system and the peripheral nervous system - in a dish that is specialized for each patient," said Bhatia. "Nobody has ever done this with adult blood. Ever.

"We can actually take a patient's blood sample, as routinely performed in a doctor's office, and with it we can produce one million sensory neurons, that make up the peripheral nerves in short order with this new approach. We can also make

central nervous system cells, as the blood to neural conversion technology we developed creates neural stem cells during the process of conversion."

His team's revolutionary, patented direct conversion technology has "broad and immediate applications," said Bhatia, adding that it allows researchers to start asking questions about understanding disease and improving treatments such as: Why is it that certain people feel pain versus numbness? Is this something genetic? Can the neuropathy that diabetic patients experience be mimicked in a dish?

It also paves the way for the discovery of new pain drugs that don't just numb the perception of pain. Bhatia said non-specific opioids used for decades are still being used today.

"If I was a patient and I was feeling pain or experiencing neuropathy, the prized pain drug for me would target the peripheral nervous system neurons, but do nothing to the central nervous system, thus avoiding non-addictive drug side effects," said Bhatia.

"You don't want to feel sleepy or unaware, you just want your pain to go away. But, up until now, no one's had the ability and required technology to actually test different drugs to find something that targets the peripheral nervous system and not the central nervous system in a patient specific, or personalized manner."

Bhatia's team successfully tested their process using fresh blood, but also cryopreserved (frozen) blood. Since blood samples are taken and frozen with many clinical trials, this allows them "almost a bit of a time machine" to go back and explore questions around pain or neuropathy to run tests on neurons created from blood samples of patients taken in past clinical trials where responses and outcomes have already been recorded".

In the future, the process may have prognostic potential, explained Bhatia, in that one might be able to look at a patient with Type 2 Diabetes and predict whether they will experience neuropathy by running tests in the lab using their own neural cells derived from their blood sample.

"This bench to bedside research is very exciting and will have a major impact on the management of neurological diseases, particularly neuropathic pain," said Akbar Panju, medical director of the Michael G. DeGroote Institute for Pain Research and Care, a clinician and professor of medicine.

"This research will help us understand the response of cells to different drugs and different stimulation responses, and allow us to provide individualized or personalized medical therapy for patients suffering with neuropathic pain."

This research was supported by the Canadian Institutes of Health Research, Ontario Institute of Regenerative Medicine, Marta and Owen Boris Foundation, J.P. Bickell Foundation, and the Ontario Brain Institute and Brain Canada.

http://www.eurekalert.org/pub_releases/2015-05/cp-obw051415.php

Our bond with dogs may go back more than 27,000 years

Dogs' special relationship to humans may go back 27,000 to 40,000 years

Dogs' special relationship to humans may go back 27,000 to 40,000 years, according to genomic analysis of an ancient Taimyr wolf bone reported in the Cell Press journal Current Biology on May 21.

Earlier genome-based estimates have suggested that the ancestors of modern-day dogs diverged from wolves no more than 16,000 years ago, after the last Ice Age.

The genome from this ancient specimen, which has been radiocarbon dated to 35,000 years ago, reveals that the Taimyr wolf represents the most recent common ancestor of modern wolves and dogs.

"Dogs may have been domesticated much earlier than is generally believed," says Love Dalén of the Swedish Museum of Natural History. "The only other explanation is that there was a major divergence between two wolf populations at that time, and one of these populations subsequently gave rise to all modern wolves."

Dalén considers this second explanation less likely, since it would require that the second wolf population subsequently became extinct in the wild.

"It is [still] possible that a population of wolves remained relatively untamed but tracked human groups to a large degree, for a long time," adds first author of the study Pontus Skoglund of Harvard Medical School and the Broad Institute.

The researchers made these discoveries based on a small piece of bone picked up during an expedition to the Taimyr Peninsula in Siberia.

Initially, they didn't realize the bone fragment came from a wolf at all; this was only determined using a genetic test back in the laboratory. But wolves are common on the Taimyr Peninsula, and the bone could have easily belonged to a modern-day wolf. On a hunch, the researchers decided to radiocarbon date the bone anyway. It was only then that they realized what they had: a 35,000-year-old bone from an ancient Taimyr wolf.

The DNA evidence also shows that modern-day Siberian Huskies and Greenland sled dogs share an unusually large number of genes with the ancient Taimyr wolf.

"The power of DNA can provide direct evidence that a Siberian Husky you see walking down the street shares ancestry with a wolf that roamed Northern Siberia 35,000 years ago," Skoglund says. To put that in perspective, "this wolf lived just a few thousand years after Neandertals disappeared from Europe and modern humans started populating Europe and Asia."

Join the conversation about this paper on Twitter using #ancientwolf. Want more info? Ask lead author Pontus Skoglung @pontus_skoglund.

http://bit.ly/1BjDimY

Dog Domestication Much Older than Previously Known

Genetic information from a 35,000-year-old wolf bone found below a frozen cliff in Siberia is shedding new light on humankind's long relationship with dogs

By Will Dunham Editing by Sandra Maler

WASHINGTON - Genetic information from a 35,000-year-old wolf bone found below a frozen cliff in Siberia is shedding new light on humankind's long relationship with dogs, showing canine domestication may have occurred earlier than previously thought.

Today's dogs, from the Chihuahua to the Great Dane, are believed to have descended from wild wolves domesticated by humans in prehistoric times, but when this took place has been a matter of debate.

Scientists said on Thursday they pieced together the genome of the wolf that lived on Russia's Taimyr Peninsula and found that it belonged to a population that likely represented the most recent common ancestor between dogs and wolves.

Using this genetic information, they estimated that dog domestication occurred between 27,000 and 40,000 years ago.

Previous research based on genetic data from modern-day wolves and dogs had estimated that dogs were first domesticated 11,000 to 16,000 years ago based on an estimate of how quickly mutations occurred across the genome.

Swedish Museum of Natural History geneticist Love Dalén said the Taimyr wolf genome showed that the rate of mutation was only about half of what previously had been assumed, indicating domestication occurred much earlier.

"The difference between the earlier genetic studies and ours is that we can calibrate the rate of evolutionary change in dog and wolf genomes directly, and we find that the first separation of dog ancestors must have been in the older range," Harvard Medical School geneticist Pontus Skoglund added.

Dalén found the wolf bone fragment, likely a part of a rib, in the Siberian permafrost.

The wolf likely belonged to a population that roamed the Eurasian steppe tundra during the last Ice Age, hunting large prey like bison, musk ox and horses, Dalén said.

"I think one of the simplest explanations is that hunter-gatherers may have caught wolf pups, which is extremely easy to do, and kept them in captivity as sentinels against the large predators that roamed the landscapes of the last Ice Age - bears, cave lions, etc. as well as other dangerous mammals - mammoths, woolly rhinos, other humans," Dalén said.

Skoglund said Siberian Huskies and Greenland sled dogs share a large number of genes with the Taimyr wolf. "The most likely explanation is that the Siberian domestic dog populations interbred with local wolves when they followed early human groups into northern latitudes," Skoglund said.

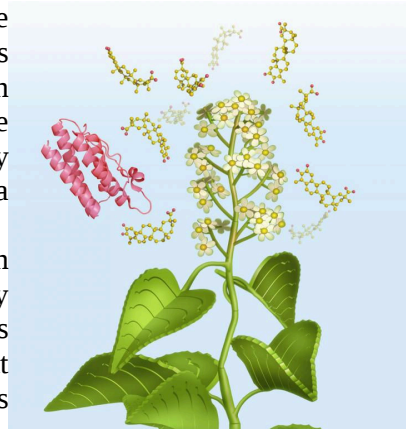
Current Biology, Skoglund et al.: "Ancient wolf genome reveals an early divergence of domestic dog ancestors and admixture into high-latitude breeds" http://dx.doi.org/10.1016/j.cub.2015.04.019

http://www.eurekalert.org/pub_releases/2015-05/cp-tgv051515.php

Thunder god vine used in traditional Chinese medicine is a potential obesity treatment

Extract of thunder god vine reduces food intake and causes up to a 45% decrease in body weight in obese mice

An extract from the thunder god vine, which has a long history of use in traditional Chinese medicine, reduces food intake and causes up to a 45% decrease in body weight in obese mice. The weight-loss compound, called Celastrol, produces its potent effects by enhancing the action of an appetite-suppressing hormone called leptin. The findings, published May 21 in Cell, are an early indicator that Celastrol could be developed into a drug for the treatment of obesity.



***An artist's depiction of the thunder god vine* 雷公藤 *and leptin molecule.* Credit: Eric Smith**

"During the last two decades, there has been an enormous amount of effort to treat obesity by breaking down leptin resistance, but these efforts have failed," says senior study author Umut Ozcan, an endocrinologist atBoston Children's Hospital and Harvard Medical School.

"The message from this study is that there is still hope for making leptin work, and there is still hope for treating obesity. If Celastrol works in humans as it does in mice, it could be a powerful way to treat obesity and improve the health of many patients suffering from obesity and associated complications, such as heart disease, fatty liver, and type 2 diabetes."

Leptin is a fat-cell-derived hormone that signals to the brain when the body has enough fuel and energy. Humans and mice that lack leptin signaling eat voraciously and become morbidly obese, suggesting that leptin-enhancing drugs may be effective for treating obesity. But leptin does not reduce hunger or food intake in obese individuals despite high levels of the hormone in the bloodstream,

leading many researchers to speculate that leptin insensitivity is the root cause of obesity.

Despite longstanding research efforts, drugs that can effectively alleviate leptin resistance have not yet been found. However, one potential clue to this problem came several years ago when Ozcan and his team discovered that leptin resistance is associated with a stress response in a cell structure called the endoplasmic reticulum (ER).

In the new study, Ozcan and his team screened an existing database containing whole-genome gene expression profiles from human cells that were treated with more than one thousand small molecules.

They found that Celastrol was the most effective at producing an expression profile that could be associated with improved ER function and leptin sensitivity in human cells. Within only one week of Celastrol treatment, obese mice reduced their food intake by about 80% compared to untreated obese mice. By the end of the third week, treated mice lost 45% of their initial body weight almost entirely by burning fat stores.

This dramatic weight loss is greater than that produced by bariatric surgery -- an operation on the stomach and/or intestines that helps patients with extreme obesity to lose weight. Moreover, Celastrol decreased cholesterol levels and improved liver function and glucose metabolism, which collectively may translate into a lower risk of heart disease, fatty liver, and type 2 diabetes.

Even though Celastrol did not produce toxic effects in mice, Ozcan strongly urges caution for now because in-depth toxicology studies and controlled clinical trials are needed to demonstrate the compound's safety in humans. "Celastrol is found in the roots of the thunder god vine in small amounts, but the plant's roots and flowers have many other compounds," he says. "As a result, it could be dangerous for humans to consume thunder god vine extracts to lose weight."

In future studies, Ozcan and his team will investigate the molecular mechanisms by which Celastrol improves leptin sensitivity and produces weight loss. "We have been heavily focusing on this line of research in my laboratory and hope that this approach will help us to understand the mechanisms in nature that are leading to the development of obesity," Ozcan says.

"In the end, my main goal is to see this research leading to a novel and powerful treatment for obesity in humans."

This work was supported by Boston Children's Hospital, the National Institutes of Health, the American Diabetes Association, and the Fidelity Biosciences Research Initiative.

Cell, Liu et al. "Treatment of Obesity with Celastrol" http://dx.doi.org/10.1016/j.cell.2015.05.011

http://nyti.ms/1KsCEM4

New Approach Trains Robots to Match Human Dexterity and Speed

In an engineering laboratory here, a robot has learned to screw the cap on a bottle, even figuring out the need to apply a subtle backward twist to find the thread before turning it the right way.

By JOHN MARKOFF MAY 21, 2015

BERKELEY, Calif. - This and other activities — including putting a clothes hanger on a rod, inserting a block into a tight space and placing a hammer at the correct angle to remove a nail from a block of wood — may seem like pedestrian actions. But they represent significant advances in robotic learning, by a group of researchers at the University of California, Berkeley, who have trained a two-armed machine to match human dexterity and speed in performing these tasks.

The significance of the work is in the use of a so-called machine-learning approach that links several powerful software techniques that make it possible for the robot to learn new tasks rapidly with a relatively small amount of training.

The new approach includes a powerful artificial intelligence technique known as "deep learning," which has previously been used to achieve major advances in both computer vision and speech recognition. Now the researchers have found that it can also be used to improve the actions of robots working in the physical world on tasks that require both machine vision and touch.

The group, led by the roboticist Pieter Abbeel and the computer vision specialist Trevor Darrell, with Sergey Levine, a postdoctoral researcher, and Chelsea Finn, a graduate student, said they were surprised by how well the approach worked compared with previous efforts.

By combining several types of pattern recognition software algorithms known as neural networks, the researchers have been able to train a robot to perfect an action such as correctly inserting a Lego block into another block, with a relatively small number of attempts. "I would argue this is what has given artificial intelligence the whole new momentum it has right now," Dr. Abbeel said. "All of a sudden there are all of these results that are better than expected."

Roboticists said that the value of the Berkeley technology would be in quickly training robots for new tasks and ultimately in developing machines that learn independently.

"It used to take hours on up to months of careful programming to give a robot the hand-eye coordination necessary to do a task," said Gary Bradski, a roboticist and computer vision specialist who founded OpenCV, a freely available software library for machine vision. "This new work enables robots to just learn the task by doing it."

Previously, the Berkeley lab had received international attention for training a robot to fold laundry. Although it was viewed almost one million times on YouTube, the laundry-folding demonstration noted that the video had been sped up more than 50 times. The new videos show the robots performing tasks at human speeds.

Despite their progress, the researchers acknowledge that they are still far away — perhaps more than a decade — from their goal of building a truly autonomous robot, such as a home worker or elder care machine that could perform complex tasks without human supervision.

The researchers said that while their new approach represents an important leap, it is also fragile. For example, the bottle cap-threading technique will work reliably when the bottle is moved from one location to another or if the bottle is of a different color. But if the bottle is tilted at an angle before it is picked up, the robot will completely fail. “There is nothing better to ask a roboticist, ‘If you change the conditions, will it still work?’ ” Dr. Abbeel said.

To explain the new approach, the researchers draw the analogy of how baseball players track and then catch balls. Humans do not do mathematical calculations to discern the trajectory of the ball. Rather, they fix the ball in their field of vision and adjust their running speed until they arrive at the spot where the ball lands.

This, in effect, short-circuits a complicated set of relations between perception and motion control, substituting a simple technique that works in a wide variety of situations without having to worry about details like wind resistance or the ball’s velocity.

Until now, robots have generally learned with a variety of techniques that are laboriously programmed for each specific case. The Berkeley researchers, who will present their results in a paper at the IEEE Robotics and Automation Society’s conference next week in Seattle, instead connected the neural networks, which learn from both visual and sensory information, directly to the controller software that oversees the robot’s motions. As a result, they achieved a significant advance in speed and accuracy of learning.

“We are trying to come up with a general learning framework that allows the robot to learn new things on its own,” Dr. Abbeel said.

The advance underscores the rapid impact that the deep-learning approach has had on the field of artificial intelligence. Pioneered several decades ago by a small group of cognitive scientists, the techniques were blended in 2012 with the “big data” power offered by cloud computing systems. Researchers were then able to capture billions of images or samples of human language. Their software was able to show rapid progress in accuracy in recognizing objects and in understanding human speech.

Now computer scientists are pushing the techniques in new directions, including self-driving cars and a host of other applications. In December 2013, Deepmind, a British start-up, first demonstrated deep-learning techniques that could be used to play video games with more skill than most human players. The company, which Google acquired for an undisclosed sum in 2014, published a paper describing its advance in the journal Nature in February.

http://bit.ly/1Rev74o

Brain implant allows paralysed man to sip a beer at his own pace

A brain implant that can decode what someone wants to do has allowed a man paralysed from the neck down to control a robotic arm with unprecedented fluidity – and enjoy a beer at his own pace.

- **19:10 21 May 2015 by Helen Thomson**

Video: Robotic arm moves by the power of thought

Erik Sorto was left unable to move any of his limbs after an accident severed his spinal cord 12 years ago. People with similar injuries have previously controlled prosthetic limbs using implants placed in their motor cortex – an area of the brain responsible for the mechanics of movement. This is far from ideal because it results in delayed, jerky motions as the person thinks about all the individual aspects of the movement. When reaching for a drink, for example, they would have to think about moving their arm forward, then left, then opening their hand, then closing their hand around the cup and so on.

Richard Andersen at the California Institute of Technology in Pasadena and his colleagues hoped they could achieve a more fluid movement by placing an implant in the posterior parietal cortex – a part of the brain involved in planning motor movements.

"We thought this would allow us to decode brain activity associated with the overall goal of a movement – for example, 'I want to pick up that cup', rather than the individual components," said Anderson at the NeuroGaming Conference in San Francisco, California, where he presented the work this month.

Neuron control

Andersen's team placed two implants measuring 4 millimetres squared into Sorto's posterior parietal cortex. Each contained electrodes that recorded the activity of hundreds of individual neurons. "We weren't actually sure what we would find as it's entirely new territory," said Andersen. "The posterior parietal cortex is a fascinating area as it doesn't control the muscles so much as the plans you make to do something."

For nearly two years, the team recorded the patterns of electrical activity from each neuron firing while Sorto imagined making different arm and eye movements associated with a movement.

"We found there was amazingly specific activity for specific gestures," says Andersen. For example, certain neurons were active when Sorto imagined moving his right hand to the back of his head, while others were active when he thought about moving his left hand to his lips.

Some neurons were responsible for the intended goal of a movement, and others for the trajectory of the movement – whether Sorto wanted to reach for something overarm or underarm, for example. In addition, some neurons responded only when he imagined moving one of his arms – information that might be useful for controlling two prosthetic limbs at the same time.

Rock, paper, scissors

Next, the team sent information from the implant to a computer, which translated it into instructions to move a separate robotic arm.

This enabled Sorto to control the speed and trajectory of the arm, allowing him to shake hands with people, play rock, paper, scissors and to switch on a blender to make a smoothie. Most importantly to him, he was able to smoothly pick up a beer and take a swig. "The one thing he said he wanted to be able to do at the start of the experiment was to drink a beer with his friends and control how fast he drank it, rather than having to rely on others, says Andersen.

"It's awesome, it's awesome," Sorto repeated, after drinking his beer. "I would hope some day that people with these conditions will have a robotic arm and regain some sort of independence. I want to push the limit – I have high hopes for myself," he says.

One unexplored possibility is that the posterior parietal cortex might also encode other kinds of intentions. In their paper, Anderson's team hypothesises that as the world becomes increasingly technologically connected it might be possible to also decode non-motor intentions to control one's environment – for example, could we identify the brain activity that corresponds with the thought of wanting to watch a film, and have that trigger the television to switch on?

Touchy feely

For now though, the next step is to give people like Sorto back their sense of touch. Tactile feedback is essential if the person is to have full control over a prosthetic limb. It also makes it easier for them to consider it as their own.

Previously, scientists have stimulated nerves in the wrist to give touch back to people whose hands had been amputated, but this is not possible for people with a spinal injury because the messages from the nerves cannot reach the brain.

It might be possible to stimulate the brain directly instead. In 2011, Miguel Nicolelis at Duke University Medical Centre in Durham, North Carolina, showed that stimulating the somatosensory cortex – an area that processes feelings of touch – let monkeys feel the texture of virtual objects without physically touching anything.

Other experiments have suggested the same might apply to humans: people undergoing brain surgery have had their somatosensory cortex stimulated and reported feeling things such as "a wind rushing over my hand" or "my finger being wrapped in something".

Andersen and his colleagues are the first to attempt to harness this brain area to simulate touch in people. At the conference, Andersen announced that the team has placed an implant in their first volunteer and begun preliminary experiments to identify what kind of brain stimulation is required to replicate real sensation.

Journal reference: Science, DOI: 10.1126/science.aaa5417

http://bit.ly/1LyA4Ca

First evidence that dinosaurs laid colourful blue-green eggs

Vivid hue may have been colouring eggs long before any birds evolved

22:00 21 May 2015 by Jeff Hecht

The American robin lent its name to a striking shade of blue, but the vivid hue may have been colouring eggs long before the bird evolved – perhaps long before any birds evolved. It may have appeared in the dinosaur ancestors of birds that lived 150 million years ago.

Used to be raptor egg blue **(Image: Tzu-Ruei Yang, University Bonn)**

Although recent studies have revealed the colours of dinosaur feathers, skin and scales, we had known nothing about the original colour of their eggs.

Ornithologists once assumed early birds, and the dinosaurs they evolved from, laid white eggs. But we know that some of the most ancient groups of birds still around – including the tinamou and emu – actually lay coloured eggs, points out Mark Hauber, an animal behaviourist at Hunter College in New York.

His group has discovered the chemical origin of the avocado-green from emu's eggs, as well as the blue of robin's eggs, the brown of chicken's eggs and the pinks and purples from the eggs of other birds belonging to ancient living groups. The colours come from the way that two pigments in the shell – biliverdin and protoporphyrin – blend with each other and with the calcium carbonate that makes most of the shell.

True colours

But when were the two pigments first added to egg shells? Martin Sander of Bonn University in Germany has an idea. In a separate study, he looked at eggs from

three prehistoric nesting sites in China where oviraptor dinosaurs – close relatives of modern birds – gathered to lay their eggs millions of years ago.

Sander chose the site because the eggs there are very pale. Dinosaur eggs found elsewhere are typically deep brown or black, because minerals have seeped into them over time and stained them, obscuring pigment molecules in the shell. The pigment molecules were more likely to be observed in the pale eggs from China – although in a fossilised state they would no longer colour the eggs in the same way they did when the egg was fresh..

Sander's student, Jasmina Wiemann, found the oviraptor eggs contained both biliverdin and protoporphyrin. Most protoporphyrin came from the protein layer or cuticle still coating the fossil egg, as it does in modern bird eggs. Biliverdin came mostly from the calcium carbonate, also as in modern birds. Collectively the pigment evidence suggests oviraptors had blueish-green eggs.

The blue ones are mine

The similarity to modern birds probably reflects similarity in lifestyle, says Sander. Like most modern birds, the Chinese dinosaurs incubated their eggs in open nests, rather than burying them in the ground the way turtles or crocodiles do. Coloured eggs are an advantage in that situation, because they are much less obvious to the eager eyes of predators than white eggs. That means a brooding parent can slip away from the nest occasionally to snatch a meal.

Egg colour has other benefits: it can help the parent recognise and eject eggs that another species might add to the nest surreptitiously – like cuckoos and cowbirds do today. The protoporphyrin also helps strengthen the shells.

"This is our first knowledge of anything about dinosaur egg colours," says David Varricchio of Montana State University, who was not involved in either study. Others failed to find colours in the past, he says, but techniques for identifying biomolecules have improved greatly since then.

He echoes Sander's views on the link between coloured eggs and nesting behaviour – suggesting that it was dinosaurs switching to open nests that ultimately led to robin egg blue.

Journal references: Hauber's study: Biology Letters, DOI: 10.1098/rsbl.2015.0087; Sander's study: PeerJ Preprint 1080v1

http://www.eurekalert.org/pub_releases/2015-05/esoc-cip051915.php

Cognitive impairment predicts worse outcome in heart failure

Risk of all-cause death and heart failure readmission was elevated by 7.5-fold

Seville, Spain - Cognitive impairment predicts worse outcome in elderly heart failure patients, reveals research presented today at Heart Failure 2015 by Hiroshi Saito, a physiotherapist at Kameda Medical Centre in Kamogawa, Japan. Patients with cognitive impairment had a 7.5 times greater risk of call cause death and heart failure readmission.

Heart failure patients with cognitive impairment may get progressively worse at adhering to medications, leading to poorer prognosis.

Heart Failure 2015 is the main annual meeting of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) and takes place 23 to 26 May in Seville, Spain. The scientific programme is available here.

Mr Saito said: "Systematic reviews have shown that cognitive impairment is common in patients with chronic heart failure. However, the impact of cognitive impairment on the prognosis of heart failure patients is not known. Our study investigated whether cognitive impairment independently predicted the outcome of elderly patients with heart failure."

The study retrospectively included 136 patients aged 65 years or over with heart failure who were admitted to Kameda Medical Centre. The Mini Mental State Examination (MMSE) was conducted to evaluate the presence of cognitive disorder in all patients before discharge. Patients were divided into two groups: those with cognitive disorder (score below 27 on the MMSE) and those without (score 27 or above).

Patients were 82 years old on average and 47% were men. According to the MMSE, 101 patients (74%) had cognitive disorder. After a follow up of 161 days, 33 patients (24%) were readmitted due to heart failure or died.

The researchers found that the prognosis of patients in the cognitive impairment group was significantly worse than the non-cognitive impairment group. They also showed that cognitive impairment predicted a 7.5 times greater risk of worse prognosis in elderly patients with heart failure. The risk remained even after adjusting for other prognostic factors including age, gender, body mass index, albumin, haemoglobin, brain natriuretic peptide (BNP), C-reactive protein (CRP), ejection fraction, estimated glomerular filtration rate (eGFR) and blood urea nitrogen (BUN).

Mr Saito said: "Our study shows that cognitive impairment is common in elderly patients with heart failure, occurring in three-quarters of patients. We also found that cognitive impairment is an independent predictor of worse prognosis in elderly heart failure patients, who had a 7.5 times greater risk of all cause death or heart failure readmission."

He added: "We expect that heart failure patients with cognitive impairment tend to get progressively worse at adhering to medications. It is possible that this could explain why they have a worse prognosis. Cardiologists and other medical staff should assess the cognitive status of elderly heart failure patients."

Mr Saito continued: "When cognitive status is impaired we should provide education on disease management to families to prevent heart failure readmission of their loved ones. The three major components of this are medication, nutrition, and exercise. Of these three components, medication is an especially important element. It is necessary for families to enhance medication adherence for patients who are unable to manage their medication by themselves."

He concluded: "There are no specific treatments for cognitive impairment in heart failure patients. If patients do not have shortness of breath resulting from their heart failure, we often recommend mild exercise such as walking to maintain their cognitive function. Clinicians need to be more aware of the cognitive status of their heart failure patients and families can play an important role in ensuring that patients take their medication, get some exercise and eat well."

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http://bbc.in/1Syk5ZB

Ayr Hospital surgeon amputated leg with 'rusty hacksaw'

A hospital surgeon allegedly used a "rusty hacksaw" to amputate a patient's leg after attempting to get a suitable instrument from B&Q.

The Ayr Hospital surgeon was cutting into the pensioner's limb when the knife struck a metal plate in his leg. After B&Q was found to be closed, the operation went ahead with the sterilised saw found in a storage area. NHS Ayrshire and Arran said it was investigating an incident "where standard procedures were not followed".

A health board source said: "An elderly man who was a patient at Crosshouse Hospital needed a leg amputation and was taken to Ayr Hospital for the operation, because that's where the vascular surgeons are based. "The operating theatre was prepared, he was anaesthetised and the operation began but it was halted after the surgeon had difficulty cutting further. "That's when he discovered he'd hit a metal plate that they didn't know about. So he frantically sought advice from the consultant orthopaedic surgeon, who suggested going to B&Q."

'Simply incredible'

However, the store was closed because the operation was being carried out after 21:00 so the surgeon decided to use the saw which was from old hospital stock."

The source added: "The saw was sterilised by soaking in some disinfectant solution and the surgeon proceeded to complete the amputation after cutting through the metal plate. "If this is a proper investigation it should be shared with all as learning. This should never have happened. I have never come across anything similar in my career." It is understood the patient and his relatives were told about what happened some time after the incident.

Scottish Conservatives health spokesman Jackson Carlaw said: "This is simply incredible - an indescribable way to treat any patient. "Despite the UK's advances in modern medicine this episode has all the finesse of improvised surgery on Nelson's flagship during the Battle of Trafalgar. "I would hope that NHS Ayrshire and Arran thoroughly investigates this as a matter of urgency."

Ann Gow, the board's interim nurse director, said in a statement: "NHS Ayrshire and Arran is currently conducting a significant adverse event review (SAER) into a recent incident within University Hospital Ayr, where standard procedures were not followed. "The findings of this review and any subsequent recommendations will be shared with clinicians, as well as the family of the patient."

http://www.eurekalert.org/pub_releases/2015-05/cafn-cys052115.php

Can you see what I hear? Blind human echolocators use visual areas of the brain

Canadian expert Mel Goodale determines echolocators use echoes to detect multiple properties of objects through areas of the brain associated with vision

Certain blind individuals have the ability to use echoes from tongue or finger clicks to recognize objects in the distance, and some use echolocation as a replacement for vision. Research done by Dr. Mel Goodale, from the University of Western Ontario, in Canada, and colleagues around the world, is showing that echolocation in blind individuals is a full form of sensory substitution, and that blind echolocation experts recruit regions of the brain normally associated with visual perception when making echo-based assessments of objects. Dr. Goodale's latest results were presented at the 9th Annual Canadian Neuroscience Meeting, on May 24th 2015 in Vancouver British Columbia.

"Our experiments show that echolocation is not just a tool to help visually-impaired individuals navigate their environment, but can act as an effective sensory replacement for vision, allowing them to recognize the shape, size, and material properties of objects" says Mel Goodale.

Just like multiple properties (size, expected weight, texture, composition) of an object assessed by visual cues are encoded in different brain regions, recent research done in the Goodale laboratory shows that the same is true of information obtained through the auditory cues provided by echolocation. Indeed, many of the same regions in the sighted brain that are used for the visual assessment of objects are recruited in the blind brain when objects are explored using echolocation.

To understand what an object is, and to know how to interact with this object, knowing what an object is made of, its "stuff", is equally important as knowing its structure or shape. While his initial studies have investigated how echolocators detect the shape and distance of objects, Dr. Goodale's most recent studies have investigated how they perceive the material or "stuff" that different objects are made of.

"Remarkably, expert blind echolocators can tell whether something is hard or soft, dense or not, just by listening to the echoes bouncing back from that material" notes Dr. Goodale.

While sighted individuals use visual cues to get information about the composition of objects, such as the sheen of metal, or the fuzziness of fur, echolocators must rely on the auditory cues that result from the echoes of the clicks they emit. To determine how the brains of echolocators process these cues, researchers have recorded the echoes produced by echolocator's clicks on different materials (a blanket, fake foliage and a whiteboard) and looked at the response these sounds produced in the brains of sighted people, of blind non-echolocators and of blind echolocators. To view which brain regions were activated in these individuals, an advanced brain imaging technique called functional magnetic resonance imaging (fMRI) was used.

These studies show that material-related signals activate a region of the brain called the parahippocampal cortex (PHC) in blind expert echolocators, but not in sighted people or blind non-echolocators. PHC activation is associated with scene perception in sighted individuals. Just as in sighted individuals using vision, the brain regions that play a critical role in processing the structure and geometry of objects are distinct from the brain regions that process the cues that signal the material properties of objects in blind echolocators.

Interestingly, other studies in the Goodale lab have shown that blind expert echolocators are also subject to illusions, for example the size-weight illusion in which the perception of mass is influenced by the size of an object. If two objects of equal weight are presented to both a sighted and a blind echolocator, both will find the smaller object feels heavier when they lift it using a string attached to a pulley. This illusion, thought to be based on the lifter's cognitive expectations, and the fact that it is also present in blind echolocators, but not in blind non-echolocators, shows that echolocation is an effective form of sensory substitution for vision.

Because echolocation allows blind individuals to perceive objects from a distance, it can be used as an alternative to vision, allowing the perception of distant objects that would be impossible through touch. In fact, some echolocators are proficient enough to use this ability to perform complex tasks such as riding a bicycle - or even sinking a basketball!