http://bit.ly/2DPIBpu

Blood pressure: Early treatment advised by US guidelines has no survival benefits

When is high blood pressure dangerous? Medical associations offer widely differing answers.

In the USA, for example, patients are seen as hypertensive much sooner than in Germany. A team working with Prof. Karl-Heinz Ladwig of the Technical University of Munich and the Helmholtz Zentrum München has concluded that treating patients sooner does not reduce the risk of deadly heart disease. It could even negatively affect their mental health.

In 2017 the American College of Cardiology added a new category to its guidelines for high blood pressure: "Stage 1 Hypertension". Under the new standards, doctors are advised to place patients in this category (130-139 mmHg / 80-89 mmHg) on treatment. For the European Society of Cardiology, that range is defined as "high normal" blood pressure, with no specific action recommended.

"The idea behind the US guidelines is to lower blood pressure as early as possible and, by presenting patients with a diagnosis, to encourage them to adopt a healthier lifestyle," explains Prof. Karl-Heinz Ladwig, a researcher at the Clinic for Psychosomatic Medicine and Psychotherapy at the TUM University Clinic rechts der Isar at the Helmholtz Zentrum München.

Motivation factor questionable

Using data from approximately 12,000 patients, Ladwig and his team assessed the situation in Germany. "We studied the 10-year risk of mortality from cardio-vascular disease (CVD) among people in the various hypertension categories in the context of the other risk factors affecting them," says Seryan Atasoy, the first author of the study, who is working as an epidemiologist at Helmholtz Zentrum München and Ludwig-Maximilians-Universität München.

In the newly created category "Stage 1 Hypertension", the CVD mortality risk was not significantly higher than among patients with normal blood pressure. "The motivation effect is questionable, too," says Karl-Heinz Ladwig. Patients in the high-risk category "Stage 2 Hypertension", where medication is recommended under both the US and the European guidelines, have a much greater risk of dying of heart disease, he explains. "At the same time, risk factors such as smoking and a lack of exercise are far more frequent in that group. That shows that many people do not change their lifestyles despite the diagnosis."

Dangerous depression

Although the incidence of depression is generally lower among people with dangerously high blood pressure than in the general population, depression was significantly more common in one subset of that group: those taking medication to treat their serious hypertension. Here, depressive moods were reported by around half of all patients, as opposed to just one-third of those not receiving treatment.

"We believe that this should be seen as a labeling effect," says Ladwig. "When people are officially labeled as 'sick', that has an impact on their mental health." A previous study by Ladwig and his team showed that, in terms of mortality risk from cardio-vascular disease, depression is comparable to high cholesterol levels or obesity.

New guidelines mean more sick people

"The American College of Cardiology itself has calculated that the proportion of adults diagnosed with high blood pressure will increase from 32 to 46 percent," says Karl-Heinz Ladwig. "That means 14 percent more who have to deal with the additional mental stress - although their risk of developing a potentially deadly cardio-vascular condition is not significantly higher, and despite no real expectation of extra motivation through the diagnosis." For those reasons,

Ladwig believes that it would be a serious mistake to adopt the US guidelines in Europe.

Publication:

S. Atasoy, H. Johar, A. Peters, K.-H. Ladwig. "Association of hypertension cut-off values with 10-year cardiovascular mortality and clinical consequences: a real-world perspective from the prospective MONICA/KORA study". European Heart Journal *(2018). DOI:10.1093/eurheartj/ehy694*

http://bit.ly/2FLDE3w

Purported birth of world's first gene-edited babies proclaimed on YouTube

It was a birth announcement like no other.

Rebecca Robbins @rebeccadrobbins

In a promotional video posted on YouTube on Sunday, Chinese researcher He Jiankui revealed new details about the two babies he claims to have genetically modified as embryos using the gene-editing technology known as CRISPR.

In the video, He said that the twin girls — named Lulu and Nana — were born a few weeks ago after a normal pregnancy. They are now at home with their mother, a woman named Grace, and their father, Mark, a man who is HIV-positive and did not want to pass his infection to his offspring, He said.

He told the Associated Press, however, that the parents did not want to be identified or interviewed. He, who studied in the U.S. before starting a lab at Southern University of Science and Technology of China in Shenzhen, would not tell the AP where the parents live or where the gene editing was performed.

If true, the birth of gene-edited babies would be a landmark — and a deeply controversial step for science and society.

He's promotional video, filmed in a laboratory setting, was heavy on emotion and short on evidence. At one point in the video, He said that Mark never thought he could be a father, and has now found "a reason to live, a reason to work, a purpose" in the birth of his daughters. (In fact, relatively simple ways exist to keep HIV-positive parents from infecting their children that do not involve altering DNA.)

He said the babies had their genomes sequenced after birth, which confirmed that the gene editing had worked safely and had been isolated to disabling the gene CCR5 — which allows HIV to enter a cell. "The girls are safe and healthy as any other babies," He said in the video, though he provided no evidence to back up those claims.

But there's reason to think that the reality is more complicated than the rosy picture painted by He's video.

In the interview with the Associated Press, He said one of the girls had both copies of CCR5 altered, while the other had only one copy altered. It's still possible for people with only one copy of CCR5 to get HIV, though preliminary research indicates that they may stay healthier for longer if they do get it.

Moreover, several scientists who reviewed documentation that He provided to the Associated Press said it appears that the editing was not complete and that there's not yet enough evidence to tell whether the editing worked as intended or was safe.

The existence of He's clinical trial in which the editing took place was first reported by MIT Technology Review's Antonio Regalado on Sunday evening. A few hours later, the Associated Press was first to report He's claim that the first genetically modified babies had been born. The news comes on the eve of an international conference on gene editing in Hong Kong.

http://bit.ly/2Arf8Pc

Reports out of China suggest first human gene-edited babies have been born

CRISPR technology supposedly used to edit gene associated with HIV resistance.

John Timmer - 11/27/2018, 5:31 AM

On Sunday, news reports indicated that the first gene-edited human babies had been born in China. As of right now, the information on

what, exactly, has been accomplished is confusing. The scientist behind the announcement has made a variety of claims but has not submitted his data to the community in order for his claims to be verified. But even in its current state, the announcement has set off a firestorm of criticism within the scientific and ethics communities. Most scientists feel that the technology isn't ready for use in humans and that there are better ways to deal with the problem the work was addressing: HIV infection.

Editing genes

The most complete report we currently have comes from the Associated Press. Its reporters talked to the researcher behind the announcement, He Jiankui of Shenzhen, China, in advance of his public announcement. That public announcement came at the start of the Second International Summit on Human Genome Editing, taking place this week in Hong Kong. The summit is intended to help work out the "science, application, ethics, and governance of human genome editing," but He apparently chose to go ahead in advance of those being settled.

He is expected to present more details of his work on Wednesday, but it's clear that he used biotechnology called CRISPR to perform the gene editing. CRISPR is a system that evolved in bacteria to protect them from viruses by allowing them to recognize and cut viral DNA. By changing part of the CRISPR system, it's possible to direct it to cut an arbitrary DNA sequence. That can include sequences within the human genome.

Cells interpret the resulting break in their DNA as damage and attempt to repair it. In many cases, this repair is inexact and results in the deletion of a handful of individual base pairs within the targeted sequence. Depending on the precise details of this deletion, this can disable a targeted gene. (There are also means of replacing the targeted sequence, but those weren't needed for the work described here.)

This is where the first ethical issue of the work comes in. The frequency of successful editing in early work on human cells was only about five percent. And just this year, a study involving human cells showed that CRISPR editing can also make arbitrarily large deletions that affect neighboring genes or trigger complex rearrangements of the genome that can be difficult to detect if they aren't specifically looked for. All of this suggests that accurate editing of a single targeted gene isn't guaranteed, and we're still working out how to screen for it.

Is this really necessary?

That should be a large enough ethical problem to block the work. But there were more, including the reason for doing the editing in the first place. The researchers targeted a gene called *CCR5*, which encodes an immune system protein that the HIV virus latches onto in order to enter cells. People with mutations in *CCR5* are notable because they have low rates of HIV infection and tend to have the disease progress extremely slowly (or not at all) if infected.

He Jiankui claims to have used volunteer couples in which the male partner has an HIV infection. He then targeted *CCR5* for editing in an embryo generated through IVF.

There are a huge number of issues with this. To begin with, offspring of HIV-positive male parents are not considered to be at risk of picking up the infection during fertilization. And, once born, it's relatively easy for them to avoid infection, even when sharing a home with an infected individual. Thus, the editing being done here doesn't seem to address a significant risk. If infection does occur, we now have viable, long-term treatments, making this approach even less necessary.

Compounding matters are indications that the loss of *CCR5* leaves individuals at heightened risk of infection from other viruses, including West Nile. So, rather than simply eliminating a risk, the work here seems to involve exchanging risks.

Or that would be the case if He had limited his work to instances in which the editing was successful. He claims that a pair of twins were born following the editing procedure (other couples tried but have not yet brought a baby to term). But the AP showed data obtained from He to a number of scientists, who indicated at least one of the twins born was a mosaic—editing took place after the embryo started cell divisions, making that individual a patchwork of edited and unedited cells.

"In that child, there really was almost nothing to be gained in terms of protection against HIV, and yet you're exposing that child to all the unknown safety risks," Kiran Musunuru of the University of Pennsylvania told the AP. Harvard's George Church suggested that the "main emphasis was on testing editing rather than avoiding this disease." That's consistent with He's video, linked above, in which he describes the need for this editing for treating incurable genetic diseases—something that doesn't describe this work.

An ethical train wreck

So how did this get past the ethics authorities at the institutions where He worked? It's not clear that it has. *Tech Review* indicated that the Shenzhen City Medical Ethics Expert Board was beginning an investigation, saying that the hospital that supposedly granted approval for the research did not do a full reporting of its approval process. And the university that employs He has suspended him without pay, saying his work "seriously violates ethical and academic standards and regulations."

Meanwhile, scientific and ethical communities have nearly universally come out against He's work. One hundred Chinese scientists quickly organized an open letter in which they say, "We can only use the word 'crazy' to describe the experiment conducted directly on human beings."

Meanwhile, two of the people who helped pioneer development of CRISPR technology have also come out against He's work. The Broad Institute's Feng Zhang is calling for a moratorium on gene editing in embryos, while UC Berkeley's Jennifer Doudna released a statement saying "this work reinforces the urgent need to confine the use of gene editing in human embryos to settings where a clear unmet medical need exists and where no other medical approach is a viable option."

More details will likely become available after He's talk on Wednesday in Hong Kong or as they leak out through various channels in the meantime. We will continue providing updates as appropriate.

https://go.nature.com/2BBNZe4

Beware the rise of the radical right

Academic freedom is on the hit list when radical politicians gain office — as they have done in Europe.

Hidden inside a 1970s office block close to London's Waterloo station is a tiny organization that has helped tens of thousands of academics find sanctuary from conflict. Co-founded 85 years ago by the economist William Beveridge and physicist Ernest Rutherford, the organization, now called the Council for At-Risk Academics (CARA), enabled many notable twentieth-century scientists — including biochemist Hans Krebs and philosopher Karl Popper — escape the Nazis and settle at British universities. In recent years it has reached out to the Middle East and receives the largest volume of applications from Yemen and Iraq.

The rise of the far right in Poland highlights the increasing threat to academic freedom in Europe. **Sean Gallup/Getty**

CARA and its counterparts in other countries exist because governments in the host nations value three of the pillars on which democracy rests: the rule of law, a free press and, as we explore in a Comment article, freedom of academic enquiry. If the British government were to decide not to support even one of these, CARA would struggle to carry on.

Such an alarming scenario is not purely hypothetical. For at least the past two decades, citizens of countries in the European Union have increasingly been voting for parties of the extreme right (also known as the populist right or radical right). From almost no representation in the 1990s, these parties are in governing coalitions in 10 out of the EU's 28 member states, including in Austria, Hungary, Italy and Poland. Next May sees elections to the European Parliament in which right-wing parties are expected to increase their combined tally of 78 seats in the 751 seat chamber.

When parties of either the extreme right or extreme left take power, any one of democracy's foundational pillars can be knocked away. Journalists and their families are intimidated. Judges are demonized and replaced with allies. People from minority groups are singled out for their alleged disloyalty. And action is taken against academics: universities are brought under direct state control and staff are subjected to loyalty tests.

It's a classic playbook to quash dissent. Take Poland for example, where the state has moved to exert control over the media and judiciary. Academic freedom is under threat too. A barometer for the risk it could face will be how much protest the Polish government allows, if any, over its pro-coal stance — which climate scientists have warned against — during the annual United Nations climate talks to be held in Poland next month.

Although there has been much media attention on the phenomenon of the populist right, the implications for academic freedom have gone largely unreported. Even where there has been widespread coverage — such as the case of Hungary's Central European University which was forced to enrol new students in Vienna rather than Budapest — EU institutions such as the European Council and the European Parliament have been largely powerless to take action. Europe's heads of government are biting their lips, and their reasons for doing so are understandable, even if European agreements or conventions are being violated. There is, of course, the principle of non-interference in the affairs of a sovereign state. But, in addition, the EU works through the collective solidarity of its member states. This is what has enabled the organization to enact progressive policies in climate change, anti-discrimination legislation and employee rights.

But collective progressivism breaks down when one-third of EU governments include political parties with scant commitment to protecting democratic institutions. Now that EU governments include parties who do not believe in the rights of people from minority groups, the consensus on climate change, or, indeed, academic freedom, it will become more difficult for the EU as a whole to either advance, advocate or protect policies in these fields.

"What's wrong with the world is not nationalism itself," noted Michael Ignatieff, the embattled rector of the Central European University. What's wrong, he added, "is the kind of nation, the kind of home that nationalists want to create and the means they use to seek their ends."

Ignatieff wrote these words more than 20 years ago in *Blood and Belonging* (BBC Books, 1993), at the end of a series of journeys into some of Europe's conflict zones. But he remains optimistic about the continent's future. "I don't want to predict doom and gloom," he told *Nature*. "Regimes come and go, but universities remain."

Academics everywhere will hope he's right. They, and us, can help by speaking out against injustice and specific cases where academic freedom is threatened — by any regime.

Nature ***563***, *599 (2018) doi: 10.1038/d41586-018-07527-2*

http://bit.ly/2BBY9LY

How ancient viruses got cannabis high

Ancient viruses contributed to the evolution of hemp and marijuana

World's first cannabis chromosome map reveals the plant's evolutionary past and points to its future as potential medicine.

THC and CBD, bioactive substances produced by cannabis and sought by medical patients and recreational users, sprung to life thanks to ancient colonization of the plant's genome by viruses, U of T researchers have found.

Modern day hemp and marijuana evolved distinct chemistry thanks to ancient viruses that colonized the ancestral cannabis genome millions of years ago. **Michael Fischer**

The finding is only one of the insights revealed by the long-awaited cannabis genome map detailing gene arrangement on the chromosomes, published recently in the journal *Genome Research*. Among other revelations are discovery of a gene responsible for the production of cannabichromene, or CBC, a lesser known cannabinoid, as the active substances in cannabis are known, and new insights into how strain potency is determined.

"The chromosome map is an important foundational resource for further research which, despite cannabis' widespread use, has lagged behind other crops due to restrictive legislation," says Tim Hughes, a professor in the Donnelly Centre for Cellular and Biomolecular Research and co-leader of the study. Hughes is also a professor in the Department of Molecular Genetics and Senior Fellow at the Canadian Institute for Advancement of Research.

The researchers expect the map will speed up breeding efforts to create new strains with desired medical properties as well as varieties that can be grown more sustainably, or with increased resistance to diseases and pests.

The study was a three-part collaboration between Tim Hughes' team and those of Jonathan Page, of Aurora Cannabis and the University of British Columbia , and Harm van Bakel, of the Icahn School of Medicine at Mt Sinai in New York.

Hughes, Page and van Bakel first got together in 2011 when they released the first draft of cannabis genome which was too fragmented to reveal gene position on chromosomes.

The new map reveals how hemp and marijuana, which belong to the same species Cannabis sativa, evolved as separate strains with distinct chemical properties. Cannabis plants grown for drug use ("marijuana") are abundant in psychoactive tetrahydrocannabinol, or THC, whereas hemp produces cannabidiol, or CBD, popular of late for its medicinal potential. Some people use CBD to relieve pain and it is also being tested as a treatment for epilepsy, schizophrenia and Alzheimer's.

The enzymes making THC and CBD are encoded by THCA and CBDA synthase genes, respectively. Both are found on chromosome 6 of the ten chromosomes the cannabis genome is packaged into. There, the enzyme genes are surrounded by vast swathes of garbled DNA which came from viruses that colonized the genome millions of years ago. This viral DNA, or retroelements as it is known, made copies of itself that spread across the genome by jumping into other sites in the host cell's DNA.

"Plant genomes can contain millions of retroelement copies," says van Bakel, an assistant professor in the Icahn Institute for Data Science and Genomic Technology in New York and in the department of Genetics and Genome Sciences.

"This means that linking genes on chromosomes is analogous to assembling a huge puzzle where three quarters of the pieces are nearly the same color. The combination of a genetic map and PacBio sequencing technology allowed us to increase the size of the puzzle pieces and find enough distinguishing features to facilitate the assembly process and pinpoint the synthase genes."

The researchers believe that gene duplication of the ancestral synthase gene and expanding retroelements drove ancient cannabis to split into chemically distinct types. Humans subsequently selected for plants containing desirable chemistry such as high THC.

The gene sequences for the THCA and CBDA synthases are nearly identical supporting the idea that they come from the same gene which was duplicated millions of years ago. Over time, one or both gene copies became scrambled by invading retroelements, and by evolving separately, they eventually came to produce two different enzymes - CBDA synthase found in hemp (fibre-type), and THCA synthase in drug-type (marijuana).

Because the enzymes are so similar at the DNA level, until this study it was not even clear if they are encoded by separate genes or by two versions of the same gene. Adding to the confusion was the fact that most strains produce both CBD and THC despite breeders' efforts to grow hemp varieties free from the mind-altering THC for users looking to avoid it.

The chromosome map now clearly shows that two distinct genes are at play which should make it possible to separate them during breeding to grow plants without THC.

Some psychoactive effects in medical strains could be coming from CBC, a lesser known cannabinoid that has unusual pharmacology including anti-inflammatory properties. The discovery of the gene responsible for CBC synthesis will make it possible for breeders to tailor its content in future varieties.

"Mainstream science has still not done enough because of research restrictions," says Page, of UBC and Chief Scientific Officer at Aurora, one of Canada's largest producers of medical cannabis. "Legalization and looming ease of research regulation really provide for opportunities for more research to be done. And Canada is leading the way."

http://bit.ly/2KGKXbk

Certain dietary or nutritional supplements could improve sperm quality

These are the results of an analysis of 28 nutritional intervention studies involving 2,900 participants and headed by the Universitat Rovira i Virgili; these supplements may increase male fertility

Infertility affects 15% of the world population and is recognised by the World Health Organisation as a global health problem.

In recent years, studies of sperm quality in different populations from developing countries have shown a decrease that could have consequences for the survival of the human species. The decrease in sperm quality has been related to unhealthy lifestyles. Stress, the consumption of drugs, tobacco and alcohol and unhealthy diets seem to be the principal modifiable factors.

Despite the current lack of scientific evidence regarding the effect of dietary and nutritional supplements on sperm quality, many fertility clinics offer dietary recommendations and supplements before providing their patients with in-vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

Recently, researchers at the Human Nutrition Unit of the Universitat Rovira i Virgili (URV) and the Pere i Virgili Health Research Institute (IISPV), which are both members of the Ciber Obn Network of the Carlos III Institute, and researchers at the Clinical Department of Human Reproduction and Infant Growth at the Universidad de Guadalajara (Mexico) have carried out the most extensive and systematic review to date of randomised clinical studies into the

effects of different nutrients and dietary supplements on sperm quality and male fertility.

After qualitatively analysing the results of 28 nutritional studies involving 2900 participants, researchers have concluded that supplementing the diet with omega 3 and coenzyme Q10 (in either liquid or tablet form) can have a beneficial effect on the quantity of spermatozoids in semen.

Supplementing the diet with selenium, zinc, fatty acids, omega-3 and coenzyme-Q10 is associated with an increase in spermatozoid concentration; supplementing the diet with selenium, zinc, omega-3, coenzyme-Q10 and carnitines has been associated with an improvement in sperm mobility, and finally, selenium, fatty acids, omega-3, coenzyme-Q10 and carnitines has a positive effect on the morphology of spermatozoids.

According to the researchers, their study suggests that dietary supplements have a modulating effect on sperm quality and provides an extensive and up-to-date review of the existing scientific evidence. The results suggest that certain dietary supplements can have a beneficial effect on sperm quality, although it remains to be demonstrated whether this increases the likelihood of conceiving a child naturally or through assisted reproduction techniques.

The researchers believe that further studies need to be carried out with larger samples so that a more accurate conclusion can be drawn. The results of the present study, headed by Albert Salas-Huetos, post-doctoral researcher currently at the University of Utah and Jordi Salas-Salvadó, professor and director of the Human Nutrition Unit at the URV, have been published in the November edition of the scientific journal *Advances in Nutrition*.

Reference: Salas-Huetos A, Rosique-Esteban N, Becerra-Tomás N, Vizmanos B, Bulló M, Salas-Salvadó J. The Effect of Nutrients and Dietary Supplements on Sperm Quality Parameters: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Advances in Nutrition, 2018; 9(6), 833-848. DOI: 10.1093/advances/nmy057

http://bit.ly/2raPTwd

Study identifies sepsis symptoms that lead to death

Using data science, researchers quantify the relationship between organ dysfunction signs and risk for in-hospital mortality for patients with sepsis.

Using patient records from 210,289 hospital visits between 2013 and 2016, Drexel University researchers have identified the specific symptoms that put patients at the greatest risk of dying from sepsis - and they're not what many clinicians might think.

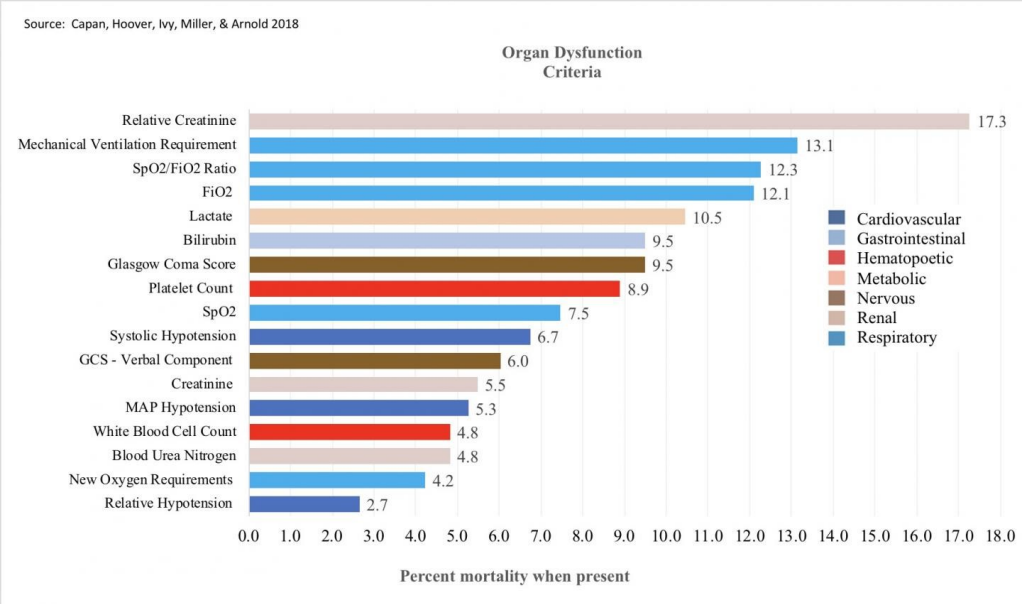
Sepsis, a life-threatening condition caused by the body's response to an infection, is one of the most frequent causes of death in the hospital and one of the most expensive conditions to treat. Early recognition can save lives, but patients require close, consistent monitoring, and providers can easily miss the insidious, gradual signs of the disease. Complicating matters, the definition of sepsis is in dispute amongst experts. This can lead to muddied treatment guidelines and a lack of care for patients whose symptoms do not fit the standard checklist for a sepsis diagnosis, but who, in fact, may be at high risk for death.

The new study by Drexel researchers, published this month in Critical Care, shows that impaired kidney function is one of the leading predictors of sepsis patient mortality. The data offers an advanced analytical model for detecting early warning signs of sepsis and for differentiating between different organ dysfunctions' contribution to in-hospital morality.

"We now have large-scale evidence that many of these organ system failures that are typically underappreciated - particularly the renal and respiratory systems - actually have the highest association with death," said study co-principal investigator Ryan Arnold, MD, an emergency medicine doctor and faculty member at Drexel College of Medicine. "That means that symptoms related to these systems

need to be raising a red flag for doctors. We're saying, 'Hey, this is the type of patient you need to be paying more attention to.'"

The researchers found that the more well-known symptoms of sepsis, such as low blood pressure, were linked to lower mortality rates in the population they studied.



This graph shows hospitalization visits during the study period (July 2013 to April 2016) with infection that met at least one organ dysfunction criteria, color-coded for each individual organ system, and associated percentage of visits that resulted in mortality. **Drexel University**

"That likely speaks more to the health care providers' response to the symptom, than the low blood pressure itself actually being a protective factor," Arnold added. "With sepsis, patients generally don't fall off of a cliff. Instead, it's a day by day, gradual deterioration. Maybe someone has a small increase in creatinine today, and tomorrow it's a little worse. Those subtle changes that don't get detected, we found, lead to death."

To quantify the association between organ dysfunctions and health outcomes, the research team used retrospective Electronic Health Record data for adult patients hospitalized within Delaware's Christiana Care Health System from July 2013 to April 2016. They analyzed the relationship between in-hospital mortality and symptoms with seven organ systems: cardiovascular, metabolic, hematopoietic, nervous, gastrointestinal, renal and respiratory.

Of the 210,289 visits during the study period, 62,057 patients (30 percent) were treated for an infection, and 48,680 (78 percent) experienced organ dysfunction. Of the patients treated for an infection, 1,955 (3 percent) died during this period. Patients with worsening kidney function (increase in creatinine levels by 50 percent from baseline) had the highest mortality rate (17 percent), followed by mechanical ventilation requirement (13 percent). Patients with hypotension had the lowest incidents of death. The researchers also found that treating patients for an infection within 24 hours of being admitted to the hospital significantly lowered their risk of dying.

The study paves the way for the creation of a clinical decision support system that can give providers real-time alerts about patients that might be high-risk for dying from sepsis, according to study co-principal investigator Muge Capan, PhD, an associate clinical professor at Drexel's LeBow College of Business.

"The integration of analytics and clinical, translational research provides insight into developing smart and connected systems that support data-driven and personalized management of sepsis," Capan said.

The research team is now building a model that assigns different "weighted risk" to individual organ system dysfunctions that are observed simultaneously, allowing clinicians to plug in combinations of symptoms and create an individualized picture for each sepsis patient. For instance, a patient with dysfunction of both kidney and respiratory systems, would require more close monitoring than a patient suffering from kidney dysfunction and low blood pressure.

"Now, when a new patient walks into the hospital, we can use our math and analytic skills to match that patient's fingerprint and really see: 'What is that person's individualized risk of in-hospital death?' and 'What is that person's individual risk of developing septic shock?' That is very useful, and very exciting," Capan said.

http://bit.ly/2TT6hPm

Scientists Wrote an Equation to Find the Funniest Word in English. The Results Will Make You Fart.

Don't laugh, but professor Chris Westbury's newest psychology study is about farts.

By Brandon Specktor, Senior Writer | November 26, 2018 07:25am ET

It's also about snots, chortles, wienies, heinies and bozos; things that are wriggly, jiggly, flappy and slaphappy; things that waddle, things that slobber; things that puke, cluck, squawk and dingle.

That's because Westbury studies funny words — and, more specifically, what makes some words funny and others not.

"As schoolboys of a certain age rediscover repeatedly, there is a sense in which simply uttering the word fart is a one-word joke," Westbury and Geoff Hollis, both professors at the University of Alberta in Canada, wrote in a new study published Oct. 18 in the Journal of Experimental Psychology: General.

But what, Westbury wondered, makes the word "fart" so funny? He already knew from a 2016 study he co-authored that part of a word's funniness could be explained by the popular theory of humor known as incongruity theory — the idea that something becomes funnier the more it subverts your expectations. In that study, students rated the funniness of several thousand meaningless, computer-generated words, or "nonwords." The nonwords with surprising letter combinations that looked least like known English words — such as "snunkoople," "hablump" and "jumemo" — were consistently rated funniest.

Dirty-sounding nonwords like "whong," "dongl" and "focky" also performed very well, suggesting that a word's perceived connotation played a role in humor, even for words that had no real meaning. In their new study, Westbury and Hollis delved further into the relationship between word sounds, meanings and humor — this time, working with tens of thousands of real English words.

The science of booty tinkles

They started with a list of 4,997 common words previously compiled by a team of psychologists at the University of Warwick in the U.K. and scored with funniness ratings by a panel of 800 online participants. The Warwick psychologists found that words like "booty," "tinkle" and "nitwit" were consistently ranked as being very funny, while words like "pain," "torture" and "deathbed" were ranked as being decidedly humorless.

Westbury and Hollis looked at each one of the nearly 5,000 words under a humorist microscope, categorizing them based on 20 different factors, including how long the word itself was, how positive or negative the word's meaning was, how common each letter or combination of letters was in English, and whether the word contained a crude or profane-sounding string of characters within it (like "pike" and "bunghole," for example).

With these factors and the pre-existing humor scores for the words in the entire list, the researchers devised several different equations that could, theoretically, predict the humorousness of any given word. They tested two of their humor equations on a list of more than 45,000 words, then ranked the results in their new paper. One algorithm decided the top five funniest words on the list were:

1. Upchuck
2. Bubby
3. Boff
4. Wriggly
5. Yaps

The second equation, which was written with the help of a special data-modeling program Hollis and Westbury co-created in 2006, predicted the funniest words were:

1. Slobbering
2. Puking
3. Fuzz
4. Floozy
5. Cackling

Among the highest- and lowest-rated words, several clear patterns emerged. Both equations agreed that the least-funny words were those with highly negative meanings — such as "violence," "attacks," "rape," "murder" and "harassment." Meanwhile, words with meanings related to sex, bodily functions, insults, animals and partying were consistently predicted to induce giggles (actually, "giggle" was the seventh-funniest word in English, according to the first data model).

Word sounds (or "phonemes") played a huge role, too. Echoing Westbury's 2016 nonword study, words with an emphasis on relatively uncommon letters — like k, j and y — consistently appeared funny. The single funniest phoneme in English turned out to be the vowel sound /u/, as in "guffaw," "humph" and "lummox." This vowel sound appeared in nearly 20 percent of the words judged most funny, the authors wrote.

The perfect funny word, the authors concluded, is "a short, infrequent word composed of uncommon letters," and has a meaning that is "human and insulting, profane, diminutive and/or related to good times."

With that much settled, Westbury and Hollis hope to extend their research into quantifying the humor values of word pairs — "such as toothy weasel, muzzy muffin and fizzy turd," they wrote — and eventually entire jokes. How funny is a chicken crossing a road, anyway? Evidently, that depends on whether it farts on the other side.

http://bit.ly/2FPtSqT

Unicorns did exist – until they didn't

A monstrous rhino species survived until much more recently than thought.

Stephen Fleischfresser reports.

What's four metres long, 2.5 metres high, weighs 3.5 tonnes and has a preposterously large horn in the middle of its face? A really massive unicorn, that's what. Research published in the journal *Nature Ecology and Evolution* has now uncovered the details of the life, history and extinction of a spectacular species dubbed the "Siberian Unicorn".

An artist's impression of the Siberian unicorn. **Nature Ecology and Evolution**

A team of international researchers from a range of institutions including the universities of New South Wales and Adelaide in Australia, the University of Durham in the UK, and Leiden University in the Netherlands, led by senior author Adrian Lister of London's Natural History Museum and lead author Pavel Kosintsev of the Russian Academy of Sciences, have unlocked the secrets deep in the bones of *Elasmotherium sibiricum*, an extinct member of the rhinoceros family.

E. sibiricum is known colloquially as the Siberian unicorn because of its unusually large horn. It was the largest rhinoceros of the Quaternary period – which ran from roughly 2.5 million to 12 thousand years ago.

huge size it was lithe and seemed adapted to running across its homelands of central Asia: Kazakhstan, western and central Russia, Ukraine, Azerbaijan and Uzbekistan, and possible areas of Mongolia and China.

Until now, *E. sibiricum* had been thought to have gone extinct about 200,000 years ago as part of the natural extinction rate that preceded the arrival of humanity, and no one really knew what niche in the ecosystem it inhabited.

For the new work, the researchers sampled 25 examples of *E. sibiricum* bones, extracting collagen for radiocarbon dating and even DNA for a study of the unicorn's evolutionary history.

The latter has shows that the animal belonged to a sister taxon to Rhinocerotinae, the group to which all modern rhinoceros belong. The two were thought to have split about thirty-five million years ago, but the current research indicates an even earlier divergence of forty-seven million years ago.

The radiocarbon dating yielded some surprising results, suggesting that the unicorn was still kicking until 39,000 years ago. This places its extinction "firmly within the late Quaternary extinction event", between 50,000 and four thousand years ago, in which nearly half of Eurasian mammalian megafauna died out. Interestingly, this adds to the evidence of the decline of megafauna just before the ice sheets of the last ice age reached their maximum extension.

And this might help us to understand the reasons for the unicorn's demise.

The shape of, and the isotopes within, the remains of *E. sibiricum* suggest that it found its home in herb- and grass-covered steppes, with an extreme adaptation for feeding close to the ground. Perhaps it dug up vegetation up to consume it roots and all.

However, starting about 35 thousand years ago, as the deep cold extended further south, the steppe became more like tundra, denying the unicorn its primary food source, and this was perhaps a decisive factor in its extinction.

The authors also speculate that human might have had something to do with it, although they acknowledge a dearth of supporting evidence.

"The extinction of *E. sibiricum*," they write, "could in theory have been exacerbated by human hunting pressure, given the replacement of *H. neanderthalensis* by *H. sapiens* in Eurasia around 45–40 [thousand years ago]".

http://bit.ly/2E4KPlH

Males can pass on mitochondrial DNA

Thought to be an exclusively maternal process, in rare circumstances mtDNA can pass down the paternal line. Nick Carne reports.

Passing on mitochondrial DNA was thought to be an exclusively maternal process, but new research suggests otherwise.

Paternal transmission of mitochondrial DNA (mtDNA) may be possible, a new study suggests – contradicting the accepted view that it is passed on exclusively through maternal inheritance.

The find, made by a team led by Taosheng Huang from Cincinnati Children's Hospital Medical Centre, and Paldeep Atwal, from Mayo Clinic Hospital, Jacksonville, both in the US, may stimulate further study of mtDNA genetics that leads to alternative treatments for mitochondrial diseases.

Writing in the journal *Proceedings of the National Academy of Sciences*, the researchers present evidence of biparental inheritance of mitochondrial DNA in 17 members of three unrelated multi-generation families. The findings were independently validated using multiple approaches for whole mtDNA sequencing.

"Our results suggest that, although the central dogma of maternal inheritance of mtDNA remains valid, there are some exceptional cases where paternal mtDNA could be passed to the offspring," they write.

Mitochondria, the energy-producing organelles of cells that play a critical role in numerous cellular functions, contain their own compact genomes that are separate from the nuclear genome.

In nearly all mammals, this genome is inherited exclusively from the mother, and transmission of paternal mitochondria or mtDNA has not to date been convincingly demonstrated in humans.

The authors are not going overboard, noting that their results "will need to be brought in agreement with the fact that maternal inheritance remains absolutely dominant on an evolutionary timescale and that occasional paternal transmission events seem to have left no detectable mark on the human genetic record".

But that does not hide the fact, they suggest, that this remains an unprecedented opportunity in the field.

"Elucidation of the molecular mechanism by which this biparental transmission occurs will expand our fundamental understanding of the process of mitochondrial inheritance and may provide an alternative approach to minimise the consequences of the transmission of pathogenic maternal mtDNA in humans," they write.

"Whatever the mechanism of this unusual phenomenon may be, it is clear that years of research will be required to fully understand and exploit the ramifications of this discovery."

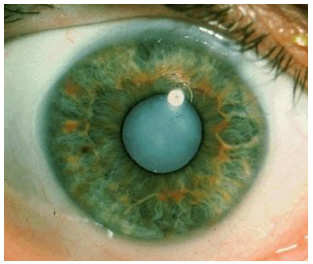
http://bit.ly/2E6xclX

How changing labs revealed a chemical reaction key to cataract formation

Researchers studying eye lens find a new function for a protein previously thought to be inert

Researchers working to understand the biochemistry of cataract formation have made a surprising finding: A protein that was long believed to be inert actually has an important chemical function that protects the lens of the eye from cataract formation.

The lens is made up of cells packed with structural proteins called crystallins. Crystallins within each lens cell form a protein-dense gel, and the gel's optical properties -- like its transparency and the way it refracts light -- help focus light onto the retina.



But when crystallin proteins clump together, they are no longer so transparent. If enough of the proteins go from their usual water-soluble, densely packed organization to clumpy aggregates, they begin to scatter incoming light, forming cloudy deposits known as cataracts.

When damaged by oxidative stress or UV light, an eye lens protein called gamma-crystallin, can begin to aggregate, forming the cloudy clumps that we call cataracts. Researchers have recently uncovered a chemical function for gamma-crystalline that helps reduce clumping unless the protein is already damaged. Their work may lead to new treatments that can delay cataract surgery. **Қазақша: Кәрілік катаракта**

According to Harvard postdoctoral fellow Eugene Serebryany, lead author on a recent study in the *Journal of Biological Chemistry*, for a long time researchers believed that crystallin proteins were chemically inert. That is, except for aggregating as an individual ages, the proteins were not believed to interact much with fellow proteins.

Serebryany said, "This was the model: (crystallin's) real function is to remain monomeric and transparent and avoid aggregating for as long as possible."

Back when he was a graduate student at MIT, Serebryany used a mutant form of the lens protein gamma-crystallin to mimic UV damage to the protein. While studying how that mutation leads crystallin to aggregate into clumps, Serebryany found something surprising: The mutant was more likely to aggregate if wild-type, or undamaged, protein was also present.

Harvard professor Eugene Shakhnovich, who collaborated with Serebryany and his graduate adviser, Jonathan King, on the earlier studies, described the finding as "a fairly striking phenomenon" and explained: "If you had these damaged proteins in a test tube, they would not aggregate for a while. If you had the wild-type protein, it would not aggregate forever. But then, when you mix the two, you

see rapid and precipitous aggregation." In other words, the healthy version of a protein everyone had thought was inert was somehow causing a slightly damaged version to get much worse -- and fast.

When Serebryany graduated, Shakhnovich hired him to continue working to understand how a supposedly inactive protein could cause this effect. Serebryany said, "The first thing I had to do was basically try to get the experiments from my Ph.D. lab to work in this (new) lab."

"They're just two stops apart on the subway!" Shakhnovich joked.

But, for some reason, Serebryany had trouble replicating the results. "It's a different place, it's a different set of instruments, a slightly different set of procedures. You see where this is going," he said. "All of a sudden, experiments that were highly reproducible before were giving a lot of variability."

Indeed, in the Harvard lab sometimes the wild-type crystallin caused mutant crystallin to aggregate, and sometimes it didn't. The scientists were mystified.

Serebryany said, "Obviously, if there is suddenly variability, there is a hidden variable that we didn't see before." He set up a series of experiments trying to pinpoint that variable.

A close comparison of the molecular weights of the wild-type protein that caused the mutant to clump and the protein that didn't revealed a difference equivalent to the weight of two hydrogen atoms. This gave the researchers a hint that the redox state - whether two sulfur atoms within a protein molecule were bound to one another instead of to hydrogen atoms -- might make a difference.

"By carrying out isotopically resolved mass spectrometry experiments, we got more than we bargained for," Serebryany explained. "Not only did the aggregation-prone mutant acquire one internal disulfide bond per molecule during the aggregation reaction, but the aggregation-promoting wild-type protein lost its disulfide at the same time."

By mutating the sulfur-containing cysteine amino acid residues one by one to non-sulfur-containing residues, Serebryany found that two cysteine amino acids close together on the surface of gamma-d-crystallin acted as a kind of switch. When the two bound, making a structure called a disulfide bond, crystallin seemed to be able to push damaged fellow molecules toward aggregation. When the two cysteines were not bound, each instead took on a hydrogen atom, explaining the protein's tiny change in mass. Under that condition, wild-type crystallin was inert.

But how could one bond between amino acids on the surface of this protein make it drive other proteins to aggregate?

Using biophysical and biochemical techniques, the team found that although the disulfide bond forms easily, it also introduces strain into the protein's structure. This made each protein molecule likely to pass along the disulfide bond to a nearby molecule of the protein, receiving two protons in return. In this way the disulfide bond could be constantly passed around among crystallin protein molecules. The authors compared the process to passing a hot potato.

Given a whole population of healthy, undamaged crystallin proteins, this process could go on indefinitely. But if one protein was already a little damaged, the authors showed, it caught the hot potato with a different set of cysteines, which were less able to pass it on. This drove the damaged protein to clump up. The authors' previous work revealed that mutations mimicking damage caused by UV changed the stability of the protein, making it more floppy, and therefore more likely to acquire the conformation that exposes new cysteines that could catch the hot potato.

This helps us understand cataract formation. According to Shakhnovich, the team is working on peptide treatments that might keep the "hot potato" from reaching damaged proteins. Serebryany hopes such peptides "could actually soak up some of those disulfides

and delay the time that it takes to form the more aggregation-prone species." That could lead to slower cataract formation for patients.

doi: 10.1074/jbc.RA118.004551
This study was funded by the National institutes of Health.

http://bit.ly/2FRtsXl

Study suggests multiple instances of inter-breeding between Neanderthal and early humans

Evidence suggesting Neanderthals mated and produced offspring with anatomically modern humans multiple times

November 27, 2018 by Bob Yirka, Phys.org report

A pair of researchers at Temple University has found evidence that suggests Neanderthals mated and produced offspring with anatomically modern humans multiple times—not just once, as has been suggested by prior research.

In their paper published in the journal *Nature Ecology and Evolution*, Fernando Villanea and Joshua Schraiber describe their genetic analysis of East Asian and European people and how they compared to people from other places. Fabrizio Mafessoni with the Max Planck Institute for Evolutionary Anthropology offers a News and Views piece on the work done by the pair in the same journal issue.

Comparison of Modern Human and Neanderthal skulls from the Cleveland Museum of Natural History **DrMikeBaxter/Wikipedia**

In recent years, scientists have discovered that early humans moving out of Africa encountered Neanderthals living in parts of what is now Europe and Eastern Asia. In comparing Neanderthal DNA with modern humans, researchers have found that there was a least one pairing that led to offspring, which is reflected in the DNA of humans—approximately 2 percent of the DNA in non-African humans today is Neanderthal.

In this new effort, the researchers have found evidence that suggests there was more than one such encounter.

Their findings make logical sense, considering that anatomically modern humans and Neanderthals coexisted for approximately 30,000 years.

Recent research by other groups had suggested that multiple offspring-producing unions had occurred—some people in East Asia, for example, were found to have up to 20 percent more Neanderthal DNA than people of strictly European descent.

In this new effort, the researchers took a more stringent look to find out once and for all if there had been multiple pairings or just one. They pulled and analyzed data from the 1000 Genomes Project, measuring the amount of Neanderthal DNA in genetic material from volunteers.

The first step was separating the data between people of European and Asian ancestry. Doing so suggested that both groups had evidence of early multiple mating events.

The researchers then studied the rates of the two groups by creating simulations showing outcomes of differing numbers of mating events between the two groups.

Data from the simulations was then fed into a machine-learning algorithm that showed DNA percentage patterns based on the number of cross-breeding events that had occurred.

The researchers concluded that the most likely scenario was that there were multiple instances of cross-breeding between early humans in both East Asia and Europe with Neanderthals.

Fabrizio Mafessoni. Encounters with archaic hominins, Nature Ecology & Evolution (2018). DOI: 10.1038/s41559-018-0729-6

Fernando A. Villanea et al. Multiple episodes of interbreeding between Neanderthal and modern humans, Nature Ecology & Evolution (2018). DOI: 10.1038/s41559-018-0735-8

http://bit.ly/2DTuK1f

Dads (Not Just Moms) Can Pass on Mitochondrial DNA, According to Provocative New Study

Provocative new study finds that, in rare cases, dads can pass on mitochondrial DNA

By Rachael Rettner, Senior Writer | November 27, 2018 07:19am ET

It's long been thought that people inherit mitochondrial DNA — genetic material found inside cells' mitochondria — exclusively from their mothers. But now, a provocative new study finds that, in rare cases, dads can pass on mitochondrial DNA, too.

The study found evidence that 17 people from three different families appeared to inherit mitochondrial DNA from both their mother and their father. The radical findings, from researchers at Cincinnati Children's Hospital Medical Center, were then confirmed by two additional laboratories using several different testing methods.

If the findings hold up, "this fundamentally changes everything that we believed about mitochondrial inheritance, which is huge," said Dr. Sajel Lala, a clinical geneticist at Nicklaus Children's Hospital in Miami who was not involved in the study.

Still, Lala said the results will need to be replicated by more research groups, and published in additional scientific papers. But the results could have "major implications on [genetic] counseling and the field of genetics overall." The study was published yesterday Nov. 26 in the journal Proceedings of the National Academy of Sciences.

Mitochondrial DNA from dad?

Although most of our DNA resides inside the nucleus of our cells, a small amount is found in the mitochondria — the organelles that generate energy for cells. In most mammals, mitochondrial DNA is inherited from the mother, while mitochondrial DNA from the father is thought to be destroyed shortly after conception.

Scientists have occasionally found exceptions to this rule in some animals — for example, some studies have found that male mice and sheep can pass on mitochondrial DNA in rare cases.

But whether human males can also pass on mitochondrial DNA to their offspring is controversial. In 2002, doctors in Denmark published a case in The New England Journal of Medicine of a man who appeared to inherit 90 percent of his mitochondrial DNA from his father. But no additional cases of this happening were reported in the following 16 years, leading many researchers to think that the 2002 result was a result of technical errors.

But that all changed when researchers at Cincinnati Children's decided to investigate a 4-year-old boy's unusual genetic test results. The boy was suspected of having a mitochondrial disease — or a disease caused by mutations in mitochondrial DNA. When the researchers sequenced his mitochondrial DNA, they didn't find any apparent disease-causing mutations, but they noticed something very odd: It appeared as though the boy had two sets of mitochondrial DNA.

Further investigations revealed that the boy's mother had inherited mitochondrial DNA from both her father and her mother (the boy's grandfather and grandmother), and she had passed down this mixed set of mitochondrial DNA to her son.

When the researchers examined the DNA from other family members, they found that overall, 10 people in the family — from three generations — had inherited "biparental" mitochondrial DNA.

This led them to explore other unusual genetic test result from two unrelated families, where they found evidence of biparental mitochondrial DNA in seven additional people.

"Our results clearly demonstrate biparental transmission of [mitochondrial DNA] in humans, counter to the central dogma of mitochondrial inheritance," the researchers wrote.

Future research

The findings also raise the question of "how many other instances of individuals with biparental [mitochondrial DNA] inheritance have been dismissed as technical errors," the researchers said.

Indeed, it's not unusual for doctors to ignore odd results of mitochondrial testing, especially if the patient does not appear to have a known mitochondrial disease. "[When] we don't get the result that we would expect, we kind of leave it at that," Lala said.

If the findings are proved true, further research is needed to determine exactly how fathers pass on mitochondrial DNA, and how frequently this occurs.

Figuring out how this happens "will expand our fundamental understanding of the process of mitochondrial inheritance" and may lead to new ways of preventing the transmission of mitochondrial diseases, the researchers concluded.

http://bit.ly/2FRy27Z

Stone Age food was haute cuisine

Analysis of cooking gunk from six millennia ago reveals a surprisingly sophisticated palate.

Andrew Masterson reports.

The meal – or, more likely, the dish, one element of a more varied repast – was simple, but elegantly so. It comprised freshwater carp eggs, cooked in a fish broth.

The top of the earthenware bowl in which it was prepared was sealed with leaves of some sort – the eggs perhaps fried off before the stock was added, the leaves holding in steam and perhaps also adding a note or two of their own.

All up, then, the dish – a fish roe soup a little like a Korean *altang*, perhaps, or a Thai *tom yam khai pla* – likely had a pleasing and rounded depth of flavour, a certain delicacy and a beguiling aroma. It would not have been out of place on a menu in any posh restaurant from New York to Tokyo.

Except that this particular meal was cooked almost 6000 years ago, not far from what is these days Berlin.

The ingredients were identified by scientists led by Anna Shevchenko from the Max Planck Institute for Molecular Cell Biology in Dresden, Germany.

They did so by analysing the proteins contained in a thin crust of ancient food gunk found clinging to a small coarse ceramic bowl unearthed at an archaeological site called Friesack 4, in the Brandenburg region. The bowl had previously been radio-carbon dated to around 4300 BCE.

Writing in the journal *PLOS One*, Shevchenko and her colleagues note that most archaeological approaches to studying historical food substances are unable to definitively identify the species consumed.

Assumptions – often very accurate – thus have to be made on the basis of isotopes, fats and a few common biological markers, as well as indirect evidence, including artefacts, contemporary artworks or written material, the contents of latrines and middens, and so forth.

Protein analysis, a relatively new field called proteomics, however, provides much more detailed results.

Ancient proteins, the authors explain, evince age-specific modifications which allow them to be distinguished from more recent contaminants. Many proteins are also species-specific, permitting source animals and plants to be confidently identified, and changes to their biological properties, wrought by enzymes, enable educated guesses regarding cooking methods and recipes.

And the proof, it seems, if not in the pudding, is at least in the soup tureen. The ceramic bowl tested by the researchers is one of about 150,000 objects so far excavated from the Friesack 4 site. The extensive collection includes many pieces of clay and stoneware, as well as artefacts made from bone, wood, pitch and antlers.

Almost all of the pieces recovered from the site have been dated as coming from the Mesolithic period, which ran from roughly 13,000 to 300 BCE.

Initial protein analysis of the "charred organic deposits" adhering to a group of 12 shards that together comprise an unglazed, smoothed, dark brown, 10-centimetre-high pot known as *#3258* indicated an aquatic origin.

In order to properly identify age and species, and to eliminate later contaminants – including human-derived keratins, food particles from the fingers of archaeologists and previous researchers and, it turned out, a speck of hair gel – the samples had to be compared against modern equivalents.

Thus, Shevchenko and colleagues report, fresh carp roe was purchased from a fish farm in Dresden, and 125 milligrams of fish muscle tissue derived from Norwegian farmed Atlantic salmon (*Salmo salar*) was also sourced.

The latter was boiled for 30 minutes in 300 milligrams of salty water. The result would have been a nice bit of fish stock, but instead of serving it the scientists mixed it with a couple of marker compounds and separated out its components in order to use it as a standard reference.

Once all the tests had been run, the identification of carp roe inside bowl *#3258* was unequivocal. The analysis produced no evidence of microorganisms commonly associated with food fermentation, so it is very likely that the eggs were fresh when they went into the pot.

Fish roe, the researchers note, can be consumed "grilled, fired, marinated, baked, smoked, dried, cured, and also boiled in broth".

In this case, they suggest, there is clear evidence that it was "thermally processed", but more specific assumptions about preparation method are possible. It is likely, they add, that it was "cooked in a small volume of water or fish broth, for example by poaching on embers".

Electron microscopy carried out on the pot itself revealed an organic crust around the rim, suggesting that it was "probably capped with leaves". Alas, the plant species could not be determined, leaving moot the question of whether Stone Age cooks used the material just to keep the heat in, or to add another flavour profile to the dish.

A crust from another bowl subjected to proteomic analysis by Shevchenko and her colleagues suggested it had been used to cook "pork with bones, sinews or skin".

All up, the evidence gathered from the Friesack 4 ceramics suggests that stereotypic images of Mesolithic hunters chowing down on great hunks of meat cooked brutally in camp fires are substantially wrong. For some at least, poached caviar accompanied by boar spare ribs was perhaps a more likely meal.

http://bit.ly/2rczebK

Vaccination may reduce the severity of the flu in vaccinated but still infected patients

Researchers of the UB and CIBERESP have taken part in a study that analyses all severe influenza cases in twelve Catalan hospitals between the 2010-2011 and 2015-2016 campaigns

The study, published in the scientific journal *Eurosurveillance*, also counts on the participation of researchers from the Public Health Agency of Catalonia, the Lleida Institute of Biomedical Research and the Barcelona Public Health Agency.

Less ICU admissions and deaths

Each year, between 5 and 20 % of the world population catches the flu, which causes about between 3 and 5 million severe cases and between 300,000 and 500,000 deaths worldwide. The new study analyses the effectiveness of anti-influenza vaccines to reduce the most severe effects of the flu: ICU admissions and death of patients whose vaccine did not prevent them from getting infected. To do so, researchers study all severe cases of influenza in twelve Catalan hospitals during the influenza seasons in 2010-2011 and 2015-2016,

a period during which 1,727 patients over eighteen entered the hospital, 591 being ICU admissions and 223 resulting in deaths.

Results show that, among those ICU admissions and deaths, vaccination was less frequent (21.2 % of the cases) than the rest of the patients with more benign symptomatology, 29.7 % of them being vaccinated. Therefore, the effectiveness of influenza vaccination to prevent ICU admissions or death among the total people in hospital for influenza was of 23 %, and in particular, a 44 % for the group of people aged 65. "We should add the effectiveness of the vaccine to prevent the flu to these percentages. These data highlight the need of an influenza vaccine for each season for those people who are more likely to show severe types of influenza, such as people over 65, and people with other diseases, for whom the influenza vaccine was not enough to prevent the infection from appearing", note the authors.

In the study, researchers note an explanation for these results would be the role the immune system plays. "People who were previously infected by the virus or who received anti-influenza vaccines would get benefits, at least, in the pre-existing cross-reactive memory of cytotoxic T lymphocytes, which would reduce the severity of the infection, even without protective antibodies", they conclude.

http://bit.ly/2ADRkrv

91 percent response rate for venetoclax against newly diagnosed AML in older adults

91 percent response rate to the combination of venetoclax with azacitidine

Clinical trial results published in the journal *Nature Medicine* show 91 percent response rate to the combination of venetoclax with azacitidine in older adults newly diagnosed with acute myeloid leukemia (AML). Of 33 patients given combination venetoclax and azacitidine, 20 experienced a complete response (aka complete remission) and eight experienced a complete response but with continued low blood counts. Of the three patients who did not respond to treatment, two discontinued the study before the first week due to personal reasons unrelated to treatment or side-effects.

Based on these results, on November 21, the U.S. Food and Drug Administration (USFDA) granted accelerated approval for venetoclax to treat patients who are aged 75 years and older or are ineligible for intensive chemotherapy due to coexisting medical conditions. Updated clinical trial results and scientific findings will be presented December 1-4 at the 60th annual American Society of Hematology (ASH) meeting in San Diego, CA.

Traditionally, the diagnosis of AML in this population has carried an extremely poor prognosis, with median overall survival of less than a year. Already, patients on the current trial have reached a median follow-up time of 580 days. Because so many patients remain on the trial with controlled disease, it is impossible to predict the average expected duration of benefit from this new combination treatment, implying a remarkably long duration of remission.

"To date, treatment options for older patients with AML have been limited. We see this new regimen as a paradigm shift in the way we will treat this disease in this population, moving forward," says Daniel A. Pollyea, MD, MS, investigator at CU Cancer Center, clinical director of Leukemia Services at the CU School of Medicine, and the study's first author.

Azacitidine is a low-dose chemotherapy drug that has long been used in the treatment of AML, with minimal success. Venetoclax is a targeted inhibitor of the Bcl-2 protein, which earned FDA approval in 2016 for the treatment of relapsed/refractory chronic lymphocytic leukemia (CLL). The current regimen includes a course of azacitidine, followed by the ongoing use of venetoclax.

"Two patients on this study have been off all therapy for nearly three years, and others who remain on therapy seem to be on the same

trajectory, suggesting this regimen may be curative in some settings," Pollyea says.

The trial is closely related to the preclinical work of Craig Jordan, PhD, investigator at University of Colorado Cancer Center, division chief of the Division of Hematology and the Nancy Carroll Allen Professor of Hematology at the University of Colorado School of Medicine. Basic science describing the underlying mechanism of drug action is published concurrently in the journal Cancer Cell. First author of the Cancer Cell paper Courtney Jones, PhD, and others working in the Jordan lab showed that leukemia stem cells depend on amino acid metabolism to supply themselves with energy. As part of its action against Bcl-2, venetoclax blocks cells' uptake of amino acids, and thus blocks the mechanism these cells use to generate energy, killing these cells.

"Leukemia stem cells in newly diagnosed AML patients absolutely depend on amino acid metabolism, but that's not the case for healthy cells. By taking away the ability of leukemia stem cells to metabolize amino acids, we can target these cells without affecting surrounding, healthy tissues," Jordan says.

One factor limiting treatment options in this population is the severity of side-effects associated with current therapies. Newly-diagnosed AML is most often treated with intensive chemotherapy. Unfortunately, while chemotherapy is largely effective against the bulk of leukemia cells, leukemia stem cells are uniquely equipped to resist chemotherapy, and so often survive treatment, leading to relapse. Using azacitidine alone in this population shows 28 percent response rate with response duration of 10 months. At that point, treatment often includes bone marrow transplant - eradicating a patient's cancerous blood system and repopulating a new one using blood stem cells from cord blood or from a matched donor. However, bone marrow transplant can be poorly tolerated in older and/or more frail patients.

"Many of these patients, you just can't treat in that way," Pollyea says. "They would be too likely to die from the treatment, itself - it does more harm than good."

Combining venetoclax with azacitidine was associated with no more side effects than the use of azacitidine alone.

Patients whose cancers held IDH mutations were more likely to experience long-lasting response; patients with RAS mutations often experienced shorter remissions. Initial findings suggest that treatment of AML patients who have relapsed following standard therapy is a more difficult challenge, requiring more than just venetoclax and azacitidine to achieve substantially improved outcomes.

In addition to AML and CLL, venetoclax is in clinical trials to treat cancers including acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), T cell lymphoma, non-Hodgkin lymphoma, myelodysplastic syndrome, and more (full list at clinicaltrials.gov).

The Jordan lab continues to collaborate closely with CU Cancer Center clinicians including Daniel Pollyea to further optimize strategies targeting cancer stem cells in leukemia and other cancers.

https://wb.md/2zykWqE

FDA Approves Gilteritinib for FLT3+ Acute Myeloid Leukemia

Gilteritinib approved for the treatment of adult patients with* FLT3 *mutation-positive relapsed or refractory AML

Roxanne Nelson RN, BSN

The US Food and Drug Administration (FDA) has approved gilteritinib (*Xospata*, Astellas Pharma) for the treatment of adult patients with *FLT3* mutation-positive relapsed or refractory acute myeloid leukemia (AML).

An expanded indication for a companion diagnostic was also granted, to use with gilteritinib. The LeukoStrat CDx FLT3 Mutation Assay,

developed by Invivoscribe Technologies, Inc, is used to detect the *FLT3* mutation in patients with AML.

"Approximately 25 to 30% of patients with AML have a mutation in the *FLT3* gene," Richard Pazdur, MD, director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research, said in a statement. "These mutations are associated with a particularly aggressive form of the disease and a higher risk of relapse."

Pazdur added that gilteritinib is the first drug to receive approval that can be used as monotherapy in this population of AML patients.

FLT3 is the most frequently mutated gene that has been identified in AML, and *FLT3* internal tandem duplication mutations are associated with high relapse rates, short remissions, and poor survival outcomes. Gilteritinib is a highly selective FLT3 tyrosine kinase inhibitor that has demonstrated activity against *FLT3* ITD mutations, and also inhibits *FLT3* D835 mutations that can confer clinical resistance to other FLT3 inhibitors.

Improved Outcomes

The approval was based on data from the ADMIRAL study, a randomized phase 3 trial in which 138 adult patients with *FLT3*-positive relapsed/refractory AML received gilteritinib orally at 120 mg daily. Within this group, 21% of patients achieved a complete remission or complete remission with partial hematologic recovery.

In addition, of the 106 patients who required red blood cell or platelet transfusions at baseline, 31% became transfusion-free for at least 56 days.

The ADMIRAL trial itself is still ongoing, and detailed response and overall survival data are expected to be made public in the coming year.

Results from the CHRYSALIS study, an earlier, first-in-human phase 1/2 trial, involved 252 patients and showed that 49% of patients with relapsed or refractory AML and an *FLT3* mutation responded to gilteritinib. The median survival for these participants was more than 7 months. Only 12% of patients without *FLT3* mutations responded to gilteritinib, providing evidence that it acts as a selective inhibitor of mutated *FLT3*. The findings from this early trial were published in *Lancet Oncology* (*Lancet Oncol.* 2017;18:1061-1075).

Data from the CHRYSALIS trial also showed that the drug was generally well tolerated, and the most common adverse events attributed to gilteritinib were diarrhea in 41 patients (16%), fatigue in 37 patients (15%), and elevated aspartate aminotransferase and alanine aminotransferase in 33 patients (13%). These were generally mild in severity, and only 25 patients (10%) stopped their treatment because of side effects.

"Although we're waiting for the final analysis of ADMIRAL, the available data with gilteritinib show fewer and milder side effects than typically is seen with traditional chemotherapy," lead investigator Alexander Perl, MD, an associate professor of hematology-oncology in the Perelman School of Medicine at the University of Pennsylvania and the Abramson Cancer Center, in Philadelphia, said in a news release.

In the release, Perl also pointed out that gilteritinib is given in an outpatient setting, making it easier for patients to receive treatment.

"Today's approval brings a new, highly-effective, and well-tolerated treatment option to the clinic for a group of truly high-risk patients who, until today, had no specific therapies available beyond chemotherapy to treat their disease," Perl said.

In 2017, the FDA granted this application Fast Track and Priority Review designation, and gilteritinib also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

http://bit.ly/2U5DDu8

Cosmic Airburst May Have Wiped Out Part of the Middle East 3,700 Years Ago

Archaeologists have found evidence of the cosmic airburst, north of the Dead Sea

By Owen Jarus, Live Science Contributor

Some 3,700 years ago, a meteor or comet exploded over the Middle East, wiping out human life across a swath of land called Middle Ghor, north of the Dead Sea, say archaeologists who have found evidence of the cosmic airburst.

The airburst "in an instant, devastated approximately 500 km2 [about 200 square miles] immediately north of the Dead Sea, not only wiping out 100 percent of the [cities] and towns, but also stripping agricultural soils from once-fertile fields and covering the eastern Middle Ghor with a super-heated brine of Dead Sea anhydride salts pushed over the landscape by the event's frontal shock waves," the researchers wrote in the abstract for a paper that was presented at the American Schools of Oriental Research annual meeting held in Denver Nov. 14 to 17. Anhydride salts are a mix of salt and sulfates.

"Based upon the archaeological evidence, it took at least 600 years to recover sufficiently from the soil destruction and contamination before civilization could again become established in the eastern Middle Ghor," they wrote. Among the places destroyed was Tall el-Hammam, an ancient city that covered 89 acres (36 hectares) of land.

This photo shows the site of Tell el-Hammam in Jordan. New research suggests that 3,700 years ago a cosmic airburst wiped out this city and the area near it. **Photo courtesy Phillip Silvia**

Unusual pottery

Among the evidence that the scientists uncovered for the airburst are 3,700-year-old pieces of pottery from Tall el-Hammam that have an unusual appearance. The surface of the pottery had been vitrified (turned to glass). The temperature was also so high that pieces of zircon within the pottery turned into gas — something that requires a temperature of more than 7,230 degrees Fahrenheit (4,000 degrees Celsius), said Phillip Silvia, a field archaeologist and supervisor with the Tall el-Hammam Excavation Project. However, the heat, while powerful, did not last long enough to burn through entire pottery pieces, leaving parts of the pottery beneath the surface relatively unscathed.

The only naturally occurring event capable of causing such an unusual pattern of destruction, Silvia said, is a cosmic airburst — something that has occurred occasionally throughout Earth's history, such as the explosion in 1908 at Tunguska in Siberia.

Also, archaeological excavations and surveys at other towns within the impacted area suggest a sudden wipeout of life around 3,700 years ago, Silvia said. So far, no craters have been found nearby, and it's unclear whether the culprit was a meteor or comet that exploded above the ground.

The fact that only 200 square miles of land was destroyed indicates that the airburst occurred at a low altitude, possibly not more than 3,280 feet (1 km) above the ground said Silvia. In comparison, the Tunguska airburst heavily damaged 830 square miles, or 2,150 square kilometers of land.

The team's results are preliminary and research is ongoing, Silvia emphasized. The team of scientists includes members from Trinity Southwest University, Northern Arizona University, DePaul University, Elizabeth City State University, New Mexico Tech and the Comet Research Group.

http://bit.ly/2DX7O0Y

BU study: Modified malaria drug proven effective at inhibiting Ebola

Derivatives from a commonly used anti-malarial can prevent Ebola virus from entering cells

Robert Davey, professor of microbiology at Boston University School of Medicine and researcher at Boston University's National Emerging Infectious Diseases Laboratories (NEIDL), in collaboration with researchers at Nagasaki University, Tokushima Bunri University, Kagoshima University, and Texas Biomedical Research Institute, have discovered that certain derivatives of amodiaquine, a medication typically used to treat malaria, could provide a new therapeutic approach to treating patients infected with Ebola.

From 2014-2016, an Ebola epidemic swept through West Africa, infecting more than 28,000 people and killing more than 11,000 in Guinea, Liberia, and Sierra Leone alone. The outbreak attracted the attention of virologists from around the world, and several of them, including Robert Davey, noticed something intriguing: patients with Ebola who had been treated with amodiaquine were 31 percent less likely to die.

"People were saying 'it's interesting'; I wondered if it was important," says Davey. "I thought we should test some [chemical] derivatives and see if we could find some improvement over the amodiaquine performance."

Davey and collaborators set out to learn exactly which parts of the amodiaquine molecule were inhibiting Ebola virus infection. Their findings, published in *Antiviral Research*, show that modified amodiaquine derivatives are significantly less toxic and nearly 10 times more effective at blocking Ebola virus than the original amodiaquine formula that greatly reduced mortality during the West Africa outbreak.

To make the discovery, Davey teamed up with other virologists on the hunt for new antiviral therapeutics. Serendipitously, one of Davey's colleagues from Japan--Yasuteru Sakurai, from the National Research Center for the Control and Prevention of Infectious Diseases in Nagasaki--knew another Japanese researcher, Masanori Baba of Kagoshima University, who had already made a series of amodiaquine derivatives in an effort to find new treatments for HIV and other viruses.

Davey says amodiaquine inhibits the two diseases, malaria and Ebola virus disease, in related ways. All cells need to get food from their surroundings. With malaria, amodiaquine prevents the parasite from digesting food from inside red blood cells, so it basically starves to death. Ebola virus mimics food and tricks your cells into swallowing and trying to digest it. However, the virus senses this and uses it as a trigger to begin replication, avoiding digestion. So, by interfering with normal cell digestion, amodiaquine also blocks Ebola virus infection.

"With Ebola, we are affecting your own cell's digestive system, but for a short time, which the cell can survive," says Davey. "And the drugs that we developed likely improve targeting to places in the cell where Ebola virus likes to get to, whereas for malaria, the drugs are best at targeting the parasite's feeding process which it needs all the time. It's a subtle difference in chemistry, but it's important for making an effective drug treatment for patients."

Working together at Davey's former lab in San Antonio, Texas, the team--which also included Masaaki Toyama of Kagoshima University and Norikazu Sakakibara of Tokushima Bunri University--tested nearly 70 amodiaquine derivatives, mixing each one with cells infected with Ebola virus and observing the effect that each derivative had on the live virus infection.

What they found, says Davey, was encouraging. Fourteen of the compounds tested did a better job inhibiting the Zaire strain of Ebola

virus disease than straight amodiaquine. They also noticed that when two particular parts of the amodiaquine molecule were modified, the potency against the virus was further increased. Then, by combining the two features, they created further potent compounds, which appeared to completely prevent the virus from entering cells.

"If you combine those two things--less toxicity and better performance against the virus--you get something called a selective index," says Davey. "The selective index that we found easily met the criteria for clinical development."

Davey and BU researchers Manu Anantpadma and Patrick Keiser, are taking the next steps on the long road of developing the discovery from "it's interesting" to an approved therapy. Next, Davey says, will come testing in animal models, as well as testing the potent compounds against other strains of Ebola virus.

The research was supported by the National Institutes of Health.

http://bit.ly/2zCp20E

Stone tools date early humans in North Africa to 2.4 million years ago

Archaeological excavation at Ain Boucherit, Algeria.

Mathieu Duval ARC Future Fellow, Griffith University
Mohamed Sahnouni

When did early humans first arrive in the Mediterranean area? New archaeological evidence published today online by the journal Science (as a First Release) indicates their presence in North Africa at least 2.4 million years ago.

This is about 600,000 years earlier than previously thought.

The results, from the Ain Boucherit site in north eastern Algeria, provide new information on a time window involving the earliest representative of the *Homo* genus.

These discoveries are the result of excavations and intensive investigations performed under the umbrella of the Ain Hanech project since 1992.

Location of Ain Boucherit and other prehistoric sites mentioned in the text. Right: Zoom on the vicinity of El Eulma city. **Maps from Google map**

Located north of El Eulma city, the area was previously well known for providing stone tools and cut-marked bones dated to about 1.8 million years ago (Ain Hanech and El Kherba sites, see map above), which have been until now the oldest occurrences in North Africa.

In 2006 and 2009, new artefacts were found at Ain Boucherit, a few hundred metres from the other sites. They were distributed in two layers below the previous archaeological findings, suggesting an even older human presence in the area.

The new archaeological finds

Excavations of the lower and upper (AB-Up) archaeological levels yielded more than 250 stone tools and almost 600 fossil remains.

Excavations of the lower (known as AB-Lw) and upper (AB-Up) archaeological levels yielded more than 250 stone tools and almost 600 fossil remains.

A wide range of animals was identified, including elephants, horses, rhinos, hippos, wild antelopes, pigs, hyenas, and crocodiles. These animals currently occupy a relatively open savanna type habitat with permanent water nearby, suggesting similar conditions in the past.

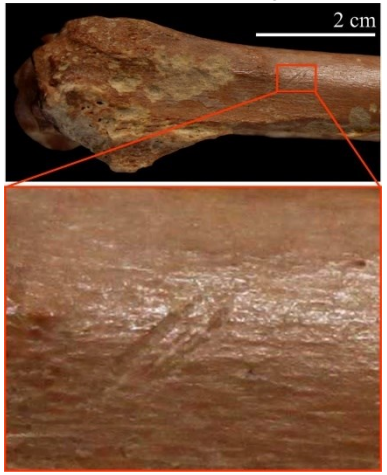
The stone tool find includes mostly chopping tools and sharp-edged cutting tools used for processing animal carcasses. Those tools are made of limestone and flint that were most likely collected nearby

from ancient stream beds. They are typical of the Oldowan stone tool technology known from East African sites and dated to between 2.6 million and 1.9 million years ago. But the Ain Boucherit find also shows some subtle variations, in particular with the presence of very peculiar tools of spheroidal shape whose function remains unknown.

Two examples of stone tools from Ain Boucherit. An Oldowan core from which sharp-edged cutting flakes were removed (left). Sharp-edged cutting flake that may be used for butchery activities on the bones (right). **Mohamed Sahnouni**

Some of the fossil bones show very specific marks that could not be of natural origin, but rather the result of an intentional activity. Two types were identified. The first were cutmarks made from sharp-edged flakes, suggesting skinning, evisceration and defleshing activities (pictured below). The second include percussion marks made from a hammerstone, suggesting marrow extractions.

These show the use by early hominins of meat and marrow from animals. This is consistent with other studies from broadly contemporaneous East African sites.



A small bovid bone with stone tool cutmarks. **sabel Caceres**

Dating the site was quite challenging, but the relative positions of AB-Up (within Olduvai event) and AB-Lw (a few metres below Olduvai) allowed us to derive an age of about 1.9 million and 2.4 million years ago, respectively.

The significance of the discovery

This new discovery modifies our understanding of the timing and diffusion of the Oldowan stone tool technology throughout Africa and outside the continent.

By pushing back by about 600,000 years the earliest occurrence of Oldowan tools in North Africa, the age difference with the oldest East African evidence suddenly becomes relatively small.

This indicates at least a somewhat rapid (or, more rapid than previously thought) expansion of this technology from East Africa, although a multiple origin scenario of stone tool manufacture in both East and North Africa might even be possible.

As a consequence, the first settlements of the southern margin of the Mediterranean area now appear to be much older than their northern counterparts.

The oldest evidence from southern Europe does not exceed about 1.4 million years ago (Atapuerca and Orce sites, in Spain), while the hominin fossils found at Dmanisi in Georgia, at the gates of Europe, are dated to 1.8 million years ago.

Who made these tools?

Since no hominin fossils were found at Ain Boucherit, we can only speculate about the possible makers of these Oldowan stone tools.

The hominin fossil record in North Africa is extremely poor, and there is currently no fossil reported in the age range of Ain Boucherit. The oldest fossils found in Algeria are dated to about 700,000 years ago. They were found at Tighennif (formerly known as Ternifine, map above). If their attribution has changed over time (initially *Atlanthropus mauritanicus* and nowadays *Homo erectus* or early *Homo heidelbergensis* depending on the authors), these fossils are too young compared with the Ain Boucherit discoveries to support any kind of connection between the sites.

All the early hominin fossil remains found in the Mediterranean area in association with Oldowan stone tools are significantly younger than Ain Boucherit, by at least 1 million years. The oldest Western

European evidence such as the partial mandible found at Atapuerca Sima del Elefante, Spain, and the isolated deciduous tooth from Barranco León, southern Spain, are dated to about 1.2 million and 1.4 million years ago, respectively.

Consequently, the best candidates are most likely to be found in East Africa, despite their geographical distance from North Africa. Several hominins are broadly contemporaneous with Ain Boucherit (a good overview may be found here), including australopithecines and different members of the genus *Homo* such as *Homo habilis*, *Homo rudolfensis* or the undefined early *Homo* from Ledi-Geraru, Ethiopia.

That said, we cannot rule out the possibility that the stone tools at Ain Boucherit come from another hominin species, belonging or not to the genus *Homo*, that has not been found yet.

We hope our future excavation at Ain Boucherit will give us the opportunity to identify these stone toolmakers.

Archéologue et professeur au National Center for Research on Human Evolution (CENIEH), Burgos., National Center for Research on Human Evolution (CENIEH)

Mathieu Duval receives funding from the Australian Research Council (ARC) Future Fellowship (FT150100215). He works for Griffith University, Australia and is an affiliate scientist (non-remunerated position) at CENIEH, Spain.

***Mohamed Sahnouni does not work for,** consult, own shares in or receive funding from any company or organisation that would benefit from this article, and has disclosed no relevant affiliations beyond their academic appointment.*

http://bit.ly/2SnJrxB

Until leaving the nest, jumping spiders suckle spider milk from their moms

Newly identified and peculiar behavior compares both functionally and behaviorally to lactation in mammals

Much like baby mammals nursing at the teats of their mothers, some baby jumping spiderlings are entirely dependent on nutritious spider milk secreted and fed to them by their mothers. What's more, spider mothers continue to care for and feed their offspring the nutritious milk-like fluid - which contains nearly four times the protein of cow's milk - into their subadult lives and long after they're able to forage on their own, a new study finds.

According to the results, this newly identified and peculiar behavior compares both functionally and behaviorally to lactation in mammals and hints to the possibility that long-term, milk-provisioning maternal care may be more common in the animal kingdom than previously believed.

For many animals, the growth, development and survival of young is wholly dependent on nutritious food often provided to them by their parents. Mammals produce their own nutritional substances, such as milk, and nurse their young until they learn to fend for themselves.

While lactation-like provisioning is known elsewhere in the animal kingdom, the intensity and duration of associated parental care is uniquely mammalian and thought to increase fitness by providing the opportunity for offspring to learn behaviors crucial for survival. Zhanqi Chen and colleagues, however, describe strikingly similar, yet particularly puzzling, milk provisioning behavior in Toxeus magnus, a species of ant-mimicking jumping spider.

Laboratory observations show the young spiderlings first drinking from droplets deposited on the nest's surface and then directly sucking from the mother's egg-laying opening.

According to Chen et al., spiderlings remained in the nest and nursed on spider milk for nearly 40 days, shortly before reaching sexual maturity. Furthermore, the authors found that while nursing was not critical to offspring's survival after becoming independent, their mother's presence during their young lives greatly assured their overall health and adult survival. The mothers' nursing and care also seemed important for maintaining numbers of adult female offspring required for optimal reproductive success of the spider; although the mothers treated all juveniles the same, only daughters were allowed to return to the breeding nest after sexual maturity, the authors observed.

http://bit.ly/2PgnE97

Scary 'New' Tick Has US Officials Worried

A species of tick native to Asia is spreading across the United States, according to a new report.

By Rachael Rettner, Senior Writer | November 29, 2018 05:44pm ET

This tick, known as the longhorned tick, or Haemaphysalis longicornis, was first identified in the U.S. in August 2017 when it was found on a sheep in New Jersey, according to the report, released today (Nov. 29) by the Centers for Disease Control and Prevention (CDC).

Since then, the tick has been detected in nine states: New York, Virginia, West Virginia, Arkansas, North Carolina, Pennsylvania, Connecticut and Maryland, the report said.

”The presence of H. longicornis in the United States represents a new and emerging disease threat," the report said.

In other parts of the world, longhorned ticks are known to spread diseases, including the bacterial infections babesiosis, ehrlichiosis, theileriosis and rickettsiosis, as well as certain viral diseases. In China and Japan, the longhorned tick transmits a disease called severe fever with thrombocytopenia syndrome (SFTS), which can be deadly.

But whether longhorned ticks in the U.S. can spread diseases is not known, because the types of diseases ticks spread can vary depending on their environment. So far, no cases of disease tied to these ticks have been reported in the U.S., the report said.

Officials are now working with experts in veterinary medicine, agricultural science and public health to better understand the potential impact of the longhorned tick in the U.S.

Indeed, the longhorned tick poses a particular threat to livestock. Unlike most tick species, longhorned ticks can reproduce asexually, and lay massive numbers of eggs. A single female longhorn tick can lay up to 2,000 eggs at a time, the CDC said. Due to these large numbers, longhorned ticks can cause severe infestations in livestock, leading to weakness, anemia or even death in the animals.

The CDC said that critical work is needed to assess the threat of longhorned ticks in the U.S. Researchers need to determine the distribution of the tick in the U.S.; the kinds of pathogens it can carry; how frequently it bites people and animals; and how to effectively control its spread.

http://bit.ly/2QeuxgI

Ancient populations from different Caucasus regions had strong social connections

Neanderthals transferred rock distances up to 250 kilometers and used it to manufacture tools

Research group from Russia and the United States analyzed samples of obsidian volcanic glass in Kabardino-Balkaria. It turned out that more than 70 thousand years ago, Neanderthals transferred this mineral to distances up to 250 kilometers and used it to manufacture tools. These findings help to understand how populations from different regions communicated in antiquity. The study was supported by the Russian Science Foundation and is published in the *Journal of Archaeological Science: Reports*.

When volcanoes erupted, the ejected lava hardens formed a mixture of various minerals, including obsidian. In the Stone Age, the ancient people used this material extensively to create tools. In fact, we use it even now: in surgery, for the manufacture of dark glass and jewelry. The elemental composition of obsidian is unique not only for each volcano, but also for each eruption. This makes it possible to determine precisely the specific archaeological site, where particular obsidian sample originated from.

According to earlier studies, in the Paleolithic in Central Europe and the Caucasus, obsidians were actively transferred from one settlement to another, and over time the distance of its transportation increased from 100 to more than 700 kilometers.

Scientists from the non-profit organization "Laboratory of Prehistory" analyzed the elemental composition of obsidian samples from various Neanderthals ites of the Central and North-Western Caucasus, which were found during several expeditions. The obsidian composition turned out to be almost identical for many tools, which indicates their common origin. New data also indicates that obsidian was transported over more than 250 kilometers from sources in the Central Caucasus to the North-West Caucasus during the Middle Paleolithic. At the same time, new studies show that the Central Caucasus populations cultural tradition differed from the Neanderthals of the North-West Caucasus. So archaeologists have yet to figure out how the interaction between these different Neanderthals groups was build in this period.

Scientists also found that in the Upper Paleolithic, people transported obsidians from the Elbrus region and the South Caucasus to the Mezmay cave, which is located in the North-West Caucasus. The length of migration was 250 and 450 kilometers respectively. The researchers suggest that in the Upper Paleolithic there was already a developed social network between groups of people from different regions.

"The study of cultural areas, the impact of innovations and mechanisms for the dissemination of new technologies is one of the most important tasks of modern research. Our work reliably shows the existence of connections of the population of different regions in antiquity. These results can be widely used in university lectures, as well as in modern textbooks for middle and high school. Also, the results of recent studies can be used in the design of expositions of museums and thematic exhibitions," summarizes Ekaterina Doronicheva, one of the authors of the work, Ph.D., research associate of the "Laboratory of Prehistory".

The work was done in collaboration with scientists from the University of California (USA) and the National Museum of the Republic of Adygea.

http://bit.ly/2FX4qPb

Stone tools linked to ancient human ancestors in Arabia have surprisingly recent date

Stone handaxes, similar to those made by early humans as much as 1.5 million years ago, have been dated for the first time in the Arabian Peninsula, to less than 190,000 years old, where their production may have endured until the arrival of Homo sapiens

Beginning more than 1.5 million years ago, early humans made stone handaxes in a style known as the Acheulean - the longest lasting tool-making tradition in prehistory. New research led by the Max Planck Institute for the Science of Human History and the Saudi Commission for Tourism and National Heritage has documented an Acheulean presence in the Arabian Peninsula dating to less than 190,000 years ago, revealing that the Arabian Acheulean ended just before or at the same time as the earliest Homo sapiens dispersals into the region.

These are handaxes from the site of Saffaqah, Saudi Arabia. **Palaeodeserts (Ian R. Cartwright)**

Much attention has been given to understanding the spread of our own species, Homo sapiens, first within Africa and then beyond. However, less attention has been given to where diverse groups of close evolutionary cousins lived in Eurasia immediately prior to the arrival of Homo sapiens. Understanding this is critical because the spatial and temporal characteristics of such groups reveal the human and cultural landscape first encountered by our species on leaving Africa.

The youngest Acheulean site in Southwest Asia

In a paper published in Scientific Reports, an international team of researchers led by the Max Planck Institute for the Science of Human History and the Saudi Commission for Tourism and National Heritage reports the first ever dates obtained from an Acheulean site in Arabia, the site of Saffaqah, situated in Central Saudi Arabia. Saffaqah is the first stratified Acheulean site to be reported in the Arabian Peninsula and the dates reveal that early humans occupied the site until at least 190,000 years ago. These dates are surprisingly recent for a region known to feature among the oldest examples of such technology outside Africa. For example, dates from the Levant document an ancient Acheulean presence from 1.5 million years ago. Conversely the site of Saffaqah features the youngest Acheulean tools yet found in southwest Asia.

Over 500 stone tools, including handaxes and other artefacts known as cleavers, were recovered from the occupation levels. Some of the stone flakes used to make handaxes were in such fresh condition that they were recovered still resting on the stone nodules from which they had been detached. These and other artefacts show that the early humans responsible for making them were manufacturing stone tools at this site.

"It is not surprising that early humans came here to make stone tools," says Dr. Eleanor Scerri of the Max Planck Institute for the Science of Human History, the lead author of the study. "The site is located on a prominent andesite dyke that rises above the surrounding plain. The spot was both a source of raw material as well as a prime location to survey a landscape that, back then, sat between two major river systems." This choice location also seems to have continued to be attractive to early humans at an even later date than those recorded by the researchers in this study. Layers containing identical stone handaxes are also found above the dense occupation layers that were dated, raising the possibility that Saffaqah is among the youngest Acheulean sites documented anywhere.

Hominins living at the edge

The new dating results both record the late persistence of the Acheulean in the Peninsula and also show that as yet unidentified hominin populations were using networks of now extinct rivers to disperse into the heart of Arabia during a time of increased rainfall in the region. This suggests that these hominins were able to live on the margins of habitable zones and take advantage of relatively brief "greening" episodes in a generally arid area. The dispersal of these hominins into the heart of Arabia may also help to explain the surprisingly late persistence of the Acheulean, as it suggests a degree of isolation.

"These hominins were resourceful and intelligent," adds Dr. Scerri, "They dispersed across a challenging landscape using technology commonly seen as reflecting a lack of inventiveness and creativity. Instead of perceiving the Acheulean this way, we should really be struck by how flexible, versatile and successful this technology was."

Cutting edge science

To date the sediments from the site of Saffaqah, the researchers used a combination of dating techniques known as luminescence methods, including a newly developed infrared-radiofluorescence (IR-RF) dating protocol for potassium rich feldspars. The method relies on the ability of such minerals to store energy induced by natural radioactivity and to release this energy in the form of light. "The application of IR-RF dating allowed us to obtain age estimates from sediments that were previously difficult to reliably date," explains Marine Frouin of the University of Oxford, one of the researchers involved in the dating program.

These discoveries and methods are already leading to new research. "One of the biggest questions we have is whether any of our evolutionary ancestors and close cousins met up with Homo sapiens, and if this could have happened somewhere in Saudi Arabia. Future field work will be dedicated to understanding possible cultural and

biological exchanges at this critical time period," says Professor Michael Petraglia of the Max Planck Institute for the Science of Human History, the director of the project which led to the discoveries at Saffaqah.

The international consortium of researchers involved in this project is headed by the Max Planck Institute for the Science of Human History, in partnership with HRH Prince Sultan bin Salman and the Saudi Commission for Tourism and National Heritage. Additional partners include King Saud University and other key institutions in the United Kingdom and Australia.

http://bit.ly/2Qr3oq7

Why patients lie to their doctors

Fear of being judged and embarrassed are among the reasons

Salt Lake City - When your doctor asks how often you exercise, do you give her an honest answer? How about when she asks what you've been eating lately? If you've ever stretched the truth, you're not alone. 60 to 80 percent of people surveyed have not been forthcoming with their doctors about information that could be relevant to their health, according to a new study. Besides fibbing about diet and exercise, more than a third of respondents didn't speak up when they disagreed with their doctor's recommendation. Another common scenario was failing to admit they didn't understand their clinician's instructions.

When respondents explained why they weren't transparent, most said that they wanted to avoid being judged, and didn't want to be lectured about how bad certain behaviors were. More than half were simply too embarrassed to tell the truth.

"Most people want their doctor to think highly of them," says the study's senior author Angela Fagerlin, Ph.D., chair of population health sciences at U of U Health and a research scientist with the VA Salt Lake City Health System's Informatics Decision-Enhancement and Analytic Sciences (IDEAS) Center for Innovation.

"They're worried about being pigeonholed as someone who doesn't make good decisions," she adds.

Scientists at University of Utah Health and Middlesex Community College led the research study in collaboration with colleagues at University of Michigan and University of Iowa. The results will be published online in *JAMA Network Open* on November 30, 2018.

Insights into the doctor-patient relationship came from a national online survey of two populations. One survey captured responses from 2,011 participants who averaged 36 years old. The second was administered to 2,499 participants who were 61 on average.

Survey-takers were presented with seven common scenarios where a patient might feel inclined to conceal health behaviors from their clinician, and asked to select all that they had ever happened to them. Participants were then asked to recall why they made that choice. The survey was developed with input from physicians, psychologists, researchers and patients, and refined through pilot testing with the general public.

In both surveys, people who identified themselves as female, were younger, and self-reported as being in poor health were more likely to report having failed to disclose medically relevant information to their clinician.

"I'm surprised that such a substantial number of people chose to withhold relatively benign information, and that they would admit to it," says the study's first author Andrea Gurmankin Levy, Ph.D., MBe, an associate professor in social sciences at Middlesex Community College in Middletown, Connecticut. "We also have to consider the interesting limitation that survey participants might have withheld information about what they withheld, which would mean that our study has underestimated how prevalent this phenomenon is."

The trouble with a patient's dishonesty is that doctors can't offer accurate medical advice when they don't have all the facts.

"If patients are withholding information about what they're eating, or whether they are taking their medication, it can have significant

implications for their health. Especially if they have a chronic illness," says Levy.

Understanding the issue more in-depth could point toward ways to fix the problem. Levy and Fagerlin hope to repeat the study and talk with patients immediately after clinical appointments, while the experience is still fresh in their minds. Person-to-person interviews could help identify other factors that influence clinician-patient interactions. For instance, are patients more open with doctors they've known for years?

The possibility suggests that patients may not be the only ones to blame, says Fagerlin. "How providers are communicating in certain situations may cause patients to be hesitant to open up," she says. "This raises the question, is there a way to train clinicians to help their patients feel more comfortable?" After all, a healthy conversation is a two-way street.

"Prevalence of and Factors Associated with Patient Nondisclosure of Medically Relevant Information to Clinicians" publishes online in JAMA Network Open *on Nov. 13, 2018.*

In addition to Fagerlin and Levy, Aaron Scherer from University of Iowa, Brian Zikmund-Fisher and Geoffrey Barnes from University of Michigan, and Knoll Larkin from Wayne State University were co-authors on the study.

http://bit.ly/2Qr4diH

Babies kicking in the womb are creating a map of their bodies

The kicks a mother feels from her unborn child may allow the baby to 'map' their own body and enable them to eventually explore their surroundings, suggests new research led by UCL in collaboration with UCLH.

For the study, published today in Scientific Reports, researchers measured brainwaves produced when newborn babies kick their limbs during rapid eye movement (REM) sleep, finding that fast brainwaves - a brainwave pattern typically seen in neonates - fire in the corresponding hemisphere.

For example, the movement of a baby's right hand causes brainwaves to fire immediately afterwards in the part of the left brain hemisphere that processes touch for the right hand. The size of these brainwaves is largest in premature babies, who at that age would usually still be in the womb.

The findings suggest that foetal kicks in the late stages of pregnancy - the third trimester - help to grow areas of the brain that deal with sensory input, and are how the baby develops a sense of their own body. The fast brainwaves evoked by the movement disappear by the time babies are a few weeks old.

"Spontaneous movement and consequent feedback from the environment during the early developmental period are known to be necessary for proper brain mapping in animals such as rats. Here we showed that this may be true in humans too," explained study author Dr Lorenzo Fabrizi (UCL Neuroscience, Physiology & Pharmacology).

Kimberley Whitehead (UCL Neuroscience, Physiology & Pharmacology) said: "We think the findings have implications for providing the optimal hospital environment for infants born early, so that they receive appropriate sensory input. For example, it is already routine for infants to be 'nested' in their cots - this allows them to 'feel' a surface when their limbs kick, as if they were still inside the womb.

"As the movements we observed occur during sleep, our results support other studies which indicate that sleep should be protected in newborns, for example by minimising the disturbance associated with necessary medical procedures."

The babies' brainwaves were measured using electroencephalography (EEG), and were recorded continuously during sleep. Active sleep was identified behaviourally according to cot side observation of rapid eye movements, largely irregular breathing and frequent, isolated limb movements.

A total of 19 newborns aged two days on average took part in the study, and they were between 31 and 42 weeks corrected gestational age when studied. Corrected gestational age takes into account their age if they were still in the womb; a baby born at 35 weeks and being one week old would have a corrected gestational age of 36 weeks.

The research was carried out at UCL Neuroscience, Physiology & Pharmacology and the Elizabeth Garrett Anderson Obstetric Wing at UCLH, and was kindly supported by the Medical Research Council. Ethical approval was obtained from the NHS Research Ethics Committee.

http://bit.ly/2E9GwFL

The fight against measles has taken a turn for the worse

An overall downward trend reversed between 2016 and 2017.

Cathleen O'Grady - 12/1/2018, 1:51 AM

In 2010, the World Health Organization (WHO) set some ambitious goals for fighting measles worldwide. By 2015, they wanted to reduce the number of deaths caused by measles by 95 percent compared to 2000. They set similarly ambitious targets for vaccination rates and measles infections.

The world has not reached these goals. And between 2016 and 2017, there was an alarming uptick in measles cases worldwide, according to a joint report by the WHO and CDC. "Complacency about the disease and the spread of falsehoods about the vaccine in Europe, a collapsing health system in Venezuela, and pockets of fragility and low immunization coverage in Africa are combining to bring about a global resurgence of measles after years of progress," said Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance, in a statement about the report.

Overall, between 2000 and 2017, there has been a lot of progress: annual global deaths have decreased 80 percent, from 545,174 to 109,638. Over this time period, measles vaccination has prevented approximately 21 million deaths globally, compared to a hypothetical world with no measles vaccines (in this world, the death rate would have been a lot higher in 2000, too). The number of cases reported annually plummeted from 145 cases per million people to just 25—although the goal was five cases per million. And 85 percent of people globally had received the first dose of the measles vaccine in 2017, compared to 72 percent in 2000.

That 85 percent is good, but lower than the 95 percent needed to create herd immunity—a vaccination rate in a population that's so high that the virus is unlikely to meet anyone to infect, leaving it unable to spread via unvaccinated people and those with compromised immune systems. The rate has "stagnated for nearly a decade," write the authors of the report. Meanwhile, coverage of the crucial second dose of the vaccine is only at 67 percent worldwide.

In 2000, 169 countries reported the number of recorded measles cases, and only 38 percent of those countries reported a rate in line with the WHO goal of 5 cases (or fewer) per million people. By 2016, that target had been reached by 69 percent of the 176 countries that reported their data. But in 2017, it took a dip, to 65 percent of the 184 reporting countries.

Part of that dip can be explained by the eight extra countries that reported their data, the authors of the report write. But that doesn't fully account for the 31 percent increase in reported cases globally. The only region to see a falling infection rate in 2017 was the Western Pacific (including Cambodia, Fiji, Micronesia, and others), while Europe saw rates more than quadruple, and in the Americas, rates were more than 64 times higher.

A large part of the increase in the Americas is driven by an ongoing outbreak in Venezuela, where the virus has now re-established itself as a regular feature. This has also led to outbreaks in neighboring countries. The researchers have concerns about a similar situation in Europe, where measles may also have been gone past infrequent outbreaks and become established again.

There is, of course, uncertainty in these findings—they rely on reporting chains with many possible links, and comparisons between

different countries and regions can be difficult to interpret, the authors note. But the slow progress and new outbreaks, they write, "highlight the fragility of gains made toward global and regional measles elimination goals."

Morbidity and Mortality Weekly Report, 2018. DOI: 10.15585/mmwr.mm6747a6 (About DOIs).

https://wb.md/2U9GvX1

Three Common Dementia Screens Faulty, Inaccurate

Three brief cognitive assessments often used in primary care settings to identify patients with cognitive impairment who could benefit from a full diagnostic workup for dementia are often inaccurate, new research shows.

Megan Brooks

The three tests are the Mini–Mental State Examination (MMSE), which assesses orientation to time and place and the ability to remember words; the Memory Impairment Screen (MIS), which focuses on the ability to remember words; and Animal Naming (AN), which involves naming as many animals as possible in 60 seconds.

"Our study found that all three tests often give incorrect results that may wrongly conclude that a person does or does not have dementia," study author David Llewellyn, PhD, of the University of Exeter Medical School, United Kingdom, said in a news release.

The study also found that each test has a different pattern of biases, so people are more likely to be misclassified by one test than another, depending on factors such as their age, education, and ethnicity.

"While these results are at first concerning, knowing the specific limitations for each test will help clinicians decide which is the most appropriate for their patient," lead author Janice Ranson, doctoral researcher in clinical epidemiology at the University of Exeter Medical School, told *Medscape Medical News.*

"There are many available brief tests, which all have some limitations and biases, and there is currently not strong enough evidence to suggest one particular test is best for everyone. From our findings, it appears that the best test depends on the clinical context and patient characteristics," said Ranson.

The study was published online November 28 in *Neurology Clinical Practice*, a journal of the American Academy of Neurology.

Huge Need for Better Tests

The study included 824 adults (mean age, 82 years) from the population-based Aging, Demographics and Memory Study (ADAMS) who underwent a comprehensive workup for dementia. The workup included physical examination, genetic testing for the *APOE* gene, psychological testing, and comprehensive memory and thinking tests. On the basis of these results, 35% of the patients were found to have dementia, and 65% were found not to.

Armed with this information, the researchers then had participants take the three brief cognitive assessment tests. They found that 35.7% of participants were wrongly classified by at least one test, 13.4% were misclassified by two or more tests, and 1.7% were misclassified by all three tests. Overall dementia misclassification rates for the MMSE, the MIS, and the AN were 21%, 16%, and 14%, respectively. These rates included both false positive and false negative results.

Years of education predicted higher rates of false negative results (odds ratio [OR], 1.23; 95% confidence interval [CI], 1.07 - 1.40) and lower rates of false positive results (OR 0.77; 95% CI, 0.70 - 0.83) on the MMSE.

Nursing home residency predicted lower rates of false negative results (OR, 0.15; 95% CI, 0.03 - 0.63) and higher rates of false positive results (OR, 4.85; 95% CI, 1.27 - 18.45) on the AN.

Across all tests, not having an informant (such as a family member or friend) weigh in on the patient's memory was associated with increased risk for misclassification.

"Each test is biased in different ways, so the accuracy of each test varies with the characteristics of the patient," said Ranson.

"There is clearly great potential for improvement of this initial stage in the diagnostic pathway for dementia. We desperately need more accurate and less biased ways of detecting dementia swiftly in clinic," he added.

"Not Surprising"

Reached for comment, Steven DeKosky, MD, McKnight Brain Institute, Florida Alzheimer's Disease Research Center, Gainesville, said he's not surprised by the data.

"We have known about this for a long time, and kudos to this group for doing this careful analysis of all three tests. The fact that only 1.7% of the cases were misdiagnosed when all three tests were used is testimony to the fact that the diagnosis is proportional to the amount of time that you spend testing a patient," said DeKosky, a fellow of the American Academy of Neurology.

"Everybody is looking for the one test that will tell you whether the patient has Alzheimer's disease or whether they are impaired, and the human brain is a little too complicated for that.

"Dementia and cognitive impairment of normal aging are multidimensional, continuous processes, and we are trying to nail a state out of what is a bunch of declining lines or stable lines of cognition. This reinforces that we don't have one simple test. There will always be some people that are missed if you use just one test," said DeKosky.

He said the study also highlights the importance of having the patient's partner provide information on whether there is memory loss or not.

"Patients will often tell you that they don't have memory loss, which is either their denial or possibly loss of insight because they are developing one, or because they just don't want to believe it. So often, the partner is a more accurate source," said DeKosky.

The study was supported by the Halpin Trust, the Mary Kinross Charitable Trust, the Engineering and Physical Sciences Research Council, and the UK National Institute for Health Research. The study authors and Dr DeKosky have disclosed no relevant financial relationships.

Neurol Clin Pract. Published online November 28, 2018. Abstract

https://nyti.ms/2zHKIZk

‘From Nothing to Gangbusters’: A Treatment for Sickle-Cell Disease Proves Effective in Africa

Already used in Western countries, hydroxyurea eased painful episodes in African children with the condition. It also reduced the risk of malaria infection.

By Donald G. McNeil Jr.

A drug that protects children in wealthy countries against painful and sometimes lethal bouts of sickle-cell disease has been proven safe for use in Africa, where the condition is far more common, scientists reported on Saturday.

More research remains to be done, experts said, but knowing that hydroxyurea — a cheap, effective and easy-to-take pill — can safely be given to African children may save millions of youngsters from agonizing pain and early deaths.

“I think this is going to be amazing,” said Dr. Ifeyinwa Osunkwo, who directs a sickle-cell disease program in Charlotte, N.C., but was not involved in the new study.

“There is currently no treatment in Africa, and a lot of children die before age 5,” said Dr. Osunkwo, who has treated children in the United States and Nigeria. “We’re going from nothing to gangbusters.”

The disease, in which blood cells twist themselves into stiff semicircular shapes, is caused by a genetic mutation thought to have arisen in Africa about 7,000 years ago.

About 300,000 babies are born with the disease each year; about 75 percent of them are in Africa, and about 1 percent in the United States.

The condition is found throughout the Americas and the Caribbean among descendants of Africans brought to this hemisphere by the slave trade. Sickle-cell disease also is found less frequently in southern Europe, the Middle East and India.

These are also places where malaria is still endemic or was until a few decades ago. People who inherit one copy of the sickle-cell gene are partially protected against malaria, which is presumably why the mutation has persisted in Africa.

But children who inherit the gene from both parents are often left breathlessly weak from anemia, prone to infections and liable to have crises in which their blood cells clump and jam capillaries in the brain, lungs and other organs.

The pain is often so excruciating that only opioids can help. Treatment may require blood transfusions or, in wealthy countries, bone marrow transplants, which themselves carry a risk of death.

Without treatment, many children die from strokes or organ damage. Hydroxyurea has been used for decades in the United States and Europe. But some early animal studies made researchers fear it would make African children more susceptible to local infections, particularly malaria.

The new study followed 600 children in Angola, Uganda, Kenya and the Democratic Republic of Congo who were given the drug for more than two years.

As with children in wealthy countries, taking the drug daily also made it far less likely they would die or need a blood transfusion because of their sickle-cell disease. They were about half as likely to suffer bouts of severe pain, and somewhat less likely to get other infections.

In an unexpected twist, investigators discovered that the children were about half as likely to get malaria while using hydroxyurea as they had been before the trial started. The reasons are not known.

”With all the malaria, malnourishment and vitamin deficiency in Africa, we couldn’t assume it would work as well as it did,” said Dr. Russell E. Ware, director of hematology at the Cincinnati Children’s Hospital and a co-author of the study, which was presented at a meeting of the American Society for Hematology and simultaneously published in the New England Journal of Medicine.

Hydroxyurea is already on the World Health Organization’s essential medicines list, is available in generic form for about 50 cents a pill and can be stored at room temperature, Dr. Ware said.

If this study raises interest in buying millions of additional doses for use in Africa, the drug could presumably be made far more cheaply, he added.

Even though the study was fairly large, it had some limitations.

It was intended to prove only that the drug was safe for children aged 1 to 10. It was not designed to test various dosages to find the ideal one, nor to determine how many lab tests are needed to monitor children taking the drug, nor to determine the long-term effects.

So further work will be needed, researchers said.

Also, the research was done without a placebo control — a group of similar children not getting the drug. Oversight boards in the four test countries felt it would be unethical to deny the drug to any child, since it was known to work elsewhere, said Dr. Leon Tshilolo, a pediatric hematologist at the Monkole Hospital Center in Kinshasa, Democratic Republic of Congo, and the study’s lead author.

To compensate for the lack of a placebo group, the researchers watched children for two months before starting them on hydroxyurea. That established the baseline rates at which the children normally suffered pain crises, needed blood transfusions and got malaria or other infections. The results “mean survival will be better even in very low-resource settings,” Dr. Tshilolo said.

Hydroxyurea was originally developed to fight blood cancers like leukemia, and people taking it must be monitored to make sure that

it does not dangerously lower their white blood cell and platelet counts.

The study, however, used moderate daily doses, and only about 5 percent of the children enrolled needed to have their dosages lowered because their blood cell counts dropped.

In 1998, the Food and Drug Administration approved the drug for American adults with sickle-cell disease; pediatricians soon began giving it off-label to children, Dr. Ware said.

Trials proving it was safe in American children were not finished until 2016, and the F.D.A. approved pediatric use last year, opening the way for a trial in children in Africa.

For years, many black Americans with sickle-cell disease were reluctant to enroll themselves or their children in drug trials, Dr. Osunkwo said, because of America's sordid history of medical experimentation on black patients — including the infamous Tuskegee Study, in which black men with syphilis were left untreated even after the invention of penicillin.

Also, she said, the drug is known to lower men's sperm counts, break off women's hair and turn fingernails dark gray. For safety reasons, it is not normally given to pregnant women even though they may suffer severe sickle-cell crises.

Dr. Osunkwo said she slowly overcame patients' reluctance by letting them help design the trials. "And," she added, "I would say, 'Being dead is worse than having dark nails.'"

In Africa, enrolling 600 children was relatively easy, Dr. Tshilolo said, because Africans with sickle-cell disease who had visited Europe had heard of hydroxyurea and knew it worked.

Sperm counts were obviously not an issue in a children's trial, he added. But African men were usually willing to use the drug once it was explained that the drops in sperm count were relatively small and rebounded when the drug was stopped.