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Ethanol: A Lethal Injection for Tumors

Researchers have shown that injecting an ethanol-based gel directly into a specific type of tumor resulted in a 100% cure rate in a model.

By Alex Berezow — September 3, 2017

In the rich world, cancer therapy is expensive. In the developing world, it may not be available at all. Not only is cutting-edge technology in short supply, but so are things like electricity and medical personnel. The lack of necessary resources for basic healthcare is made obvious by the fact that, if diagnosed with cancer, a person in the developing world is more likely to die from it than a person in the developed world.

Peter Maas/Wikipedia

To help alleviate this problem, cheap, uncomplicated, portable, and preferably non-surgical treatments that do not require electricity are needed. Now, a team of researchers from Duke University has shown that injecting an ethanol-based gel directly into a specific type of tumor, called squamous cell carcinoma, resulted in a 100% cure rate in a hamster model.

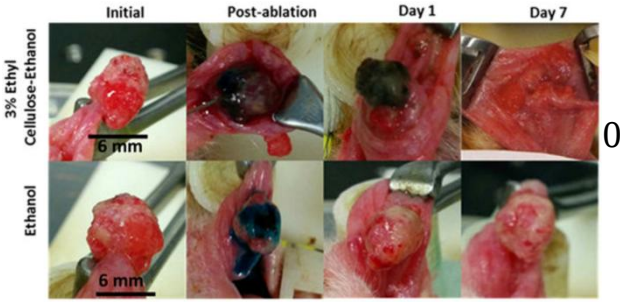
The authors were already aware of a therapy known as ethanol ablation. If ethanol (the type of alcohol found in your favorite adult beverages) is injected into a tumor, it destroys proteins and causes the cells to dehydrate and die. Ethanol ablation is used to treat one type of liver cancer, and its success rate is similar to that of surgery. Better yet, it costs less than $5 per treatment.

Ethanol ablation faces several limitations. First, it only works well for tumors that are surrounded by a fibrous capsule. Second, it requires large amounts of ethanol, which can damage nearby tissue as it leaks out. And third, it requires multiple treatments.

To overcome these hurdles, the authors mixed ethanol with ethyl cellulose, creating a solution that when injected into the watery environment of a tumor turns into a gel, which remains close to the injection site. After they practiced injecting their solution into imitation tumors (what they called "mechanical phantoms"), the authors turned to a hamster model.

The team induced the formation of oral cancer (specifically, squamous cell carcinoma) in hamster cheek pouches by rubbing them with a carcinogen called DMBA. After about 22 weeks, tumors (without capsules) formed.

In the control group, tumors were injected with pure ethanol. The results were not good. After seven days, of 5 tumors regressed completely. (Tumors injected with a large amount of ethanol -- four times the volume of the original tumor -- performed better: 4 of 12 regressed completely.) The results for the ethanol gel were far superior. After seven days, 6 of 7 tumors regressed completely. (By the eighth day, all 7 tumors were gone, for a cure rate of 100%.)



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As merely a proof-of-concept in an animal model with small sample sizes, obviously more work needs to be done. Still, the results are incredibly promising.

The team's findings suggest that merely a single injection of their special ethanol-based gel may be sufficient to cure certain types of tumors. They believe their technique may be applicable to some breast cancers and cervical precancerous lesions.

Furthermore, any technological advances that result from the team's research will have applicability not only to the developing world but to the developed one, as well.

Source: Robert Morhard, et al. "Development of enhanced ethanol ablation as an alternative to surgery in treatment of superficial solid tumors." Scientific Reports 7, Article number: 8750. Published: 18-Aug-2017. doi: 10.1038/s41598-017-09371-2

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Japan scientists develop noninvasive method to diagnose Alzheimer's disease

World's first method to diagnose Alzheimer's disease from blood

KYOTO – A team of Japanese researchers has developed what could be the world's first method to diagnose Alzheimer's disease from blood. Although the method is not currently able to provide a definitive diagnosis, it can be used in health checkups for people aged 60 or over, according to team member Takahiko Tokuda, professor at Kyoto Prefectural University of Medicine. The finding by Tokuda's team was published by a British science magazine on Monday.

Alzheimer's patients have a buildup of a type of protein called phosphorylated tau in their brains. Currently, the disease is diagnosed by the examination of extracted spinal fluid. This method is not popular and many patients are reluctant to undergo the procedure, according to the researchers.

The team managed to improve the detection sensitivity of phosphorylated tau in blood to 1,000 times the current levels by using an ultrasensitive detector developed by U.S. company Quanterix and optimizing the combination of reagents. After testing the method on 20 patients between the ages of 60 and 89, the team found that the method had an "intermediate degree of accuracy," Tokuda said.

The researchers plan to undertake large-scale testing with organizations including Osaka University and Oita University.

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Compound normalizes brain structure, function in mice with Down syndrome, Kyoto researchers say

A team of Kyoto University researchers announced Tuesday that they have discovered a chemical compound that may help nerve cells grow in the brains of people with Down syndrome and improve their learning ability.

The findings could lead to the development of drugs to treat Down syndrome in fetuses, they said, adding that it could also lead to treatment for other cerebral nerve illnesses, including Alzheimer's and Parkinson's diseases.

Down syndrome, caused in most cases by an extra copy of chromosome 21, genetically impairs intellectual ability. At present, prenatal diagnosis is possible. But there are no therapies available now for normalizing brain functions.

Masatoshi Hagiwara, professor at Kyoto University, and colleagues identified the compound, called altered generation of neurons, or ALGERNON, after screening a total of 717 candidate compounds.

Re-creating cells of people with Down syndrome from induced pluripotent stem (iPS) cells, the researchers then confirmed that the compound inhibited the target gene from restricting proliferation of neural stem cells, which become nerve cells, and increased the number of newborn neurons to almost the level without the syndrome.

The oral administration of the compound to pregnant mice with the syndrome for five days also normalized the formation of the cerebral cortex in embryos and prevented the development of abnormal behavior in offspring, the researchers said.

http://bbc.in/2qGc48b

Zika virus used to treat aggressive brain cancer

A harmful virus that can cause devastating brain damage in babies could offer up a surprising new treatment for adult brain cancer, according to US scientists.

By Michelle Roberts Health editor, BBC News online

Until now, Zika has been seen only as a global health threat - not a remedy. But latest research shows the virus can selectively infect and kill hard-to-treat cancerous cells in adult brains.

Zika injections shrank aggressive tumours in fully grown mice, yet left other brain cells unscathed. Human trials are still a way off, but experts believe Zika virus could potentially be injected into the brain

at the same time as surgery to remove life-threatening tumours, the Journal of Experimental Medicine reports.

The Zika treatment appears to work on human cell samples in the lab.

There are many different types of brain cancer. Glioblastomas are the most common in adults and one of the trickiest to treat. They are fast growing and diffuse, meaning they spread through the brain, making it difficult to see where the tumour ends and the healthy tissue begins.

Radiotherapy, chemotherapy and surgery may not be enough to remove these invasive cancers. But the latest research, in living mice and donated human brain tissue samples, shows Zika therapy can kill cells that tend to be resistant to current treatments.

It is thought that these glioblastoma stem cells continue to grow and divide, producing new tumour cells even after aggressive medical treatment. Different, healthy stem cells are found in abundance in baby brains, which probably explains why regular Zika can be so damaging to infants, say the researchers. Adult brains, however, have very few stem cells. This means Zika treatment should destroy only the cancer-causing brain stem cells without causing much collateral damage.

As an extra safety precaution, the team, from Washington University School of Medicine and the University of California San Diego School of Medicine, have already begun modifying the virus to make it more tame than regular Zika.

Researcher Dr Michael Diamond said: "Once we add a few more changes, I think it's going to be impossible for the virus to overcome them and cause disease. "It looks like there's a silver lining to Zika. This virus that targets cells that are very important for brain growth in babies, we could use that now to target growing tumours."

He hopes to begin human trials within 18 months.

Using viruses to fight cancer is not a new idea, but using Zika as the weapon of choice is. UK scientists at the University of Cambridge are beginning similar trials with Zika.

Dr Catherine Pickworth, from Cancer Research UK, said: "This promising research shows that a modified version of the Zika virus can attack brain tumour cells in the lab. "This could one day lead to new treatments for this particularly hard to treat type of cancer."

Zika

- ***Zika is a virus people can catch if they are bitten by an infected mosquito***
- ***Most people will have few or no symptoms, but the disease can pose a serious threat to babies in the womb***
- ***Affected infants have been born with abnormally small heads and underdeveloped brains - a condition known as microcephaly***
- ***The infection has been linked to severe birth defects in almost 30 countries***
- ***Although Zika is no longer "an international medical emergency", the World Health Organization says it is closely monitoring the infection***

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Aspirin-like pain reliever diflunisal blocks hearing protein

Rice University study: Commonly prescribed analgesic suppresses inner-ear protein

A Rice University study has found that the aspirin-like drug diflunisal blocks the action of prestin, a key protein that is required for hearing.

The research, which is available online in the open-access journal PLOS ONE, stemmed from a 2015 Rice study that screened more than a half-dozen nonsteroidal anti-inflammatory drugs, or NSAIDs, for possible interactions with the protein prestin. Prestin is a highly specialized protein that drives the action of outer hair cells in the cochlea, an inner-ear organ that allows people and animals to hear.

"Taking too much aspirin can cause temporary deafness, and researchers discovered more than a decade ago that this happens because salicylate, one of the primary metabolites of aspirin, interferes with prestin," said study lead author Guillaume Duret, a research scientist in Rice's Department of Electrical and Computer Engineering. "Given the number of commonly used NSAIDs that operate in a

similar way to aspirin, it seemed like a good idea to find out whether they also might inhibit prestin."

Duret said diflunisal was the only drug in the test that blocked the action of prestin. He said the findings suggest that the inhibition occurs by competing with chloride ions in prestin, a mechanism that is similar to what has been proposed for salicylate. The study also found that the dosage needed to induce a reaction was less than the aspirin dose required to induce a similar reaction.

Diflunisal is primarily prescribed as a mild pain killer and an anti-inflammatory for arthritis. But Duret said the findings come at an important time because the medical community is considering repurposing diflunisal as a possible treatment for both cancer and amyloid polyneuropathy.

"So far, it's been used in a pill form that is ingested, and the known side effects are for relatively small doses, like as if you were taking aspirin," Duret said. "For greater doses that are perhaps injected, the side effects may not yet be known."

He conducted the study's experiments in 2015 with two of the world's leading experts on prestin and outer hair cells, Rice bioengineer Rob Raphael and Baylor College of Medicine molecular biologist Fred Pereira.

The new findings weren't easy to obtain. They involved dozens of painstaking experiments in which Duret isolated and measured the activity of live outer hair cells from the cochlea of mice. To get his measurements, Duret had to find the cells under a microscope, grab hold of them with a glass pipette and apply and measure current through a process known as whole-cell patch clamping. The tests had to be performed both with and without the presence of diflunisal and before the short-lived cells died.

Raphael, who has studied prestin for more than 15 years and who made some of the first discoveries about salicylate's interference with prestin, said live-animal testing is needed to determine whether diflunisal causes deafness and at what dose.

"In addition to the potential clinical significance, Guillame's carefully done research has helped us refine our understanding of how molecules interact with prestin and how prestin itself operates," Raphael said.

He said the study also revealed a direct effect of diflunisal on the hair cell membrane, a result that may have implications for other physiological systems. "This study comes at a time where there is considerable excitement about new fields like systems and synthetic biology," said Raphael, who's lab is developing systems-level models of ion transport in the cochlea.

"This is a reminder that we still don't have a basic understanding of how commonly used drugs affect important proteins in our cell membranes," he said. "Sometimes, even the discoveries in your own lab humble you to the magnitude of what we still do not know about biological systems."

The research was supported by the National Institutes of Health.
The DOI of the PLOS ONE paper is: 10.1371/journal.pone.0183046
A copy of the paper is available at: https://doi.org/10.1371/journal.pone.0183046

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Ketogenic diet improves healthspan and memory in aging mice

Study on the effects of ketone bodies opens up new area of inquiry in aging research

A ketogenic diet significantly improved memory in aging mice and increased the animal's chances of surviving to old age. Results of the study from Eric Verdin's lab at the Buck Institute for Research on Aging in Novato, CA are published in the September 5th issue of Cell Metabolism.

Eating a ketogenic diet - which is high fat, low protein, and low carbohydrates - ramps up the production of the ketone body beta-hydroxybutyrate acid (BHB). While small studies in humans with cognitive impairment have suggested that BHB could improve memory, senior scientist and Buck President and CEO, Eric Verdin

MD, says this is the first study in aging mammals which details the positive effects of BHB on memory and lifespan. "This opens up a new field in aging research," said Verdin. "We think the health benefits of BHB may go beyond memory and could affect tissues and organ systems." Verdin added that the results also support efforts in his lab to translate the findings to the clinic. "We're looking for drug targets. The ultimate goal is to find a way for humans to benefit from BHBs without having to go on a restrictive diet."

The study was designed by lead scientist John Newman, MD, PhD, who is both a researcher in the Verdin lab and a geriatrician at University of California San Francisco. He wanted to study the long-term effects of a ketogenic diet in mice, while addressing one of the major issues that crop up in research involving diet - variability. "When studying a diet intervention, you have to pay attention to every detail," he said. Newman carefully designed three diets that were matched in every way except fat and carbohydrate content: a normal high-carbohydrate diet, a zero-carbohydrate ketogenic diet, and a high-fat, low-carbohydrate diet that was not ketogenic. Mice were fed the ketogenic diet intermittently to prevent them from becoming obese, starting at one year old - middle age for mice.

The ketogenic diet-fed mice had a lower risk of dying as they aged from one to two years old, although their maximum lifespan was unchanged. Another group of mice underwent memory testing at both middle age (one year old) and old age (two years old). Mice that had been eating a ketogenic diet performed at least as well on memory tests at old age as they did at middle age, while mice eating the normal diet showed an expected age-associated decline. Mice who ate the ketogenic diet also explored more, and their improved memory was confirmed with another test a few months later.

Newman noted that the mice were off the ketogenic diet and did not have any BHB in their blood during the testing period. "We were careful to have all of the mice eating a normal diet during the actual memory testing which suggests the effects of the ketogenic diet were lasting. Something changed in the brains of these mice to make them more resilient to the effects of age," he said. "Determining what this is, is the next step in the work."

Newman said gene expression could explain the cognitive improvement. "Looking at gene expression, the ketogenic diet suppressed the longevity-related TOR pathway and insulin signaling and up-regulated the fasting-related transcription factor PPAR-alpha, a master regulator that helps the body more efficiently metabolize fat."

Verdin said the study will open the door to new therapies for the cognitive problems of aging. "As we gain a deeper understanding of what BHB does in our body and our brain, we can intelligently design therapies to capture individual benefits while minimizing harms." The Verdin lab is currently exploring beneficial effects of a similar ketogenic diet in a mouse model of Alzheimer's disease.

The research has many caveats for humans eager to utilize diet to improve their odds of maintaining cognitive ability -- it involved a single strain and sex of mice living in an environment where it's easy to control every aspect of the diet.

Ketogenic diets are used clinically for life-threatening conditions like epilepsy, and most people should consult a health care professional before trying it on their own, said Verdin. "Exercise also creates ketone bodies - that may be one of the mechanisms why it shows such protective effects on brain function and on healthspan and lifespan," he said.

Citation: Ketogenic diet reduces mid-life mortality and improves memory in aging mice DOI: 10.1016/j.cmet.2017.08.004

Other Buck Institute collaborators include Anthony J. Covarrubias, Minghao Zhao, and Che-Ping Ng. Other collaborators include Xinxing Yu, UCSF Division of Geriatrics, San Francisco, CA; Philip Gut, Gladstone Institute of Virology and Immunology, San Francisco, CA; and Yu Huang and Saptarsi Haldar from the Gladstone Institute of Cardiovascular Disease, San Francisco, CA.

The work was supported by grants from National Institutes of Health, K08AG048354 and R24DK085610; Gladstone Institutes intramural funds, Buck Institute intramural funds, and funds from the Larry L. Hillblom Foundation, Glenn Foundation for Medical Research, the American Federal for Aging Research and the Buck Institute Impact Circle.

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Glowing cancer tool illuminates benign, but dangerous, brain tumors during pituitary surgery

Fluorescent, targeted dye illuminates molecular signature of tumor tissue in personalized surgery

PHILADELPHIA - An experimental imaging tool that uses a targeted fluorescent dye successfully lit up the benign brain tumors of patients during removal surgery, allowing surgeons to identify tumor tissue, a new study from researchers at the Perelman School of Medicine at the University of Pennsylvania shows. The tumors, known as pituitary adenomas, are the third most common brain tumor, and very rarely turn cancerous, but can cause blindness, hormonal disorders, and in some cases, gigantism.

Findings from the pilot study of 15 patients, published this week in the *Journal of Neurosurgery*, build upon previous clinical studies showing intraoperative molecular imaging developed by researchers at Penn's Center for Precision Surgery can improve tumor surgeries. According to first author John Y.K. Lee, MD, MSCE, an associate professor of Neurosurgery in the Perelman School of Medicine at the University of Pennsylvania and co-director of the Center for Precision Surgery, this study describes the first targeted, near infrared dye to be employed in brain tumor surgery. Other dyes are limited either by their fluorescent range being in the busy visible spectrum or by lack of specificity.

"This study heralds a new era in personalized tumor surgery. Surgeons are now able to see molecular characteristics of patient's tumors; not just light absorption or reflectance," Lee said. "In real time in the operating room, we are seeing the unique cell surface properties of the tumor and not just color. This is the start of a revolution."

Non-specific dyes have been used to visualize and precisely cut out brain tumors during resection surgery, but this dye is believed to be the first targeted, near infrared dye to be used in neurosurgery. The fluorescent dye, known as OTL38, consists of two parts: vitamin B9 (a necessary ingredient for cell growth), and a near infrared glowing dye. As tumors try to grow and proliferate, they overexpress folate receptors. Pituitary tumors can overexpress folate receptors more than 20 times above the level of the normal pituitary gland in some cases. This dye binds to these receptors and thus allows us to identify tumors.

"Pituitary adenomas are rarely cancerous, but they can cause other serious problems for patients by pushing up against parts of their brain, which can lead to Cushing's disease, gigantism, blindness and death," Lee explained. "The study shows that this novel, targeted, near infrared fluorescent dye technique is a safe, and we believe this technique will improve surgery."

Lee says larger studies are warranted to further demonstrate its clinical effectiveness, especially in nonfunctioning pituitary adenomas.

A big challenge with this type of brain surgery is ensuring the entire tumor is removed. Parts of the tumor issue are often missed by conventional endoscopy approaches during removal, leading to a recurrence in 20 percent of patients. The researchers showed that the technique was safe and effective at illuminating the molecular features of the tumors in the subset of patients with nonfunctioning pituitary adenomas.

The technique uses near-infrared, or NIR, imaging and OTL38 fluoresces brightly when excited by NIR light. The VisionSense IridiumTM 4mm endoscope is a unique camera system which can be employed in the narrow confines of the nasal cavity to illuminate the pituitary adenoma. Both the dye and the camera system are needed in order to perform the surgery successfully.

The rate of gross-total resection (GTR) for the 15 patients, based on postoperative MRI, was 73 percent. The GTR with conventional approaches ranges from 50 to 70 percent. Residual tumor was identified on MRI only in patients with more severe tumors, including cavernous sinus invasion or a significant extrasellar tumor.

In addition, for the three patients with the highest overexpression of folate, the technique predicted post-operative MRI results with perfect concordance.

Some centers have resorted to implementing MRI in the operating room to maximize the extent of resection. However, bringing a massive MRI into the operating room theater remains expensive and has been shown to produce a high number of false-positives in pituitary adenoma surgery. The fluorescent dye imaging tool, Lee said, may serve as a replacement for MRIs in the operating room.

Co-authors on the study include M. Sean Grady, MD, chair of Neurosurgery at Penn, and Sunil Singhal, MD, an associate professor of Surgery, and co-director the Center for Precision Surgery.

Over the past four years, Singhal, Lee, and their colleagues have performed more than 400 surgeries using both nonspecific and targeted near infrared dyes. The breadth of tumor types include lung, brain, bladder and breast.

Most recently, in July, Penn researchers reported results from a lung cancer trial using the OTL38 dye. Surgeons were able to identify and remove a greater number of cancerous nodules from lung cancer patients with the dye using preoperative positron emission tomography, or PET, scans. Penn's imaging tool identified 60 of the 66 previously known lung nodules, or 91 percent. In addition, doctors used the tool to identify nine additional nodules that were undetected by the PET scan or by traditional intraoperative monitoring.

Researchers at Penn are also exploring the effectiveness of additional contrast agents, some of which they expect to be available in the clinic within a few months.

"This is the beginning of a whole wave of new dyes coming out that may improve surgeries using the fluorescent dye technique," Lee said. "And we're leading the charge here at Penn."

This study was supported in part by the National Institutes of Health (R01 CA193556), the Institute for Translational Medicine and Therapeutics of the Perelman School of Medicine at the University of Pennsylvania, and the National Center for Advancing Translational Sciences of the National Institutes of Health (UL1TR000003).

Editor's Note: Dr. Singhal holds patent rights over the technologies presented in this article.

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New strategy for vaccinating pregnant mothers against malaria holds promise for protecting infants

Suggestions that boosting the mother's immune response to malaria will result in better protection for the infant

Washington, DC - A mother and infant in Malawi have the same repertoire of antibodies to *Plasmodium falciparum*, the malaria parasite. That suggests that boosting the mother's immune response to malaria, as via vaccination, will result in better protection for the infant. The research is published August 23rd in *Clinical and Vaccine Immunology*.

A pregnant woman's antibodies pass from her blood across the placenta, into the fetus, thereby providing some protection against infection at birth. "In sub-Saharan Africa, protection against malaria infection is very important," said corresponding author Miriam K. Laufer, MD, MPH, Director, Division of Malaria Research, Institute for Global Health, University of Maryland School of Medicine.

Malaria parasites do their damage when they invade the host's red blood cells. Each P. falciparum parasite has a handful of different surface antigens that it expresses on the surfaces of the blood cells that it has invaded. But collectively, there are lots of different malaria antigens. An individual's immune system needs to have antibodies that recognize a wide range of antigens, in order to be able to bind to all of the parasite-containing red blood cells, and thereby expunge the infection.

In the study, the investigators assayed serum from 33 mothers at delivery, and cord blood from their infants. Theirs was the first use of a customized high throughput microarray that included a wide array of malaria antigens. This enabled them to test infant seroreactivity to a large, diverse group of potential vaccine antigens that are present in P. falciparum in Africa. "Maternal antibody levels against vaccine candidate antigens were the strongest predictors of infant antibody levels," according to the report.

The investigators further showed that infant seroreactivity to any given antigen was nearly identical to mean maternal seroreactivity. This was the case regardless of whether or not the placenta had been infected during pregnancy, answering a lingering question in the field that bore heavily on how well a maternal vaccine strategy might work.

Vaccinating mothers during pregnancy "may be a very effective strategy for protecting infants from malaria," said Laufer. "This is critical because young children are at the highest risk of dying from infectious diseases such as malaria. In addition, preventing infection during infancy may help ensure healthy growth and cognitive development in infants and young children."

But so far, malaria vaccines in mothers have been ineffective at boosting immunity in infants, although the strategy has worked for other vaccines, such as tetanus. "When most researchers examine immune response to malaria, they use the most convenient malaria parasites, the ones that have been adapted to grow in the laboratory," Laufer explained. "However, these are not necessarily similar to the parasites seen in nature." She noted that a clinical trial of a vaccine that used a laboratory strain did not protect against naturally occurring strains of malaria, although it was effective against this laboratory strain. That, she said, led her research team to develop and use tools that could assay diverse surface antigens that exist in the world outside of the laboratory.

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Vaccine to prevent most cervical cancers shows long-term effectiveness

Effectiveness and safety of the Gardasil 9 vaccine were followed up to six years in more than 14,000 women around the world. These new results strengthen the promise that vaccination with Gardasil 9 can reduce 90 percent of cervical cancers.

BIRMINGHAM, Ala. - A vaccine that can literally eradicate the majority of cervical cancer cases shows long-term effectiveness in a study published today in The Lancet. This study of 14,215 women in 18 countries extends and solidifies the initial phase 3 efficacy and safety trial of the nine-valent human papilloma virus vaccine, Gardasil 9, that was published in February 2015 in The New England Journal of Medicine. These new results strengthen the promise that vaccination with Gardasil 9 can reduce 90 percent of cervical cancers.

"There is no question that the vaccine works," said primary author Warner Huh, M.D., professor and director of the University of Alabama at Birmingham Division of Gynecologic Oncology and a senior scientist at the UAB Comprehensive Cancer Center. "We're on the verge of a dramatic change that will positively affect all individuals, particularly women, in the United States. The challenge is to get the new vaccine into widespread use among young women."

The UAB Comprehensive Cancer Center and a coalition of Alabama health groups last year launched a formal call for action, urging Alabama parents and health care providers to get children -- girls and boys -- vaccinated against the sexually transmitted human papillomavirus, or HPV. The vaccine is unique in its ability to prevent certain cancers.

HPV infections cause global disease, including an estimated 266,000 deaths from cervical cancer worldwide in 2012, according to the World Health Organization. Routine screening by Pap smears or tests for HPV infection has reduced death rates in developed countries compared to less developed regions of the globe. Still, an estimated 12,200 U.S. women a year are diagnosed with cervical cancer.

Gardasil 9, marketed by Merck & Co., was approved by the U.S. Food and Drug Administration in December 2014. The vaccine immunizes against nine genotypes of HPV known to cause cervical cancer, as well as vulvar, vaginal and anal cancers and genital warts caused by HPV. It is an advance over the four-valent HPV vaccine, Gardasil, which was approved by the FDA in 2006.

Huh helped develop and test Gardasil, which targets the two HPV genotypes known to cause about 70 percent of cervical cancer and two other genotypes that cause genital warts. Gardasil 9 targets those four

genotypes and five additional ones as well. Both vaccines are prophylactic, meant to be given before females or males become exposed to possible HPV infection through intimate contact.

"Nationwide, 40 percent of girls and boys do not receive the HPV vaccine, and in the state of Alabama, almost half of girls and boys do not receive the HPV vaccine," Huh said. "With this new vaccine, there is a very legitimate opportunity to wipe out cancers that are caused by HPV, particularly cervical cancer in women.

"Seventy-five years ago, cervical cancer was a very common cause of mortality in the United States. Looking forward, with widespread vaccination, it is highly likely that cervical cancer will evolve into historical interest only, and screening, like Pap smears, might go away altogether. HPV vaccines are one of the most scrutinized vaccines ever, but multiple studies have demonstrated the vaccine to be safe and well-tolerated."

In the Lancet study, women were followed for efficacy at preventing disease for up to six years after the first vaccine shots, and they were followed for production of infection-halting antibodies against the nine genotypes of HPV for more than five years. The randomized double-blind efficacy, immunogenicity and safety study involved 105 sites in Austria, Denmark, Germany, Norway and Sweden; Brazil, Chile, Colombia and Peru; Canada, Mexico and the United States; and Hong Kong, Japan, New Zealand, South Korea, Taiwan and Thailand.

Half the women were vaccinated with the four-valent Gardasil and half with the nine-valent Gardasil 9. They were followed via gynecological exams for evidence of infections or disease, and their blood sera were tested for antibody levels against HPV.

Gardasil 9 showed 97.4 percent efficacy to prevent infections and disease caused by the five additional HPV genotypes not included in the four-valent Gardasil vaccine. Gardasil 9 vaccination produced similar antibody protection against the four HPV genotypes in Gardasil. The two vaccines also had similar safety profiles.

The nine-valent HPV vaccine has now been licensed in more than 60 countries for prevention of HPV-related anogenital cancers and precancers, and genital warts. Results of the Lancet study support the public health value of - and the need for - comprehensive vaccination programs.

The study was sponsored and funded by Merck & Co. Huh and 27 co-authors represent 21 universities in Europe, Canada, South America, Australia and the United States, as well as Merck & Co. At UAB, Huh holds the Margaret Cameron Spain Chair in Obstetrics and Gynecology.

http://bit.ly/2vSvMYI

Massive Genetic Study Shows How Humans are Evolving

Analysis of 215,000 people's DNA suggests variants that shorten life are being selected against

By Bruno Martin, Nature magazine on September 7, 2017

A huge genetic study that sought to pinpoint how the human genome is evolving suggests that natural selection is getting rid of harmful genetic mutations that shorten people's lives. The work, published in PLoS Biology, analysed DNA from 215,000 people and is one of the first attempts to probe directly how humans are evolving over one or two generations.

To identify which bits of the human genome might be evolving, researchers scoured large US and UK genetic databases for mutations whose prevalence changed across different age groups. For each person, the parents' age of death was recorded as a measure of longevity, or their own age in some cases.

"If a genetic variant influences survival, its frequency should change with the age of the surviving individuals," says Hakhamanesh Mostafavi, an evolutionary biologist at Columbia University in New York City who led the study. People who carry a harmful genetic variant die at a higher rate, so the variant becomes rarer in the older portion of the population.

Mostafavi and his colleagues tested more than 8 million common mutations, and found two that seemed to become less prevalent with age. A variant of the APOE gene, which is strongly linked to

Alzheimer's disease, was rarely found in women over 70. And a mutation in the CHRNA3 gene associated with heavy smoking in men petered out in the population starting in middle age. People without these mutations have a survival edge and are more likely to live longer, the researchers suggest.

This is not, by itself, evidence of evolution at work. In evolutionary terms, having a long life isn't as important as having a reproductively fruitful one, with many children who survive into adulthood and birth their own offspring. So harmful mutations that exert their effects after reproductive age could be expected to be 'neutral' in the eyes of evolution, and not selected against.

But if that were the case, there would be plenty of such mutations still kicking around in the genome, the authors argue. That such a large study found only two strongly suggests that evolution is "weeding" them out, says Mostafavi, and that others have probably already been purged from the population by natural selection.

Links to longevity

Why these late-acting mutations might lower a person's genetic fitness—their ability to reproduce and spread their genes—remains an open question.

The authors suggest that for men, it could be that those who live longer can have more children, but this is unlikely to be the whole story. So scientists are considering two other explanations for why longevity is important. First, parents surviving into old age in good health can care for their children and grandchildren, increasing the later generations' chances of surviving and reproducing. This is sometimes known as the 'grandmother hypothesis', and may explain why humans tend to live long after menopause.

Second, it's possible that genetic variants that are explicitly bad in old age are also harmful—but more subtly—earlier in life. "You would need extremely large samples to see these small effects," says Iain Mathieson, a population geneticist at the University of Pennsylvania in Philadelphia, so that's why it's not yet possible to tell whether this is the case.

The researchers also found that certain groups of genetic mutations, which individually would not have a measurable effect but together accounted for health threats, appeared less often in people who were expected to have long lifespans than in those who weren't. These included predispositions to asthma, high body mass index and high cholesterol. Most surprising, however, was the finding that sets of mutations that delay puberty and childbearing are more prevalent in long-lived people.

To see a genetic link to delayed childbearing is intriguing, says Jonathan Pritchard, a geneticist at Stanford University in California. The link between longevity and late fertility has been spotted before, but those studies could not discount the effects of wealth and education, because people with high levels of both tend to have children later in life. The latest genetic evidence makes Pritchard think there is an evolutionary trade-off between fertility and longevity, which had previously been studied only in other animals. "To actually find this in humans is really pretty cool," he says. "I think it's a really nice study."

Studying ongoing evolution in humans is notoriously difficult. Scientists who want to observe selection directly would need to measure the frequency of a mutation in one generation, and then again in all that generation's children and, better still, grandchildren, says Gil McVean, a statistical geneticist at the University of Oxford, UK. "That would be very hard to do well," he says. "You would need vast samples".

http://bit.ly/2vSl8B7

Parkinson's severity assessed through drawing

Researchers combined measurements of drawing speed and pen pressure to diagnose Parkinson's disease severity

Researchers in Australia asked volunteers to draw a spiral on a sheet of paper. By analyzing how long it took them to draw the spiral and

how hard they pressed on the paper with the pen, the team could not only tell which volunteers had Parkinson's disease, they could also tell how severe it was.

Parkinson's disease is a neurodegenerative disorder that causes shaking, muscle rigidity and difficulty with walking. Many treatment options for Parkinson's are only effective when doctors diagnose the disease early, and when symptoms are very noticeable it may be too late. It's also important for doctors to be able to tell how severe the disease is, to make the right treatment decisions, and to follow-up the progression of symptoms.

The researchers developed specialized software and combined it with a tablet computer that can measure writing speed, and a pen that can measure pressure on a page. They used the system to measure pen speed and pressure during a simple spiral sketching task in a sample of healthy volunteers and Parkinson's patients with different levels of disease severity. **Courtesy of Dinesh Kumar and Ms. Poonam Zham of the 'Affordable diagnostics' group in RMIT University, Melbourne, Australia**

One way to contribute to the diagnosis of Parkinson's involves getting patients to use a pen. Certain symptoms that appear early in the disease, such as rigidity, can interfere with a patient's ability to write or sketch. Handwriting can be influenced by a person's level of education and language proficiency, so a better alternative involves sketching a shape, such as a spiral.

One drawback to this approach is that only an expert can interpret the sketches, meaning that routine check-ups at a doctor's surgery aren't possible. However, even for an expert, it can be difficult to tell how severe the disease is from the sketches alone, especially at the early stages of the disease.

Previous research has found that Parkinson's patients tend to move their pen more slowly when sketching, and they also use less pressure on the page. While these factors are useful for telling if someone has Parkinson's or not, so far researchers have not been able to reliably gauge how severe someone's disease is, using pen speed or pressure.

In a new study, recently published in Frontiers in Neurology, a team of researchers in Australia set out to develop an automatic system to contribute to the diagnosis of Parkinson's, and to asess its severity, from the comfort of a community doctor's office. "Our aim was to develop an affordable and automated electronic system for early-stage diagnosis of Parkinson's disease, which could be used easily by a community doctor or nursing staff," explains Poonam Zham, a researcher involved in the study.

The researchers developed specialized software and combined it with a tablet computer that can measure writing speed, and a pen that can measure pressure on a page. They used the system to measure pen speed and pressure during a simple spiral sketching task in a sample of healthy volunteers and Parkinson's patients with different levels of disease severity. In a world-first, the system also mathematically combines pen speed and pressure into one measurement, which the team calls the Composite Index of Speed and Pen-pressure (CISP) score.

The system measured slower pen speeds, pen pressures and CISP scores in the Parkinson's patients, compared with the healthy volunteers, and all three measurements clearly indicated whether a participant had Parkinson's or not. On their own, pen speed and pressure were not sufficiently different between patients with different levels of Parkinson's severity, for the system to distinguish between them.

However, using the new CISP score, the system could tell whether the patients had level 1 or level 3 Parkinson's, using a particular disease severity scale. "The system can automatically provide accurate Parkinson's diagnosis and could also be used by community doctors to monitor the effect of treatment on the disease," says Zham. "This simple device can be used by community doctors for routine screening

of their patients every few years after the patients are above middle-age."

http://go.nature.com/2xaM3HO

Biomedical literature: Testers wanted for article search tool

We invite the scientific community to test a search engine we have developed

- **Peter Brown & Yaoqi Zhou**

Subject terms: Publishing Databases Research management

We invite the scientific community to test a search engine we have developed for the biomedical literature (see http://pubmed.ict.griffith.edu.au). The aim of this Article-based PubMed Search Engine is to find only those publications that are most relevant to any particular article.

By extracting keywords from a paper's title and abstract, the search engine reveals every related study indexed in PubMed up to 26 July 2017 - typically as many as 60 publications per paper. We then refine the results by asking researchers to score them for relevance, which takes just a few minutes. All such evaluations will be curated into a benchmark data set that can be downloaded and distributed for free.

The web server has attracted several thousand visitors from more than 50 countries since its launch in July. Preliminary data indicate an overall success rate of 80% in identifying relevant articles.

- *Nature 549, 31 (07 September 2017) doi:10.1038/549031c*

http://bit.ly/2jb9NWH

The colon of patients with IBS reacts differently to bacteria

Intestinal barrier of patients with the gastrointestinal disease allows bacteria to pass more freely than in healthy people

The intestinal barrier of patients with the gastrointestinal disease IBS allows bacteria to pass more freely than in healthy people, according to a study led by researchers at Linköping University in Sweden. The study, published in the scientific journal Gastroenterology, is the first to investigate IBS using living bacteria.

IBS, or irritable bowel syndrome, disturbs bowel function. The condition leads to repeated episodes of abdominal pain, and usually gives rise to constipation or diarrhoea. Around 10% of people in Sweden suffer from IBS, and it is twice as common among women as among men.

"People affected by IBS have been regarded as a rather diffuse group. Our study has shown that people with IBS are clearly different from healthy people in the way in which the part of the intestine known as the colon (or large intestine) reacts to bacteria," says Åsa Keita, researcher at the Department of Clinical and Experimental Medicine (IKE). She has led the study together with Susanna Walter, specialist in gastrointestinal diseases at Linköping University Hospital and also a researcher at IKE.

It is still unclear why the condition arises, but there is increasing evidence that changes in the way in which the brain interacts with the bacterial flora in the gut play a role. The large intestine has a layer of mucous, which constitutes the first line of defence against the bacteria in the intestine. Behind this, there is a layer of epithelial cells known as enterocytes, and behind these is tissue that contains immune cells. The present study has looked at this layer of epithelial cells, and examined how permeable it is to bacteria.

The researchers investigated small samples of tissue taken from the large intestine of 37 women with IBS, and compared them with samples from women with no intestinal symptoms. They studied the membranes in an instrument known as a Ussing chamber, in which it is possible to measure the transport of substances and bacteria through living tissue.

Infection with the pathogenic bacterium Salmonella typhimurium is a risk factor for developing IBS, and this led the researchers to investigate how this Salmonella strain interacts with the intestinal membrane. They also studied a strain of E. coli (Escherichia coli HS),

which is usually present in the intestine. Both bacteria passed through the intestinal mucosa of patients with IBS around twice as rapidly as was the case for healthy subjects.

"Patients with IBS in our study had a higher passage of bacteria in the model system. But we cannot transfer this result directly to clinical practice, and further research is needed. What we can say, however, is that there is something that makes one layer of the intestinal mucosa of patients with IBS more sensitive to bacteria than in healthy subjects," says Åsa Keita.

The researchers also looked at mast cells, a type of immune cell that is an important component of the innate immune defence, which protects against micro-organisms. They found that mast cells appear to play a significant role in regulating the passage of bacteria across the intestinal membrane, in both healthy subjects and in people with IBS. The mechanism seems, however, to be more active in those with IBS.

The study has been carried out in collaboration with scientists at the Universitat Autònoma de Barcelona in Spain and at the David Geffen School of Medicine at UCLA in the US. Funding for the research has been provided by, among other sources, Stiftelsen Hälsofonden and Diarrheal Disease Research Centre (Region Östergötland, Linköping University), AFA Insurance and Bengt-Ihre Research Fellowship.

The article: Vasoactive Intestinal Polypeptide and Mast Cells Regulate Increased Passage of Colonic Bacteria in Patients With Irritable Bowel Syndrome, Olga Bednarska, Susanna A. Walter, Maite Casado-Bedmar, Magnus Ström, Eloísa Salvo-Romero, Maria Vicario, Emeran A. Mayer, Åsa V. Keita, published online 13 July 2017, doi: 10.1053/j.gastro.2017.06.051 https://doi.org/10.1053/j.gastro.2017.06.051

http://bit.ly/2ja767W

Substance in coffee delays onset of diabetes in laboratory mice

In recent years, researchers have identified substances in coffee that could help quash the risk of developing Type 2 diabetes.

But few of these have been tested in animals. Now in study appearing in ACS' *Journal of Natural Products*, scientists report that one of these previously untested compounds appears to improve cell function and insulin sensitivity in laboratory mice. The finding could spur the development of new drugs to treat or even prevent the disease.

Some studies suggest that drinking three to four cups of coffee a day can reduce the risk of developing Type 2 diabetes, a disease that afflicts nearly 30 million Americans. Initially, scientists suspected that caffeine was responsible for this effect. But later findings discounted this possibility, suggesting that other substances in coffee may have a more important role. In a previous laboratory study, Fredrik Brustad Mellbye, Søren Gregersen and colleagues found that a compound in coffee called cafestol increased insulin secretion in pancreatic cells when they were exposed to glucose. Cafestol also increased glucose uptake in muscle cells just as effectively as a commonly prescribed antidiabetic drug. In this new study, the researchers wanted to see if cafestol would help prevent or delay the onset of Type 2 diabetes in mice.

The researchers divided mice that are prone to develop Type 2 diabetes into three groups. Two of the groups were fed differing doses of cafestol. After 10 weeks, both sets of cafestol-fed mice had lower blood glucose levels and improved insulin secretory capacity compared to a control group, which was not given the compound. Cafestol also didn't result in hypoglycemia, or low blood sugar, a possible side effect of some antidiabetic medications. The researchers conclude that daily consumption of cafestol can delay the onset of Type 2 diabetes in these mice, and that it is a good candidate for drug development to treat or prevent the disease in humans.

The authors acknowledge funding from Aarhus University. Abstract available here.

http://bit.ly/2eLDsko

Tick tock

Biologists show wildlife loss and climate change can synergistically increase tick abundance and the risk of tick-borne disease

Around the world, ticks are one of the most important vectors of zoonotic diseases - animal diseases communicable to humans - and they're everywhere.

While North Americans worry about Lyme disease carried by blacklegged or deer ticks, on the other side of the globe, people

contend with a different variety of tick-borne fevers. A new study by UC Santa Barbara researchers and colleagues suggests that the abundance of ticks that carry certain fevers are likely to rise in the future, thanks to a combination of wildlife loss and climate change.

The study used a large-scale experimental test to demonstrate synergistic effects of those phenomena on ticks and their pathogens. The investigators found that total tick abundance and abundance of infected ticks increased dramatically when large animals were lost -- and that this effect was exacerbated in dryer, low-productivity areas. Their analysis appears in the Proceedings of the Royal Society B.

"Our research suggests that large mammal conservation may prevent increases in tick abundance and tick-borne disease risk," said lead author Georgia Titcomb, a graduate student in UCSB's Department of Ecology, Evolution, and Marine Biology (EEMB). "These results are timely and relevant in light of widespread wildlife declines and unpredictable regional climatic shifts in a steadily warming world."

For their investigation, the scientists used a long-term, size-selective herbivore exclosure experiment at the Mpala Research Centre in Kenya to examine impacts to the abundance of ticks and two regionally important tick-borne pathogens, Coxiella burnetii and Rickettsia spp., the causative agents of Q fever and spotted fevers, respectively.

The experiment included four plot treatments. The first excluded all but the smallest rodent-sized herbivores, mostly mice; the second permitted intermediate-size animals such as hares and small antelope. In the third treatment, all animals but mega- herbivores such as giraffes and elephants were allowed to penetrate the plot. The control had no animal restrictions. The researchers spend more than a year conducting monthly hour-long tick drags in each plot.

The results showed that total wildlife exclusion increased total tick abundance by 130 percent at sites with a moderate amount of moisture and by 225 percent at dry, low-productivity sites. For a subset of months when differing degrees of exclusion were tested, total tick abundance increased from 170 percent in the plot with mega-herbivores to 360 percent when all large wildlife were excluded.

"This suggests that exposure risk will respond to wildlife loss and climate change in proportion to total tick abundance," said co-author Hillary Young, an EEMB associate professor and Titcomb's adviser. "We've shown these interacting effects increase disease risk, but they also highlight the need to incorporate ecological context when making predictions about the effects of wildlife loss on zoonotic disease dynamics."

This research was supported by grants from the National Geographic Society, the National Science Foundation, the Morris Animal Foundation and the Natural Sciences and Engineering Research Council of Canada.

http://bit.ly/2eKitOI

New study finds improved vaccine that protects against nine types of HPV

Long-term study show the nine-valent HPV vaccine greatly reduces the risk of HPV infection and HPV-associated diseases

TAMPA, Fla. - Cervical cancer is the second most common cause of cancer-related death worldwide, with almost 300,000 deaths occurring each year. More than 80 percent of these deaths occur in developing nations. The advent of human papillomavirus (HPV) vaccines has significantly reduced the number of those who develop and die from cervical cancer. And thanks to an international effort to improve the vaccine, the medical community is one step closer to preventing more HPV-associated diseases. The researchers, including those from Moffitt Cancer Center, published the final results of a study showing the newest vaccine is highly effective at preventing HPV infection and disease. The study was published this week in The Lancet.

HPV is an extremely common virus. It is estimated that by age 50, four out of five women have been infected with the virus at one point throughout their lifetimes. HPV causes ailments such as genital and anal warts and, in some instances, continued infection can lead to the development of benign or cancerous growths of the cervix, vulva, vagina, anus, penis, tonsils, and base of the tongue. There are more

than 100 types of HPV, but only approximately 13 types are associated with cancer development. HPV 16 and 18 alone are estimated to cause 70 percent of all cervical cancers.

Two existing HPV vaccines, Cervarix® and Gardasil®, are effective at preventing disease caused by HPV types 16 and 18, while Gardasil also protects against genital warts caused by HPV 6 and 11. However, these vaccines do not protect against all HPV types that are associated with cancer. Scientists developed an improved vaccine called 9vHPV that targets HPV 16, 18, 6, and 11, and an additional 5 HPV types that are the next most commonly associated with cervical cancer (HPV 31, 33, 45, 52 and 58). "Based on epidemiological studies, the 9vHPV vaccine could prevent approximately 90 percent of cervical cancer, 90 percent of HPV-related vulvar and vaginal cancer, 70 to 85 percent of high-grade cervical disease in females, and approximately 90 percent of HPV-related anal cancer and genital warts in males and females worldwide," explained Anna R. Giuliano, Ph.D., Director of the Center for Infection Research in Cancer at Moffitt.

Researchers from 18 countries and 105 study sites conducted a phase 3 study to compare the activity of the new 9vHPV vaccine against the older vaccine that protected against four HPV types (Gardasil). The study randomized 14,215 women 16 to 26 years of age to either 9vHPV or Gardasil, and the study participants were medically followed for 6 years after vaccination.

The study found that the 9vHPV vaccine has long-term activity against HPV infection and disease. The 9vHPV vaccine reduced the risk of developing HPV 31/33/45/52/58-related cervical, vulvar, and vaginal disease by 97.7 percent when compared to Gardasil®, and the two vaccines had similar activity at preventing HPV 6/11/16/18-associated disease. The 9vHPV vaccine was also highly effective at reducing the risk of having HPV 31/33/45/52/58-associated cervical cell abnormalities, biopsies, and definitive therapies.

9vHPV, known as Gardasil 9, became available in 2015 to protect females and males ages 9 through 26 years against HPV-associated cancers and genital warts. Scientists hope its continued use will greatly reduce the incidence and mortality of HPV-associated diseases. "The 9vHPV vaccine is licensed in over 40 countries for the prevention of HPV-related anogenital cancers and pre-cancer, and genital warts. The results of this study support comprehensive vaccination programs and inform public health decision related to implementation," said Giuliano.

http://bit.ly/2wdSw0l

'Vampires' may have been real people with this blood disorder

Dana-Farber/Boston Children's researchers and collaborators have identified a genetic mutation that may be responsible for vampire folklore

Porphyrias, a group of eight known blood disorders, affect the body's molecular machinery for making heme, which is a component of the oxygen-transporting protein, hemoglobin. When heme binds with iron, it gives blood its hallmark red color.

The different genetic variations that affect heme production give rise to different clinical presentations of porphyria -- including one form that may be responsible for vampire folklore.

A clinical cause for nocturnal blood drinking?

Erythropoietic protoporphyria (EPP), the most common kind of porphyria to occur in childhood, causes people's skin to become very sensitive to light. Prolonged exposure to sunshine can cause painful, disfiguring blisters. "People with EPP are chronically anemic, which makes them feel very tired and look very pale with increased photosensitivity because they can't come out in the daylight," says Barry Paw MD, PhD, of the Dana-Farber/Boston Children's Cancer and Blood Disorders Center. "Even on a cloudy day, there's enough ultraviolet light to cause blistering and disfigurement of the exposed body parts, ears and nose."

Staying indoors during the day and receiving blood transfusions containing sufficient heme levels can help alleviate some of the

disorder's symptoms. In ancient times, drinking animal blood and emerging only at night may have achieved a similar effect -- adding further fuel to the legend of vampires.

Now, Paw and his team of international investigators report -- in a paper in the Proceedings of the National Academy of Sciences (PNAS)-- a newly discovered genetic mutation that triggers EPP. It illuminates a novel biological mechanism potentially responsible for stories of " vampires" and identifies a potential therapeutic target for treating EPP.

The nature of EPP's "supernatural" symptoms

To produce heme, the body goes through a process called porphyrin synthesis, which mainly occurs in the liver and bone marrow. Any genetic defects that impact this process can interrupt the body's ability to produce heme; the decreased heme production leads to a buildup of protoporphyrin components. In the case of EPP, type of protoporphyrin called protoporphyrin IX accumulates in the red blood cells, plasma and sometimes the liver.

When protoporphyrin IX is exposed to light, it produces chemicals that damage surrounding cells. As a result, people with EPP experience swelling, burning and redness of the skin after exposure to sunlight -- even trace amounts of sunlight that pass through window glass.

Some genetic pathways leading to build-up of protoporphyrin IX have already been described, but many cases of EPP remain unexplained. By performing deep gene sequencing on members of a family from Northern France with EPP of a previously unknown genetic signature, Paw's team discovered a novel mutation of the gene CLPX, which plays a role in mitochondrial protein folding.

"This newly-discovered mutation really highlights the complex genetic network that underpins heme metabolism," says Paw, who was co-senior author on the study. "Loss-of-function mutations in any number of genes that are part of this network can result in devastating, disfiguring disorders."

Myth vs. reality

Paw suggests that identifying the various gene mutations that contribute to porphyria could pave the way for future therapies that could correct the faulty genes responsible for these related disorders.

"Although vampires aren't real, there is a real need for innovative therapies to improve the lives of people with porphyrias," says Paw.

In addition to Paw, other authors on the PNAS paper are: co-first authors, Yvette Yien (Brigham and Women's Hospital) and Sarah Ducamp (Université Paris Diderot); Lisa van der Vorm (BWH); Julia Kardon (Massachusetts Instiute of Technology); Hana Manceau (Université Paris Diderot); Caroline Kannengiesser (Université Paris Diderot); Hector Bergonia (University of Utah School of Medicine); Martin Kafina (BWH); Zoubida Karim (Université Paris Diderot); Lauren Gouya (Université Paris Diderot); Tania Baker (MIT); Hervé Puy (Université Paris Diderot); John Phillips (U of U School of Medicine); and co-senior author, Gaël Nicolas (Université Paris Diderot).

This work was supported by grants from the National Institutes of Health (U54 DK110858, F32 DK098866, K01 DK106156, F32 DK095726, R01 GM049224, R01 DK020503, U54 DK083909, R01 DK070838, P01 HL032262), the Netherlands Society for Biochemistry and Molecular Biology (Nora Baart Foundation), the RadboudUMC Master thesis prize, the Radboud University Master thesis award, the Dutch Stomach Liver Bowel Foundation, the Public Health and Consumer Protection Directorate Public Health Executive Agency of the European Commission, ANR-GIS Maladies Rares (ANR07-MRAR-008-01), the Laboratoire d'Excellence Gr-Ex (ANR-11-LABX-0051), the program "Investissements d'Avenir" of the French National Research Agency (ANR-11-IDEX-0005-02) and the Howard Hughes Medical Institute.

http://bit.ly/2wNCjCL

Lost Languages Discovered in One of the World's Oldest Continuously Run Libraries

The centuries-old texts were erased, and then written over, by monks at Saint Catherine's Monastery in Egypt

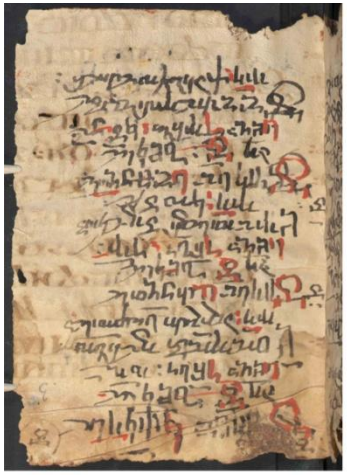
By Brigit Katz smithsonian.com

Saint Catherine's Monastery, a sacred Christian site nestled in the shadow of Mount Sinai, is home to one of the world's oldest continuously used libraries. Thousands of manuscripts and books are kept there—some of which contain hidden treasures.

Now, as Jeff Farrell reports for the Independent, a team of researchers is using new technology to uncover texts that were erased and written over by the monks who lived and worked at the monastery. Many of

these original texts were written in languages well known to researchers—Latin, Greek, Arabic—but others were inscribed in long-lost languages that are rarely seen in the historical record.

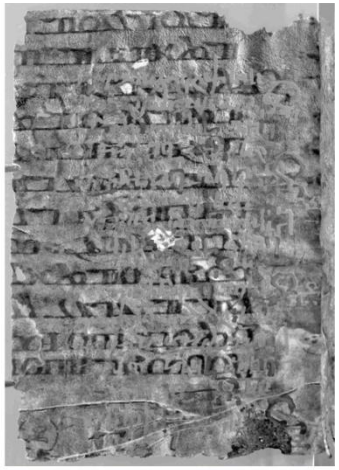
Manuscripts with multiple layers of writing are known as palimpsests, and there are about 130 of them at St. Catherine's Monastery, according to the website of the Early Manuscript Electronic Library, which has been leading the initiative to uncover the original texts. As Richard Gray explains in the Atlantic, with the rise of Islam in the 7th century, Christian sites in the Sinai Desert began to disappear, and Saint Catherine's found itself in relative isolation. Monks turned to reusing older parchments when supplies at the monastery ran scarce.



Georgian NF 71, f. 3r, a palimpsest manuscript from the New Finds, St. Catherine's Monastery of the Sinai. Georgian written over Christian Palestinian Aramaic. (Folio is rotated, so that undertext is right-side-up.)

Pseudocolor of Georgian NF 71, f. 3r (Keith Knox).

Undertext appears in red.



"Sharpie" of Georgian NF 71, f. 3r (Keith Knox).

Undertext appears in black.

To uncover the palimpsests' secret texts, researchers photographed thousands of pages multiple times, illuminating each page with different-colored lights. They also photographed the pages with light shining onto them from behind, or from an oblique angle, which helped "highlight tiny bumps and depressions in the surface," Gray writes. They then fed the information into a computer algorithm, which is able to distinguish the more recent texts from the originals.

Since 2011, researchers have photographed 74 palimpsests, which boast 6,800 pages between them. And the team's results have been quite astonishing. Among the newly revealed texts, which date from the 4th to the 12th century, are 108 pages of previously unknown Greek poems and the oldest-known recipe attributed to the Greek physician Hippocrates.

But perhaps the most intriguing finds are the manuscripts written in obscure languages that fell out of use many centuries ago. Two of the erased texts, for instance, were inked in Caucasian Albanian, a language spoken by Christians in what is now Azerbaijan. According to Sarah Laskow of Atlas Obscura, Caucasian Albanian only exists today in a few stone inscriptions. Michael Phelps, director of the Early Manuscripts Electronic Library, tells Gray of the Atlantic that the discovery of Caucasian Albanian writings at Saint Catherine's library has helped scholars increase their knowledge of the language's vocabulary, giving them words for things like "net" and "fish."

Other hidden texts were written in a defunct dialect known as Christian Palestinian Aramaic, a mix of Syriac and Greek, which was discontinued in the 13th century only to be rediscovered by scholars in the 18th century. "This was an entire community of people who had a literature, art, and spirituality," Phelps tells Gray. "Almost all of that has been lost, yet their cultural DNA exists in our culture today. These palimpsest texts are giving them a voice again and letting us learn about how they contributed to who we are today."

The Sinai Palimpsests Project, as the team's initiative is known, has taken on new urgency in recent years, as the Islamic State's presence in the Sinai Peninsula has made Saint Catherine's monastery even harder to reach. Phelps and his fellow researchers are making images of the palimpsests available online, so scholars can explore the secret writings that have recently been brought to light.

http://bit.ly/2wdQVYE

The Unlikely Medical History of Chocolate Syrup

How the sundae staple went from treatment to just treat

By Maya Wei-Haas smithsonian.com

At first glance, nothing seems particularly odd about the December 1896 edition of *The Druggists Circular and Chemical Gazette*, a catalog of products that any self-respecting pharmacy ought to carry. But look closer: Hiding among medical necessities like McElroy's glass syringes and Hirsh Frank & Co's lab coats, you'll find some more curious finds—including Hershey's cocoa powder.

"Perfectly soluble," boasts the ad in bold, capital lettering. "Warranted absolutely pure." It reads as if it was peddling medicine—and in fact, it sort of was.

Druggists of the day often used the dark powder to whip up a syrup sweet enough to mask the flavor of objectionable remedies, explains Stella Parks, a pastry chef with the food and cooking website *Serious Eats*. Parks happened upon these vintage advertisements while she was researching her new book, *BraveTart: Iconic American Desserts*, which features lesser-known histories of our favorite sweet treats. The Hershey's ad intrigued her.

"What in the world are these guys doing advertising to druggists?" she recalls wondering at the time. By digging into the history and tracking down more pharmaceutical circulars and magazines, she discover the rich history of chocolate syrup, which began not with ice cream and flavored milk—but with medicine.

(The Druggists' Circular and Chemical Gazette, Volume 40, 1896)

Our love of chocolate goes back over 3,000 years, with traces of cacao appearing as early as 1500 B.C. in the pots of the Olmecs of Mexico. Yet for most of its early history, it was consumed as a drink made from fermented, roasted, and ground beans. This drink was a far cry from the sweetened, milky stuff we call hot chocolate today: It was rarely sweetened, and likely very bitter.

Still, the roughly football-sized pods that cradled the beans were held in high esteem; the Aztecs even traded cacao as currency. Chocolate didn't become popular overseas, however, until Europeans ventured into the Americas at the end of the 15th century. By the 1700s, the ground beans were avidly consumed throughout Europe and the American colonies as a sweetened, hot drink that was vaguely reminiscent to today's hot cocoa.

At the time, chocolate was touted for its medicinal properties and prescribed as treatment for a range of diseases, says Deanna Pucciarelli, a professor of nutrition and dietetics at Ball State University who researches the medicinal history of chocolate. It was often prescribed for people suffering from wasting disease: The extra calories assisted in weight gain, and the caffeine-like compounds helped perk patients up. "It didn't treat the actual illness, but it treated the symptoms," she explains.

Yet for pharmacists, it wasn't only the supposed health benefits but also the rich, velvety flavor that held such appeal. "One thing about medicines, even going way back, is that they are really bitter," says Diane Wendt, associate curator of the division of medicine and science at Smithsonian's National Museum of American History. Many medications were originally derived from plants and fall in a class of compounds known as alkaloids, which has an acrid, mouth-puckering flavor. The first of these alkaloids, isolated by a German chemist in the early 1800s, was none other than morphine.

Chocolate, it turns out, effectively covered the toe-curling taste of these foul flavors. "Few substances are so eagerly taken by children or invalids, and fewer still are better than [chocolate] for masking the

taste of bitter or nauseous medicinal substances," according to the 1899 text, *The Pharmaceutical Era*.

It's unclear exactly when pharmacists first combined cocoa powder and sugar to brew the sticky syrup. But its popularity was likely helped along by the invention of cocoa powder. In 1828, Dutch chemist Coenraad J. Van Houten patented a press that successfully removed some of chocolate's natural fats, reducing its bitter flavor and making it easier to dissolve with water. Still, the result wasn't exactly the "same kind of smooth mellow chocolate we have now," says Parks; to make it palatable, pharmacists would mix cocoa powder with at least eight times more sugar than chocolate.

The popularity of chocolate syrup exploded in the second half of the 19th century, coinciding with the golden age so-called patent medicines. These are named after the "letters of patent" the English crown awarded to inventors of supposedly curative formulas. The first English medicine patent was awarded in the late 1600s, but the name later came to refer to any over-the-counter drugs. American "patent medicines" went by the same name, but were not typically patented under this system.

Patent medicines emerged at a time when public need for treatments and cures outpaced medical knowledge. Many of these "cures" did more harm than good. Often marketed as cure-alls, the concoctions could contain anything from pulverized fruits and veggies to alcohol and opioids. At the time, the common use of these addictive substances in remedies was legal; regulation didn't come about until the 1914 passage of the Harrison Narcotic Act.

One popular remedy featuring tincture of opium as its active ingredient was Stickney and Poor's Paregoric. This syrup was marketed as a treatment for many ills, and given to cholicky infants as young as five days old. "Remedies" like this weren't completely ineffective. The inclusion of narcotics and alcohol in the cures did indeed give customers temporary relief from illness—and, more sinisterly, their addictive nature kept them coming back for more.

The boom of factory mass production in the 1900s brought with it the rise of easy-to-swallow medical pills. But before that, "pill making by hand is pretty labor intensive," says Wendt. "To actually make a pill of a certain dose—to mix it up and cut the pills, and roll the pills, and dry the pills, and coat the pills—that's a pretty lengthy process." That's why, during this time, medications were mostly served up in liquid or powder form, says Wendt.

Druggists would mix each liquid remedy with a base of sugary flavored syrups, like chocolate, and take it either by the spoonful or mixed into a beverage, says Wendt. Alternatively, powders could be directly poured into your refreshment of choice.

The base for these medicinal drinks could be anything from plain water to tea to a couple fingers of whiskey. But over the course of the 1800s, one particular drink was gaining popularity as a medicine masker: carbonated water.

Vintage Hershey's ad showing chocolate syrup as a "stepping stone to health." **(Hershey's Company)**

Not unlike chocolate, soda water was initially considered a health drink in its own right. The carbonated beverage mimicked the mineral-rich waters bubbling up in natural springs that had become known for its curative and healing powers. Soda became a truly widespread phenomenon in America around the turn of the century thanks to the pharmacist Jacob Baur, who invented the process necessary to sell tanks of pressurized carbon dioxide.

Part health drink, part delicious treat, sweetened carbonated water began spreading like wildfire in the form of soda fountains, Darcy O'Neil writes in his book *Fix the Pumps*.

Syrups became ever more popular to keep pace with the soda craze. Many of these flavors are still common today: vanilla, ginger, lemon

and, of course, chocolate. By the late 1800s hardly a pharmacist publication went without some mention of chocolate syrup, Parks writes in *Bravetart*. And hardly a drug store went without a soda shop: Soda fountains served as a lucrative side business for druggists and pharmacists who commonly struggled to make ends meet, says Parks.

At the time, carbonated concoctions were largely still seen as cures. "Soda is an excellent medium for taking many medicines," according to the 1897 book, *The Standard Manual of Soda and Other Beverages*. "For example, the best method of administering castor oil is to draw a glass of sarsaparilla soda in the usual manner and pour in the requisite amount of oil." (Sarsaparilla, a flavor derived from the root of a tropical vine, is still used today in some root beer variants.)

One example still very much available today is Coca Cola: Originally mixed up with cocaine, the fizzy drink was touted it as a healthful stimulant to revive the brain and body.

At the turn of the century, however, chocolate syrup began to shift from treatment to treat. "It just seemed to naturally segue into all the ice cream [desserts] that pharmacists had to keep on hand just to stay afloat," says Parks.

A fortuitous mix of events helped elevate the state of chocolate to commercial confection. First, in the early 20th century, concerns over false health claims and downright dangerous cures helped lead to the passage of the 1906 Pure Food and Drug Act, which required druggists to disclose the remedy ingredients with clear and accurate labels. Similarly, a clamp down on American patent medicines may have further driven the chocolatey transition.

At the same time, other forms of chocolate were gaining traction as confections in their own right. As the industrial revolution ushered in machinery that took over the time-intensive process of turning cacao to cocoa, prices began to fall, explains Pucciarelli. "It all comes together," she says. "The price of manufacturing drops, the price of sugar drops, and then you have [chocolate] bars."

In 1926, Hershey's began marketing pre-mixed chocolate syrup in both single and double strength varieties for commercial businesses. The cans were shelf stable, meaning druggists (and soda jerks) didn't need to continually mix up new batches. By 1930, both Hershey's and other chocolate companies like Bosco's had begun marketing chocolate syrup for home use.

The rest is sweet, sweet history. These days, despite many modern claims of health benefits—some founded and some unfounded—chocolate is considered more confection than cure. Chocolate accounts for the "vast majority" of the $35 billion confection market in the United States, according to the National Confectioners association.

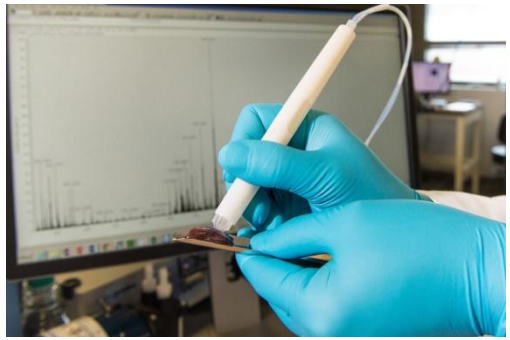
Yet the use of a sweet cover for medications remains isn't completely dead. You can find sweetness masking medicine in many forms, from cherry cough syrup to bubblegum-flavored amoxicillin. It seems Mary Poppins was right: A spoonful of sugar—or in this case, chocolate—really does help the medicine go down.

http://bit.ly/2weIAUh

Cancer pen could tell surgeons where they should cut in seconds

A pen-sized device could soon help cancer surgeons tell whether the tissue they plan to cut out of a person is cancerous or healthy.

By Andy Coghlan



Testing some tissue **Vivian Abagiu/University of Texas at Austin**

It usually takes several days for pathologists to analyse a tissue sample to decide if it's cancerous. But the new device, which gives instant feedback, could be used by surgeons to make sure they cut out the whole tumour, preventing relapses caused by missed tissue.

The device has a disposable nozzle on its tip. When placed on suspected tissue, a tiny drop of water on the nozzle soaks up biological material – such as fats, proteins and sugars – from the tissue surface.

These samples can then be transferred to a mass spectrometer, which compares the combination of biomolecules with a database of similar data. Algorithms can produce a conclusion on whether the tissue is likely to be safe or cancerous within 10 seconds. “It gave the right answer 96 per cent of the time,” Livia Eberlin, of the University of Texas, whose team has tested their pen on 253 human tissue samples.

Preventing relapses

These samples included cancerous cells from lungs, ovaries, thyroids and breasts, as well as healthy tissue. The team have also used to pen to guide tumour removal surgeries in mice, and hope to test it in hospitals next year.

“The speed and accuracy of our device could really help on treatment options and decisions,” says Eberlin. Around 10 per cent of relapses result from the re-growth of tissue missed during surgery, she says.

“Once this pre-clinical data has been validated in clinical trials, the pen-size mass spectrometry might improve diagnosis during operations, and help identify micro-metastatic cancer deposits,” comments Nicola Valeri, a cancer surgeon at the Royal Marsden NHS Trust in London. He agrees that this could lead to more precise operations to remove various types of cancer.

Journal reference: Science Translational Medicine, DOI: 10.1126/scitranslmed.aan3968

http://bit.ly/2xiK6tA

Undiagnosed spine fractures often cause pain in older men

Fewer than a quarter of new vertebral fractures are clinically diagnosed, yet they often cause symptoms.

In a study of older men in the general population now published in the Journal of Bone and Mineral Research, clinically undiagnosed vertebral fractures that were evident on x-rays were associated with higher likelihood of back pain and limited physical activity.

The findings build on similar results previously reported in older women and point to the need for more effective strategies to detect and prevent vertebral fractures.

"Preventing these fractures may reduce back pain and related disability in older men," wrote the authors.

http://bit.ly/2eRPjRO

Dissolve the Dead? Controversy Swirls around Liquid Cremation

California state bill seeks to legalize liquefaction of corpses

By Devin Powell on September 7, 2017

SAN DIEGO—Eight times a year a funeral director sets off by boat from Camp Pendleton Marine Corps base carrying about two dozen plastic bags filled with unusual human remains. The powder he pours overboard is from corpses that have been “cremated”—not by fire, but by liquid.

That’s how the University of California, Los Angeles, disposes of bodies donated to science: by dissolving the flesh off their bones. The bones are then ground to dust and scattered into the sea two miles offshore, forming white rings that slowly float away into the Pacific Ocean.

U.C.L.A. is the only place in California that liquefies the dead. But after five years and hundreds of bodies processed, Dean Fisher, director of the university’s Donated Body Program, hopes to change that. He has been working with state legislators on a bill allowing funeral homes to use this process, called alkaline hydrolysis. The state Senate has until September 15 to consider the legislation, which has already sailed through California’s lower house with a vote of 71 to 3.

“The science says this technology is safe and has environmental benefits,” Fisher says. If California approves the new death rite, it would join a club that includes parts of Canada and several U.S. states: Colorado, Florida, Georgia, Idaho, Illinois, Kansas, Maine,

Maryland, Minnesota, Missouri, Nevada, Oregon, Vermont and Wyoming.

But this means of final disposition crosses uncomfortable lines for some. Consider the case of Edwards Funeral Service in Columbus, Ohio, which started offering alkaline hydrolysis in 2011: Owner Jeff Edwards dissolved 19 corpses before the Ohio Department of Health suddenly stopped granting permits for the process, and the Ohio Board of Embalmers and Funeral Directors accused him of "immoral or unprofessional conduct." A messy legal battle left him with $150,000 worth of equipment that is gathering dust, he says. He now transports bodies across state lines, to Chicago, for the procedure.

A 2010 bill to legalize alkaline hydrolysis in California failed, as reported by the Los Angeles Times, largely due to concerns over lack of data about how the liquid waste it creates might affect aging sewer pipes and employees' health at crematoria—safety concerns that Fisher says he has addressed after years of testing with the City of Los Angeles. A second bill in 2013 for a pilot program in five funeral homes also failed to make it across the finish line. And the California Catholic Conference is urging the state's Senate to vote "no" on the latest legislation, concerned that alkaline hydrolysis "does not appear to respectfully treat human remains."

Proponents note that traditional cremation is trending upward in the U.S. In 2015 more people in this country were burned than put in the ground for the first time, according to a report by the National Funeral Directors Association. This fad is driven in part by price: A fire cremation usually costs less than a third of a burial, according to an industry report by market research firm IBISWorld. It also saves on some natural resources; a burial requires land as well as the stone, steel, cloth and wood used to make the casket and gravestone.

Some see alkaline hydrolysis—versions of which go by the names biocremation, aquamation and resomation—as the next big thing for those who want to make an environmentally friendly exit.

The technique has its origins in an 1888 patent for making fertilizer and gelatin, which describes dissolving animal parts in an alkaline solution such as potassium hydroxide. In the 1990s two researchers began disposing of lab animals this way at Albany Medical College in New York State. Their work informed the construction of the first machine that could handle a single human body, built by a company called WR2 and first used in the Mayo Clinic's anatomical bequest program in Rochester, Minn., in 2006.

Such machines break down tissue using lye (water mixed with a small quantity of potassium hydroxide or sodium hydroxide), which snaps the chemical bonds that hold together proteins, fats, DNA and other bodily building blocks. Multiple mechanisms can be used: The most expensive machines boil the lye at high pressure and 150 degrees Celsius, which can disintegrate a body in few hours. Cheaper models—unpressurized and operating below boiling point—might take a day (and are frowned on by some of those championing the pressurized approach, who are not convinced the budget-friendly models will always fully digest the remains). Some machines keep the body horizontal; others tip it into the lye. But with any of these approaches what comes out should be a brown soup of simple organic molecules that can be poured into a sewer system. The bones, however, do not dissolve. They can be pulverized and given to the family of the deceased.

Companies marketing the technique trumpet its low greenhouse gas emissions compared with flame crematoriums that burn natural gas. Alkaline hydrolysis uses energy primarily to heat and cool the lye—and thus emits about 80 percent less carbon dioxide—according to an estimate by TNO, an independent research and development consulting organization in the Netherlands. "If you're concerned about gas emissions, the choice is pretty obvious," says California Assemblyman Todd Gloria. He wrote California's new bill after being approached by Qico, a company in San Diego prototyping alkaline hydrolysis technology.

But how much carbon is actually emitted in both processes? The Dutch numbers, which are usually cited by those championing alkaline hydrolysis, suggest cremations by fire account for only a few thousandths of a percent of total carbon emissions in the U.S. Every person who becomes liquid instead of ash would keep about 180 kilograms of carbon dioxide out of the atmosphere, according to the TNO report. That's about as much as the typical U.S. citizen is responsible for emitting in just a few days.

There are other benefits to alkaline hydrolysis, proponents say: Inorganic materials like tooth fillings and breast implants are left behind by the process. That could ease fears of toxic chemicals such as mercury from burned tooth fillings polluting the air near crematoriums—and of pacemakers exploding inside crematoria.

Alkaline hydrolysis produces no smoke to worry about. But is the soapy soup it dumps into the sewer safe? Disease should not be a problem because the roiling lye sterilizes the organic material, says Joe Wilson, CEO of Bio-Response Solutions. The company, based in Danville, Ind., built many of the low-cost units now used in funeral homes, including Jeff Edwards's in Ohio. "It's hot as hell in there, and alkali is a powerful sterilant at temperature," Wilson says. Testing on animal carcasses, much of which has been peer-reviewed, seems to back his claims. "Even the hardiest pathogen, an anthrax spore, is easily killed," he says, adding that the process also breaks down toxic chemicals such as embalming fluid.

One worry might be amount of water used in the process—about 300 gallons per corpse. Gloria says this might be a consideration during droughts but is otherwise a drop in the bucket. "If every Californian who died in one year used water cremation, it would amount to 64 million gallons of water in that year," he says. "One L.A. [water] treatment plant uses more than 500 million gallons in a day."

Of greater concern is the high pH involved in the process, which scuttled the first California bill seeking to legalize alkaline hydrolysis. The machine at U.C.L.A. discharges waste that is a stronger base than a typical household drain unclogging fluid; it exceeds pH 11, the limit for discharge into the environment set by Los Angeles to protect against corrosion of skin and metal. Other cities have even stricter standards. In San Francisco nothing beyond pH 9 can go down the drain. Fisher's device can add acid to lower pH before disposing of the remains; others bubble in carbon dioxide. But California is not taking chances. Responding to concerns from the California Association of Sanitation Agencies, the new bill requires funeral homes offering alkaline hydrolysis to apply to their local water authority for a permit to send the liquid remains into the sewer on-site—or to pay a company experienced in biological waste disposal to get rid of them.

How we treat our dead is a delicate issue. The "yuck factor" that often accompanies thinking about what happens to bodies of our loved ones was invoked by an Indiana lawmaker (and casket maker) to derail alkaline hydrolysis there. "We're going to put them in acid [sic] and just let them dissolve away, and then we're going to let them run down the drain out into the sewers and whatever," said state Rep. Dick Hamm, as reported by The Indianapolis Star. But Gloria doesn't see anything icky about new tech; he hopes to help establish a new norm, and he is starting with the man in the mirror. "I plan to be cremated," he says. "It would be poetic if I could take advantage of my own bill."

http://s.nikkei.com/2j9iDEq

Rise in diabetes in Asia fuels demand for tests

Greater need for diagnostics in India, Southeast Asia along with prosperity

TOKYO -- Japanese manufacturers of diagnostic tests for diabetes and other illnesses are ramping up operations in the rest of Asia, as they hope to catch up with global players by tapping into emerging markets. In Southeast Asia, CMIC Holdings is launching a diabetes diagnostics business geared toward the affluent. The company recently received regulatory approval for its diabetes tests in the Philippines and Vietnam. CMIC will offer a service that can predict kidney disease,

based on artificial intelligence that analyzes data collected at hospitals using its tests.

CMIC is expanding its diagnostics business across Southeast Asia.

As incomes rise in emerging nations, so are the number of diabetes patients. In Vietnam alone, there are an estimated 2 million diabetics. Hospitals often struggle to keep up with the growing number of patients due to limited types of tests as well as a shortage of technicians to operate equipment. CMIC believes that treatment efficiency could be improved by narrowing its focus on potential patients.

Konoike Transport, meanwhile, is partnering with Tokyo-based J-VPD to launch a clinical testing business in India. Konoike will fly blood and tissue samples of patients to Japan, where partner companies will test for more than 1,000 indicators, including tumor markers. Results are delivered in about three days. The partners will also train laboratory technicians in India and offer trainees opportunities to study in Japan.

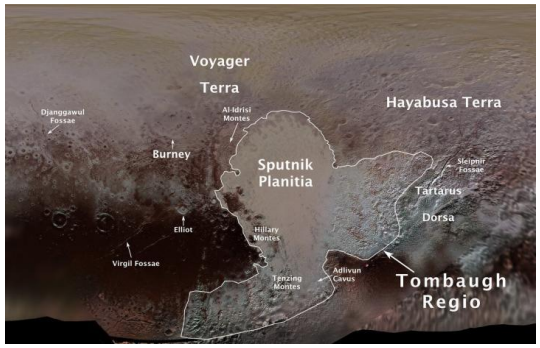
According to Fuji Keizai, a Tokyo-based research firm, the global market for clinical laboratory testing is estimated to grow by 13% from 2015 figures to $70.4 billion in 2020. Asian markets outside of Japan are expected to drive the market's growth, as developed nations will mainly see replacement demand. Meanwhile, the global market is dominated by such major players as Switzerland's F. Hoffmann-La Roche and U.S.-based Abbott Laboratories. Japanese companies aim to catch up to them by unearthing new demand.

http://bit.ly/2jaKdS1

Pluto features given first official names

The IAU has assigned names to fourteen geological features on the surface of Pluto.

The names pay homage to the underworld mythology, pioneering space missions, historic pioneers who crossed new horizons in exploration, and scientists and engineers associated with Pluto and the Kuiper Belt. This is the first set of official names of surface features on Pluto to be approved by the IAU, the internationally recognised authority for naming celestial bodies and their surface features.



NASA's New Horizons team p roposed the names to the IAU following the first reconnaissance of Pluto and its moons by the New Horizons spacecraft.

Pluto's first official surface-feature names are marked on this map, compiled from images and data gathered by NASA's New Horizons spacecraft during its flight through the Pluto system in 2015. **ASA/JHUAPL/SwRI/Ross Beyer**

Some of the names were suggested by members of the public during the Our Pluto campaign, which was launched as a partnership between the IAU, the New Horizons project and the SETI Institute. Other names had been used informally by the New Horizons science team to describe the many regions, mountain ranges, plains, valleys and craters discovered during the first close-up look at the surfaces of Pluto and its largest moon, Charon.

"We're very excited to approve names recognising people of significance to Pluto and the pursuit of exploration as well as the mythology of the underworld. These names highlight the importance of pushing to the frontiers of discovery," said Rita Schulz, chair of the IAU Working Group for Planetary System Nomenclature. "We appreciate the contribution of the general public in the form of their their naming suggestions and the New Horizons team for proposing these names to us."

More names are expected to be proposed to the IAU, both for Pluto and for its moons. "The approved designations honour many people and space missions who paved the way for the historic exploration of Pluto and the Kuiper Belt, the most distant worlds ever explored," said Alan Stern, New Horizons Principal Investigator from the Southwest Research Institute (SwRI) in Boulder, Colorado.

The approved Pluto surface feature names are listed below.

Tombaugh Regio *honours Clyde Tombaugh (1906-1997), the U.S. astronomer who discovered Pluto in 1930 from Lowell Observatory in Arizona.*

Burney *crater honors Venetia Burney (1918-2009), who as an 11-year-old schoolgirl suggested the name "Pluto" for Clyde Tombaugh's newly discovered planet. Later in life she taught mathematics and economics.*

Sputnik Planitia *is a large plain named after Sputnik 1, the first space satellite, launched by the Soviet Union in 1957.*

Tenzing Montes *and* ***Hillary Montes*** *are mountain ranges honouring Tenzing Norgay (1914-1986) and Sir Edmund Hillary (1919-2008), the Indian/Nepali Sherpa and New Zealand mountaineer who were the first to reach the summit of Mount Everest and return safely.*

Al-Idrisi Montes *honours Ash-Sharif al-Idrisi (1100-1165/66), a noted Arab mapmaker and geographer whose landmark work of medieval geography is sometimes translated as "The Pleasure of Him Who Longs to Cross the Horizons."*

Djanggawul Fossae *defines a network of long, narrow depressions named for the Djanggawuls, three ancestral beings in indigenous Australian mythology who travelled between the island of the dead and Australia, creating the landscape and filling it with vegetation.*

Sleipnir Fossa *is named for the powerful, eight-legged horse of Norse mythology that carried the god Odin into the underworld.*

Virgil Fossae *honors Virgil, one of the greatest Roman poets and Dante's fictional guide through hell and purgatory in the Divine Comedy.*

Adlivun Cavus *is a deep depression named for Adlivun, the underworld in Inuit mythology.*

Hayabusa Terra is *a large land mass saluting the Japanese spacecraft and mission (2003-2010) that returned the first asteroid sample.*

Voyager Terra *honours the pair of NASA spacecraft, launched in 1977, that performed the first "grand tour" of all four giant planets. The Voyager spacecraft are now probing the boundary between the Sun and interstellar space.*

Tartarus Dorsa *is a ridge named for Tartarus, the deepest, darkest pit of the underworld in Greek mythology.*

Elliot crater *recognises James Elliot (1943-2011), an MIT researcher who pioneered the use of stellar occultations to study the Solar System -- leading to discoveries such as the rings of Uranus and the first detection of Pluto's thin atmosphere.*

http://bit.ly/2xhtySM

Dietary approach found as effective as medications for treating type of reflux disease

Little difference in reduction of reflux symptoms between treatment with a Mediterranean-style diet and treatment with proton pump inhibitors

Among patients with laryngopharyngeal reflux, there was no significant difference in the reduction of reflux symptoms between patients treated with alkaline water and a plant-based, Mediterranean-style diet and those treated with proton pump inhibitors, according to a study published by JAMA Otolaryngology-Head & Neck Surgery.

Laryngopharyngeal reflux (LPR) is a common disorder that is the reflux (backing up) of stomach acid into the throat (pharynx) or voice box (larynx). Treatment of this disease has remained controversial, with few studies demonstrating that the current predominant regimen of proton pump inhibition (PPI) has a statistical advantage over other treatment methods. The treatment of LPR using this approach has significant economic ramifications, with PPI therapy alone costing more than 13 billion dollars in the United States in 2009.

Craig Zalvan, M.D., of New York Medical College, Valhalla, N.Y., and colleagues examined whether treatment with a diet-based approach alone can improve symptoms of LPR compared with treatment with PPI. The study included two treatment groups: 85 patients with LPR that were treated with PPI and standard reflux precautions (PS); and 99 patients treated with alkaline water, 90 percent plant-based, Mediterranean-style diet, and standard reflux precautions (AMS). The outcome was based on change in the Reflux Symptom Index (RSI).

The researchers found that the percentage of patients achieving a clinically meaningful reduction in RSI was 54.1 percent in PS-treated patients and 62.6 percent in AMS-treated patients. The average reduction in RSI was 27.2 percent for the PS group and 39.8 percent in the AMS group.

"Because the relationship between percent change and response to treatment has not been studied, the clinical significance of this difference requires further study. Nevertheless, this study suggests that a plant-based diet and alkaline water should be considered in the treatment of LPR. This approach may effectively improve symptoms and could avoid the costs and adverse effects of pharmacological intervention as well as afford the additional health benefits associated with a healthy, plant-based diet," the authors write.

The study notes some limitations, including the inherent biases of retrospective chart reviews, such as selection, information, and exclusion group biases. As rigorous as exclusion criteria were, patients with dual diagnoses may have been enrolled in the study, thus confounding results.

http://bit.ly/2qTFEam

Ship exhaust makes oceanic thunderstorms more intense

New research finds lightning strokes occurred nearly twice as often directly above heavily-trafficked shipping lanes

WASHINGTON D.C. -- Thunderstorms directly above two of the world's busiest shipping lanes are significantly more powerful than storms in areas of the ocean where ships don't travel, according to new research.

A new study mapping lightning around the globe finds lightning strokes occur nearly twice as often directly above heavily-trafficked shipping lanes in the Indian Ocean and the South China Sea than they do in areas of the ocean adjacent to shipping lanes that have similar climates.

The difference in lightning activity can't be explained by changes in the weather, according to the study's authors, who conclude that aerosol particles emitted in ship exhaust are changing how storm clouds form over the ocean.

The new study is the first to show ship exhaust can alter thunderstorm intensity. The researchers conclude that particles from ship exhaust make cloud droplets smaller, lifting them higher in the atmosphere. This creates more ice particles and leads to more lightning.

The results provide some of the first evidence that humans are changing cloud formation on a nearly continual basis, rather than after a specific incident like a wildfire, according to the authors. Cloud formation can affect rainfall patterns and alter climate by changing how much sunlight clouds reflect to space.

"It's one of the clearest examples of how humans are actually changing the intensity of storm processes on Earth through the emission of particulates from combustion," said Joel Thornton, an atmospheric scientist at the University of Washington in Seattle and lead author of the new study in Geophysical Research Letters, a journal of the American Geophysical Union.

"It is the first time we have, literally, a smoking gun, showing over pristine ocean areas that the lightning amount is more than doubling," said Daniel Rosenfeld, an atmospheric scientist at the Hebrew University of Jerusalem who was not connected to the study. "The study shows, highly unambiguously, the relationship between anthropogenic emissions - in this case, from diesel engines - on deep convective clouds."

Mapping lightning and exhaust

All combustion engines emit exhaust, which contains microscopic particles of soot and compounds of nitrogen and sulfur. These particles, known as aerosols, form the smog and haze typical of large cities. They also act as cloud condensation nuclei - the seeds on which clouds form. Water vapor condenses around aerosols in the atmosphere, creating droplets that make up clouds.

Cargo ships crossing oceans emit exhaust continuously and scientists can use ship exhaust to better understand how aerosols affect cloud formation.

In the new study, co-author Katrina Virts, an atmospheric scientist at NASA Marshall Space Flight Center in Huntsville, Alabama, was analyzing data from the World Wide Lightning Location Network, a network of sensors that locates lightning strokes all over the globe, when she noticed a nearly straight line of lightning strokes across the Indian Ocean.

Virts and her colleagues compared the lightning location data to maps of ships' exhaust plumes from a global database of ship emissions. Looking at the locations of 1.5 billion lightning strokes from 2005 to 2016, the team found nearly twice as many lightning strokes on average over major routes ships take across the northern Indian Ocean, through the Strait of Malacca and into the South China Sea, compared to adjacent areas of the ocean that have similar climates.

More than $5 trillion of world trade passes through the South China Sea every year and nearly 100,000 ships pass through the Strait of Malacca alone. Lightning is a measure of storm intensity, and the researchers detected the uptick in lightning at least as far back as 2005. "All we had to do was make a map of where the lightning was enhanced and a map of where the ships are travelling and it was pretty obvious just from the co-location of both of those that the ships were somehow involved in enhancing lightning," Thornton said.

Forming cloud seeds

Water molecules need aerosols to condense into clouds. Where the atmosphere has few aerosol particles - over the ocean, for instance - water molecules have fewer particles to condense around, so cloud droplets are large.

When more aerosols are added to the air, like from ship exhaust, water molecules have more particles to collect around. More cloud droplets form, but they are smaller. Being lighter, these smaller droplets travel higher into the atmosphere and more of them reach the freezing line, creating more ice, which creates more lightning. Storm clouds become electrified when ice particles collide with each other and with unfrozen droplets in the cloud. Lightning is the atmosphere's way of neutralizing that built-up electric charge.

Ships burn dirtier fuels in the open ocean away from port, spewing more aerosols and creating even more lightning, Thornton said.

"I think it's a really exciting study because it's the most solid evidence I've seen that aerosol emissions can affect deep convective clouds and intensify them and increase their electrification," said Steven Sherwood, an atmospheric scientist at the University of New South Wales in Sydney who was not connected to the study.

"We're emitting a lot of stuff into the atmosphere, including a lot of air pollution, particulate matter, and we don't know what it's doing to clouds," Sherwood said. "That's been a huge uncertainty for a long time. This study doesn't resolve that, but it gives us a foot in the door to be able to test our understanding in a way that will move us a step closer to resolving some of those bigger questions about what some of the general impacts are of our emissions on clouds."

http://bit.ly/2xXtW68

Secret Vatican Manuscript's Mysterious Purple Spots Decoded

About 800 years ago, a teenage soldier named Laurentius Loricatus accidentally killed a man. …

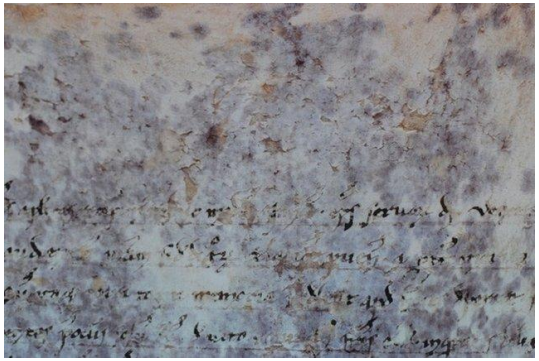
By Stephanie Pappas, Live Science Contributor

He spent the next 34 years in a cave in Italy atoning for his crime, burning his face with a hot iron and wearing a hooked chain-mail shirt directly on his skin as penance.

Loricatus' story is known today because the villagers near his cave petitioned for his sainthood on a 16-foot-long (5 meters) parchment that now resides in the Vatican Secret Archives in Vatican City. However, much of the scroll has been damaged by mysterious purple spots — and the spots are similar to ones that mar parchments made of

animal skins all over the world, said Luciana Migliore, an ecotoxicologist at the University of Rome Tor Vergata.

Using Loricatus' scroll, Migliore and her colleagues have finally pinpointed the culprit that damaged all of these parchments: salt-loving marine microbes. This was a shock, Migliore said, because the parchment had been nowhere near the sea.



"When my students came to me, saying, 'Luciana, we found marine bacteria,' I told them, 'Repeat, please; there is a mistake. There must be a mistake!'" Migliore said.

Mystery bacteria

The surprising finding was the result of applying new technology to an old problem. Migliore is a toxicologist who usually works on marine plants. At a friend's behest, she started teaching biology in a conservation-and-restoration program.

This goatskin scroll from A.D. 1244 is covered in mysterious purple spots. **G. Vendittozzi**

"I thought that I could apply the techniques that I'm used to applying to underwater plants to scrolls and old documents," Migliore told Live Science. [7 Secrets of the Dead Sea Scrolls]

Specifically, Migliore wanted to use next-generation genetic sequencing to see if she could identify the microbes that eat away at old parchments. She and her team chose to restore the Laurentius Loricatus scroll both because of its gripping content and the beauty of the document itself.

The goatskin scroll, which dates to A.D. 1244, has purple dots all along its margins, and the first and last pages are entirely obscured by the mystery pigment. Migliore's team sampled a few millimeter-size bits of the scroll that had already flaked off. They sent these samples to a lab in the United States that does fast, cheap gene sequencing.

Inside job

The findings showed much more genetic diversity, indicating a wider range of microbes, in the purple spots than in the undamaged areas of the parchment. The genetics told a two-stage story of damage: First, salt-loving, or halophilic, bacteria colonized the parchment. Next, salt-tolerant microbes, particularly the Gammaproteobacteria, took over. What shocked Migliore is that so many of these microbes were marine or aquatic.

But when they took into account how skin scrolls were made, the discovery made sense, Migliore said. The first step after removing the hide from an animal was to bathe the skin in a sea-salt bath to help preserve it, she said. This bath would have killed off most microbes that eat away at flesh — but it also introduced salt-loving and salt-tolerant marine bacteria. These little microbes huddled in the middle layers of the parchment, where the salinity was just right. When the scroll was read and stored at various monasteries throughout its lifetime, changes in temperature and humidity would have allowed the salt-loving bacteria to grow and thrive. Many of these species produce purple pigments, Migliore noted.

Eventually, though, those salt eaters would have seen their supply run out and died off. Their corpses, Migliore said, provided a whole new source of food for the next phase of bacterial colonization. The Gammaproteobacteria moved in and ate not only the dead halophilic bacteria but also the fine collagen matrix of the goatskin parchment. This caused parts of the parchment to flake off, lost forever.

Salt curing is one thing that skin parchments around the world have in common, Migliore said, so it makes sense that similar damage is seen in scrolls from all sorts of regions and time frames. (Loricatus' scroll is currently safe from further damage, as it has been kept in climate-controlled conditions since its move to Vatican City in the late 1700s.)

There's no reversing the damage to the parts of the parchment where the underlying collagen was eaten away, Migliore said. There may

still be a way to remove the purple pigments, though. She and her team are working to determine the pigment structure now.

"In this way, this work opens new perspectives, because we have to study to see if it is possible to make something of this parchment," Migliore said.

The researchers reported their findings today (Sept. 7) in the open-access journal Scientific Reports.

http://bit.ly/2qVf301

Do we need to reform international drug treaties as more countries legalize cannabis?

The future of international drug control treaties is in doubt because of recent treaty-violating decisions to legalize cannabis use in Canada, the United States and Uruguay.

Professor Wayne Hall, whose 2014 review of 20 years of cannabis research made world headlines, thinks so. If decriminalization is the way of the future, Hall advocates a cautious approach to policy reform that would involve trialling and evaluating the effects of incrementally more liberal drug policies. His suggestions, outlined below, are published online today by the scientific journal Addiction.

The international drug control treaties are endorsed by most member states of the United Nations (UN). The treaties prohibit the non-medical use of amphetamines, cannabis, cocaine and heroin. They aim to reduce the harmful use of prohibited drugs and facilitate access to these drugs for medical and scientific purposes. Critics claim that the treaties have failed to tackle non-medical use of prohibited drugs and have justified policies that conflict with UN human rights treaties by incarcerating large numbers of drug users.

Hall's paper outlines types of policies that nations could adopt to address the different types of harm that different illicit drugs cause to users and others. Some would require treaty change, while others could be accomplished by more 'flexible interpretations' of treaty provisions by member states and UN agencies. His suggestions are:

Cannabis: This is the strongest candidate for national policy experiments on different ways of regulating its sale and use. This is happening in the USA, Uruguay and Canada. Rigorous evaluations of these experiments will be useful for other countries considering legalizing cannabis for adult recreational use.

Party drugs, such as ecstasy, LSD, and novel psychoactive substances: The most important regulatory challenge for those who advocate more liberal policies is ensuring that drug manufacture and sale meet reasonable standards of consumer safety and consumers are well informed about the risks of using these drugs.

Opioids: The best way forward may be a mitigated form of prohibition. Mitigated prohibition differs from a 'war on drugs' by expanding treatment for opioid dependence, reducing some of its serious medical complications, and reducing the number of opioid users who are imprisoned.

Cocaine and amphetamines: There are no easy answers here. Proposed regulation via a modified prescription system seems unlikely to reduce harmful use. Prohibition may minimize use but it is not sufficient, because stimulants are very easy to produce illicitly. Stimulant policy needs better ways of reducing the demand for stimulants and more effective treatments for problem stimulant users.

Hall W (2017) The future of the international drug control system and national drug prohibitions. Addiction 112. doi: 10.1111/add.13941

This paper is free to download for one month after publication from the Wiley Online Library or by contacting Jean O'Reilly, Editorial Manager, Addiction, jean@addictionjournal.org, tel +44 (0)20 7848 0853.

http://bit.ly/2qSUn52

Warm Antarctic caves harbour secret life: scientists

Steam from active volcanoes has hollowed out extensive cave systems under the Antarctic ice that could be home to unique ecosystems, scientists say

A secret world of animals and plants—including unknown species—may live in warm caves under Antarctica's glaciers, scientists said Friday. The caves, hollowed out by steam from active volcanoes, are

light and could reach temperatures of 25 degrees Celsius (77 Fahrenheit), researchers said, raising the possibility of a whole ecosystem of flora and fauna deep beneath the frozen surface.

A study led by the Australian National University around Mount Erebus, an active volcano on Ross Island in Antarctica, showed extensive cave systems.

Lead researcher Ceridwen Fraser said forensic analyses of soil samples from the caves had revealed intriguing traces of DNA from algae, mosses and small animals. While most of the DNA was similar to mosses, algae and invertebrates found elsewhere in Antarctica, not all sequences could be fully identified.

"The results from this study give us a tantalising glimpse of what might live beneath the ice in Antarctica -– there might even be new species of animals and plants," she said. "The next step is to go and have a really good look and see if we can find communities living beneath the ice in Antarctica."

Despite the continent's freezing temperatures, Fraser said heat emanating from the volcanoes could make the caves quite hospitable, warm enough "to wear a t-shirt and be comfortable", with light filtering deep down where the overlying ice was thin.

Little is known about the flora and fauna that live in subglacial caves in Antarctica, and scientists say finding and exploring them is tricky

Co-researcher Charles Lee, from the University of Waikato in New Zealand, said there were many other volcanoes in Antarctica, so subglacial cave systems could be common. "We don't yet know just how many cave systems exist around Antarctica's volcanoes, or how interconnected these subglacial environments might be," he said. "They're really difficult to identify, get to and explore."

The research, published in international journal Polar Biology, said there were more than 15 volcanoes in Antarctica that were either known to be currently active or show evidence of recent activity, with new ones continuing to be found.

But despite recent advances in understanding Antarctic biodiversity, scientists still know "little about life in the continent's subglacial cave systems, which may harbour diverse and complex communities". "Our results highlight the importance of investigating these cave systems in greater detail—despite the field challenges associated with such an endeavour - to confirm the presence of living macrobiota," it said.

http://bit.ly/2whTwkc

New Genetic Discovery May Eventually End Premature Birth

An international team of researchers has identified -- for the first time -- six genes that determine the length of pregnancy and whether a baby is born preterm.

Carol Pearson

WASHINGTON - Preterm birth is a major cause of infant death and disability. Now scientists may have clues about preventing prematurity.

Researchers have found genetic mutations that affect whether a woman is likely to have her baby early or carry it to full term.

Even late preterm babies, those born between 34 and 36 weeks of gestation, are more likely to die or experience problems, even if they are the size and weight of some full-term infants born after 37 to 41 weeks in the womb. Preterm birth is the leading cause of death among children younger than 5 worldwide. These babies have higher death rates even into adolescence and beyond.

Several studies show health problems related to preterm birth persist through adult life, problems such as chronic lung disease, developmental handicaps, vision and hearing losses. The World Health Organization reports that every year, an estimated 15 million babies are born early, and this number is rising. Until now, little was

known about the causes, but these findings could help solve the mystery.

Beginning of a journey

Dr. Louis Muglia coordinated the study of the DNA of more than 50,000 pregnant women. The study identified six gene regions, which influence the length of pregnancy and the timing of birth. While the study doesn't provide information about how to prevent prematurity, Muglia says it could eventually do that. "It's just the beginning of the journey, but at least we know now, what the foundation is," he says.

Muglia is co-director of the Perinatal Institute, which focuses on preterm babies, at Cincinnati Children's Hospital Medical Center. He's also the principal investigator of one of the March of Dimes' five prematurity research centers. The March of Dimes helped pay for the study along with the National Institutes of Health, the Bill and Melinda Gates Foundation and other medical research institutes.

Muglia said scientists have known for a long time that preterm birth is a combination of genetic and environmental factors. This study showed the genes involved were from the mother.

"For the first time, we have an idea of what tissue in the mom is the one that is likely driving the one for preterm birth," Muglia says.

Selenium

One of the genes identified is involved in how the body uses selenium, a common mineral provided in food or supplements, but not currently included in vitamins women commonly take while pregnant. Selenium supplements are low-cost, and if the results are confirmed, this supplement could save millions of lives. Supplements including folic acid have been shown to greatly reduce birth defects, so much so that food in many countries is fortified with this particular B vitamin.

Another gene indicated that cells that line the uterus play a larger-than-expected role in the length of pregnancy.

The researchers were from the U.S. and from Norway, Denmark, Finland and Sweden. They only tested women of European descent, so more work needs to be done involving women of other races and ethnic origins. But their study does open up areas for researching potential diagnostic tests, new medications, improved dietary supplements or other changes that could help more women have full-term pregnancies, all areas which will require several more years of study.

The study was published in the New England Journal of Medicine.

http://bit.ly/2vXY8R6

Are we being watched? Tens of other worlds could spot the Earth

Study looks at how an alien observer might be able to detect Earth using our own methods

A group of scientists from Queen's University Belfast and the Max Planck Institute for Solar System Research in Germany have turned exoplanet-hunting on its head, in a study that instead looks at how an alien observer might be able to detect Earth using our own methods. They find that at least nine exoplanets are ideally placed to observe transits of Earth, in a new work published in the journal Monthly Notices of the Royal Astronomical Society.

Thanks to facilities and missions such as SuperWASP and Kepler, we have now discovered thousands of planets orbiting stars other than our Sun, worlds known as 'exoplanets'. The vast majority of these are found when the planets cross in front of their host stars in what are known as 'transits', which allow astronomers to see light from the host star dim slightly at regular intervals every time the planet passes between us and the distant star.

In the new study, the authors reverse this concept and ask, "How would an alien observer see the Solar System?" They identified parts of the distant sky from where various planets in our Solar System could be seen to pass in front of the Sun - so-called 'transit zones' -- concluding that the terrestrial planets (Mercury, Venus, Earth, and Mars) are actually much more likely to be spotted than the more

distant 'Jovian' planets (Jupiter, Saturn, Uranus, and Neptune), despite their much larger size.

"Larger planets would naturally block out more light as they pass in front of their star", commented lead author Robert Wells, a PhD student at Queen's University Belfast. "However the more important factor is actually how close the planet is to its parent star - since the terrestrial planets are much closer to the Sun than the gas giants, they'll be more likely to be seen in transit."

To look for worlds where civilisations would have the best chance of spotting our Solar System, the astronomers looked for parts of the sky from which more than one planet could be seen crossing the face of the Sun. They found that three planets at most could be observed from anywhere outside of the Solar System, and that not all combinations of three planets are possible.

Katja Poppenhaeger, a co-author of the study, adds, "We estimate that a randomly positioned observer would have roughly a 1 in 40 chance of observing at least one planet. The probability of detecting at least two planets would be about ten times lower, and to detect three would be a further ten times smaller than this."

Of the thousands of known exoplanets, the team identified sixty-eight worlds where observers would see one or more of the planets in our Solar System transit the Sun. Nine of these planets are ideally placed to observe transits of Earth, although none of the worlds are deemed to be habitable. In addition, the team estimate that there should be approximately ten (currently undiscovered) worlds which are favourably located to detect the Earth and are capable of sustaining life as we know it. To date however, no habitable planets have been discovered from which a civilisation could detect the Earth with our current level of technology.

The ongoing K2 mission of NASA's Kepler spacecraft is to continue to hunt for exoplanets in different regions of the sky for a few months at a time. These regions are centred close to the plane of Earth's orbit, which means that there are many target stars located in the transit zones of the Solar System planets. The team's plans for future work include targeting these transit zones to search for exoplanets, hopefully finding some which could be habitable.

http://bit.ly/2fbCy17

Meeting a microbe in the morning or in the evening: Is it all the same?

The severity of a parasite's virulence depends on what time infection occurs

Does the time of day matter when our body is infected by a parasite? According to new research from McGill University, it matters a great deal.

Our body works differently at different times of the day following our internal clocks. Researchers from McGill University and the Douglas Mental Health University Institute have now established that parasitic infections are also controlled by these clocks. The severity of a microbe's infection will thus vary whether it is encountered during the day or at night, a discovery that scientists believe could pave the way to new treatment and prevention strategies for parasitic infections.

Nicolas Cermakian, a professor at McGill's Department of Psychiatry and researcher at the Douglas Institute, made the discovery using Leishmania, a parasite that causes leishmaniasis and that is transmitted at night by the female sandfly. Every year, Leishmania infects about 1 million people, killing thousands and leaving many others with scars. Although the parasite is mostly located in tropical areas, climate change could spread Leishmania far beyond where it is found today. The parasite has already spread to certain parts of southern Europe.

When mice were injected with the parasite, Professor Cermakian's team discovered that their immune response varied greatly depending on what time of day the infection occurred.

"Our previous work showed that our immune system has its own biological clocks. Our body's defence mechanisms are more or less active at different times of the day," says Nicolas Cermakian, lead author of the new study published in Scientific Reports in

collaboration with McGill/RI-MUHC Professor Martin Olivier and Professor Nathalie Labrecque of Université de Montréal and Maisonneuve-Rosemont Hospital research centre.

Silke Kiessling, a former postdoctoral student in Professor Cermakian's lab, found that Leishmania's infection was more effective in the early night, a time when the immune response to the parasite was the strongest.

But why would the parasite be transmitted by a fly that bites at the exact time when our defences are at their strongest? Simply put, the parasite thrives when it elicits a strong immune response, attracting inflammatory cells it uses to multiply (macrophages and neutrophils) to the infection site. "We already knew that viral and bacterial infections were controlled by our immune system's circadian rhythms, but this is the first time this is shown for a parasitic infection, and for a vector-transmitted infection," Professor Cermakian adds.

Tools for better treatment and prevention

Professor Cermakian's team will now try to better define how Leishmania's circadian rhythm is controlled at the molecular and cellular levels. As a first step, they already found that the clock within cells of the immune system is directing the daily rhythm of response to Leishmania.

A better understanding of how the circadian clock controls Leishmania infection could contribute to the development of new therapeutics and better prevention approaches. Working out how time regulation of host-parasite interactions are controlled, Cermakian says, might also be useful in the fight against other diseases transmitted by insects.

This research was funded by the Canadian Institutes of Health Research

The circadian clock in immune cells controls the magnitude of Leishmania parasite infection, Silke Kiessling et al., Scientific Reports

http://bit.ly/2vX6AAa

Polio-like disease in children

Several cases of illness in children were observed that were accompanied by acute flaccid paralysis

COLOGNE - In Germany in the summer and autumn of 2016, several cases of illness in children were observed that were accompanied by acute flaccid paralysis. For the entire year 2016, 16 of such polio-like cases were registered with the Robert Koch-Institute. In an article in the current issue of Deutsches Ärzteblatt International (Dtsch Arztebl Int 2017; 114: 550-6), Johannes Hübner et al. describe this disease on the basis of two case reports, in which the neurological symptoms ranged from flaccid paralysis of the arm to tetraplegia requiring intubation and ventilation.

In the children under study, the main characteristic was damage to the anterior horn of the spinal cord as confirmed on MRI or lesions as a sign of motor neuron injury as confirmed electrophysiologically. A pathogen could almost never be detected in cerebrospinal fluid, but epidemiological associations and confirmation of viruses from stool specimens or respiratory secretions pointed at enteroviruses as the likely pathogen. The prognosis of such polio-like disease with flaccid paralysis of differing severity cannot be estimated at the beginning--it ranges from hardly detectable impairment of the arm movement to care dependency in permanent severe symptoms. Targeted therapeutic measures are not available. No sufficient evidence currently exists for the effectiveness of corticosteroids, immunoglobulins, plasmapheresis, or antiviral medications.

The authors express concern that since 2012, several cases of severe flaccid paralysis have been observed in several countries, which closely resemble the symptoms of poliomyelitis, but which are caused be different pathogens that are often not identifiable. The term "acute flaccid paralysis with anterior myelitis" has been adopted, in order to distinguish the symptoms from those of classic poliomyelitis.

https://www.aerzteblatt.de/pdf.asp?id=193181

http://bit.ly/2xXLEpY

Hurricane Harvey is gone, but it spawned a disgusting new problem in Houston

Hurricane Harvey might be a thing of the past, but the devastation it wrought still remains.

Mike Wehner @MikeWehner

Now, a new, somewhat unexpected problem is springing up for those who were in the storm's path, and it's pretty gross.

Houston, one of the hardest-hit areas, is now left to deal with an exploding population of mosquitos thanks to the incredible amount of standing water the storm left behind.

Everything from sand boxes to gardening pails were filled with water when Hurricane Harvey made its way inland, and as the city begins to repair and rebuild from the powerful storm, that water is becoming a haven for mosquitos. Officials in Houston are asking residents to clear any standing water they can, which means dumping out buckets, pails, and even discarded tires — anything that might be holding water.

"A lot of pockets of water will be formed," Mustapha Debboun, Director of the Mosquito Control Division of the Harris County Health Department, explained to Fox News. "As the water recedes from the floods there will be a lot of formation of pockets and pools of water where mosquitos will find to breed. More habitats will be available for them."

The mosquitos aren't just a nuisance, they can also spread West Nile Virus and other diseases, and the last thing the city of Houston needs right now is a bug-borne public health crisis. Even with the warning, it's impossible to clear all the new mosquito breeding grounds in time, and the population of the bugs in Houston is expected to spike in the coming weeks.

http://bit.ly/2jde7Vq

Ancient Goldsmith's Tomb Filled with Mummies Discovered in Luxor

500-year-old tomb built for a goldsmith and his wife has been discovered at an ancient cemetery el-Naga in Luxor

By Owen Jarus, Live Science Contributor

A 3,500-year-old tomb built for a goldsmith named Amenemhat and his wife Amenhotep, has been discovered at the ancient cemetery of Dra' Abu el-Naga in Luxor, the Egyptian antiquities ministry announced today (Sept. 9) at a press conference in Luxor.

Inside the tomb were also the remains of several mummies, wooden coffins, skeletal remains, pottery and small statues, according to photos released by the ministry. Jewelry and shabti figurines — which did the work of the deceased in the afterlife — were also found in the tomb, officials said.

Hieroglyphic inscriptions found inside the tomb reveal that it was originally built for a man named Amenemhat, who was a goldsmith. The inscriptions say that his wife was named Amenhotep, a name typically used in ancient Egypt for a man, officials said. However, the inscriptions said that Amenhotep held the title "lady of the house." Why Amenhotep used a name usually used for a man in ancient Egypt is unclear.

A 3,500-year-old tomb that was originally built for a goldsmith named Amenemhat and his wife has been discovered at the cemetery of Dra' Abu el-Naga in Luxor. **Egyptian antiquities ministry**

The couple lived in the 15th century B.C., during the 18th dynasty, which is part of a period in Egypt's historythat modern-day scholars call the New Kingdom, said Khaled El-Enany, Egypt's antiquities minister, during the press conference. During the New Kingdom, Egypt was united under a single pharaoh, and Egypt's power was on the rise.

The tomb was later reused during the 11th and 10th centuries B.C., during the 21st and 22nd dynasties, a time that modern-day scholars call the Third Intermediate Period, said El-Enany during the press conference. Egypt was not always united during the Third

Intermediate Period, and, at times, part of the country was ruled by Libyan groups.

Excavations inside the tomb are ongoing and more discoveries will likely be announced in the next month, El-Enany said.

The tomb was discovered by an Egyptian antiquities ministry team led by Mostafa Waziri, the head of the ministry's Luxor department. In April, Waziri's team discovered the tomb of a judge at Dra' Abu el-Naga; Waziri believes that four more tombs will be found close to where the goldsmith's tomb is located, he said during the press briefing. "If we keep digging, we'll find four more tombs in the area," Waziri said, adding "wish us luck."

Amenemhat's tomb is the second tomb belonging to an Egyptian goldsmith that has been found so far this year. In June, Live Science reported that another tomb belonging to an Egyptian goldsmith had been discovered on Sai Island in what is now Sudan.

http://bit.ly/2wU3U5l

Australian researchers say combination of treatments can stop melanoma from spreading

Researchers say a combination of new treatments can stop the world's deadliest form of skin cancer — melanoma — in its tracks and halt its spread to other organs.

SYDNEY – Results from two international drug trials conducted by the Sydney-based Melanoma Institute Australia have proved successful in preventing the disease spreading in stage three patients whose tumors had been surgically removed. Until now, these patients were at a high risk (40 to 70 percent) of the disease becoming advanced and fatal.

"Results from these clinical trials suggest we can stop the disease in its tracks — effectively preventing it from spreading and saving lives," the institute's medical director, Georgina Long, said in research published in the New England Journal of Medicine on Monday.

"Our ultimate goal of making melanoma a chronic rather than a terminal illness is now so much closer to being achieved."

One in every three cancers diagnosed is a skin cancer, according to the World Health Organization, with Australia having among the highest incidences of melanoma in the world. One Australian dies from it every five hours.

While 90 percent of people can be cured by having the primary cancer removed through surgery, it spreads in the other 10 percent because it is detected too late. "These results will change the way we treat melanoma patients as well as their quality of life," added Long. "Until now, stage three melanoma patients who have had their tumors surgically removed have simply had to play the waiting game, to see if their melanoma would metastasize or spread.

"Living with such fear severely affected them and their loved ones."

The researchers conducted two 12-month trials, one immunotherapy-based and the other with targeted therapies. Both proved successful in preventing the disease spreading.

In one of them, targeted therapies (dabrafenib and trametinib) blocked the action of a particular gene, BRAF, which is a driver for melanoma. It not only stopped stage three melanoma from recurring in those with tumors removed, but increased overall survival, the research showed.

The other trial treated patients with the immunotherapy nivolumab or ipilimumab — designed to reboot the immune system to attack melanoma cells. Results showed nivolumab decreased the chance of relapse.

"These clinical trials show we now have ammunition to prevent melanoma spreading and progressing, which until now was a critical area of disease behavior where we had no control," said Long.

"This will change how melanoma is treated around the world, as we no longer have to passively wait to see if the melanoma spreads."

The clinical trial results are due to be presented to the European Society for Medical Oncology's annual congress in Spain this week.