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ASTRO: Penn Medicine studies point to clinical advantages of proton therapy

Studies demonstrated lower toxicities, positive survival outcomes for lung, pancreatic and spine cancers

SAN ANTONIO, TEXAS - The search for evidence to support the growing use of proton therapy for more cancers at Penn Medicine continues to uncover valuable findings. New data from clinical trials conducted at the Robert Proton Therapy Center demonstrate the technology's potential advantages over conventional radiation, including less side effects and survival in some cases, for several harder-to-treat tumors: pancreatic, late-stage, non-small cell lung and chordoma and chondrosarcoma, two rare cancers found in bone or soft tissue.

The research is being presented today at the 57th American Society for Radiating Oncology (ASTRO) annual meeting, along with over 20 other abstracts from faculty and researchers in Penn's department of Radiation Oncology.

The first study, presented by Pamela J. Boimel, MD, a resident in the department of Radiation Oncology, and co-authored by John P. Plastaras, MD, PhD, an associate professor of Radiation Oncology and James Metz, MD, chair of the department of Radiation Oncology, investigated the use of proton therapy in pancreatic cancer patients whose cancer returned. Local recurrence happens in nearly 25 percent of these patients following other treatments, such as chemotherapy, surgery and radiation, and is associated with a very high morbidity. Researchers looked at 15 patients with locally recurrent pancreatic cancer who were re-irradiated with proton therapy, 10 of whom were also on chemotherapy (5-fluorouracil or capecitabine-based). The median time since the original conventional radiation was 26.7 months. Most of the patients tolerated the radiation well, with minimal side effects. The median survival was 15 months and overall survival at one year was 71.5 percent. The local-regional progression-free survival and distant-metastatic-free survival at one year was 72 and 63.8 percent, respectively.

This more than doubles the median survival for reirradiation with stereotactic body radiation therapy (SBRT), which is six to eight months. The median survival in the study also far exceeds the historical survival of patients with unresectable disease treated with chemo alone (about nine months), which is the main treatment modality offered to patients with recurrent pancreatic cancer, the authors report.

"Our data suggests that pursuing proton reirradiation may benefit these patients who have no other good treatment choices, and does so with minimal side effects," said Plastaras. "While these results are promising, larger, follow -up studies are needed to establish which people with recurrent pancreatic cancer stand to benefit most from this therapy."

Another study, presented by Jill Remick, MD, a resident in the department of Radiation Oncology, and co-authored Charles Simone, MD, an assistant professor of Radiation Oncology, and Abigail Berman, MD, an instructor in the department of Radiation Oncology, provides the first clinical report of proton therapy versus intensity modulated radiation therapy (IMRT) in the post-operative setting for late-stage, non-small cell lung cancer.

Radiation is typically given to these patients after surgery to remove a tumor; however, studies have shown that the toxicity of conventional radiation can outweigh its benefits. Proton therapy appears to be well-tolerated, while maintaining the positive clinical outcomes witnessed with IMRT, the authors report.

A total of 34 patients were part of the clinical trial: 17 underwent IMRT, while 17 underwent proton.

Patients who underwent proton and IMRT had similar, excellent short-term outcomes: One year overall survival and local recurrence-free survival were 85.7 and 94.1 percent for proton and IMRT, respectively. Side effects occurred (two patients had radiation pneumonitis and esophagitis in both sets of patients), but were less severe in the proton group.

A team from Penn Medicine also presented results from a prospective clinical of proton therapy for chordoma and chondrosarcoma. Chordoma is part of the sarcoma family, and occurs in the bones of skull and spine, while chondrosarcoma is a type of bone cancer that begins in cartilaginous tissue. Both are rare, difficult cancers to treat.

Proton therapy, with its ability to deliver high doses of radiation while sparing healthy organs, has emerged as a preferred treatment for these patients. The standard of care is surgery followed by conventional radiation, but that treatment can fail.

For the study, presented by Brian Baumann, MD, a resident in the department of Radiation Oncology, and co-authored by Michelle Alonso-Basanta, MD, PhD, an assistant professor of Radiation Oncology at Penn, the team studied 20 patients with non-metastatic chordoma and chondrosarcoma who underwent proton therapy between 2010 and 2014. Of the patients, 10 had skull base chorodomas, five had sacral chordomas, three has cervical spinal chordomas, and two had skull base chondrosarcomas.

The study yielded positive survival outcomes for the patients: local recurrence-free survival, distant metastases-free survival, and disease-free survival at two

years were 92 percent, 95 percent and 87 percent, respectively. All patients were alive at last follow up in February 2015. Some toxicities were reported in the patients, including fatigue, epistaxis and gastrointestinal issues. That toxicity data is encouraging compared with historical results using conventional radiotherapy, the authors reported.

The researchers also report that further follow-up is warranted to confirm long-term efficacy and morbidity.

"When the Roberts Proton Therapy Center opened in late 2009, we called for an increase capacity for harder-to-treat cancers, and to open new clinical trials that help pinpoint the best uses of the technology," Metz said. "These studies are prime examples of that mission, providing the field with more data to help establish the effectiveness and clinical benefits of proton therapy in more cancers."

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TSRI scientists find way to make leukemia cells kill each other

Strategy may open up new front in war on cancer

LA JOLLA, CA--Scientists at The Scripps Research Institute (TSRI) have found a way to change leukemia cells into leukemia-killing immune cells. The surprise finding could lead to a powerful new therapy for leukemia and possibly other cancers.

"It's a totally new approach to cancer, and we're working to test it in human patients as soon as possible," said senior investigator Richard A. Lerner, Institute Professor and the Lita Annenberg Hazen Professor of Immunochemistry at TSRI.

The findings, published this week in the Proceedings of the National Academy of Sciences, result from the discovery of a rare human antibody.

Unexpected Effects

The Lerner laboratory has pioneered techniques to generate and screen very large libraries of antibodies (immune system molecules), using the power of large numbers to find therapeutic antibodies that bind to a desired target or activate a desired receptor on cells.

Recently, the lab mounted an effort to find therapies for people with certain immune cell or blood factor deficiencies, by looking for antibodies that activate growth-factor receptors on immature bone marrow cells that might induce these bone marrow cells to mature into specific blood cell types. Over the past few years, Lerner and his team succeeded in identifying a number of antibodies that activate marrow-cell receptors in this way.

In the process, the scientists noted that some of these receptor-activating antibodies have unexpected effects on marrow cells, causing them to mature into radically different cell types, such as neural cells.

While why this happens is an unresolved issue, the discovery led the team to wonder if they could also use the method to convert cancerous marrow cells (leukemia cells) into non-cancerous cells.

Following the Trail

To find out, in the new study Lerner and his team, including first author Kyungmoo Yea, an assistant professor of cellular and molecular biology at TSRI, tested 20 of their recently discovered receptor-activating antibodies against acute myeloid leukemia cells from human patients. One of these antibodies turned out to have an extraordinary impact on the acute myeloid leukemia cells.

A high percentage of acute myeloid leukemia cells express the thrombopoietin (TPO) receptor, and the effective antibody was a highly potent and selective activator of this receptor on marrow cells. When the antibody was applied to healthy immature marrow cells, it caused them to mature into blood-platelet-producing cells called megakaryocytes. However, when the antibody was applied to acute myeloid leukemia cells, they matured into very different cells known as dendritic cells, key support cells in the immune system.

By itself, this could be a valuable therapeutic strategy, but it wasn't the end of the story. Lerner's team noted that, with longer exposures to the antibodies and certain other lab-dish conditions, the induced dendritic cells developed further--into cells that closely resembled natural killer (NK) cells.

NK cells represent one of the rapid-reaction forces of the immune system. They can be effective against viruses and bacteria--and cancer cells--even without prior exposure. They don't have highly specific receptors for recognizing individual targets, as T-cells do, but instead are capable of detecting, in a general way, when a nearby cell is infected or cancerous.

"That antibody could have turned those acute myeloid leukemia cells into a lot of other cell types, but somehow we were lucky enough to get NK cells," Lerner said.

'Fratricide'

The team examined these induced NK cells with electron microscopy and observed that many of the cells had extended tendrils through the outer membranes of neighboring leukemic cells--their erstwhile brethren. In lab dish tests, a modest number of these NK cells wiped out about 15 percent of the surrounding acute myeloid leukemia cell population in just 24 hours.

Curiously, the induced NK cells' cancer-killing effect appeared to be purely fratricidal. The researchers found that unrelated breast cancer cells did not die off in large numbers when in the presence of the NK cells.

Why the induced NK cells appear to target only closely related cells isn't yet clear. In principle, though, there are yet-to-be-discovered antibodies--and even small-

molecule compounds--that would turn other cancerous cell types into fratricidal NK cells, by activating other receptors expressed on those cells.

Such fratricidal therapies, which Lerner terms "fratricidins," would have several potential advantages. First, especially if they are antibodies, they could be clinically useful with little or no further modification. Second, their high specificity for their target receptors, and the resulting NK cells' specificity for related cancer cells, should reduce the likelihood of adverse side effects, possibly making them much more tolerable than traditional cancer chemotherapies.

Finally, the peculiar dynamics of fratricidin therapy, in which every cancerous cell is potentially convertible to a cancer-killing NK cell, suggests that--if the strategy works--it might not just reduce the targeted cancer-cell population in a patient, but eliminate it altogether.

"We're in discussions with pharmaceutical companies to take this straight into humans after the appropriate preclinical toxicity studies," he said.

Other co-authors of the study, "Agonist antibody that induces human malignant cells to kill one another," were Hongkai Zhang, Jia Xie, Teresa M. Jones, Chih-Wei Lin, Walter Francesconi, Fulvia Berton, Mohammad Fallahi, and Karsten Sauer, all of TSRI during the study.

The research was supported by the JPB Foundation and Zebra Biologics.

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Genomic ancestry linked to mate selection, study shows

Genetic ancestry, as well as facial characteristics, may play an important part in who we select as mates, according to an analysis from UC San Francisco, Microsoft Research, Harvard, UC Berkeley and Tel Aviv University.

Researchers used population genomics and quantitative social sciences to gauge the relatedness of parents in a study of asthma in Mexican and Puerto Rican children.

They found that the parents tended to choose partners with a similar mix of ancestry to their own, a phenomenon known as assortative mating. In the case of Mexicans, that meant having a similar proportion of mostly European and Native American ancestry, with some genomic heritage from Africa. For Puerto Ricans, that meant having similar amounts of European and African ancestry, with some Native American.

The average mix was similar enough to make the couples equivalent to between third and fourth cousins, a degree of closeness that may have implications for the perpetuation of some genetic diseases but also could have health benefits. A study done in Iceland, for example, found that the most fertile couples were about as closely related as fourth cousins.

Among the Puerto Rican, but not the Mexican couples, the researchers also found that parents had similar genes associated with facial characteristics. The strength of the ancestry assortment in both groups was stronger than education assortment, a powerful factor in mate selection that has been well documented.

The researchers said their findings could affect a wide range of disciplines that employ population genomics.

"To avoid mathematical complexities, population and medical geneticists typically assume that people choose their mates randomly when modeling everything from demographic history to the diseases in a population," said Noah Zaitlen, PhD, an assistant professor of medicine at UCSF. "We now have evidence that these choices may not be random at all, and we should incorporate this new understanding to more accurately model human history and improve our understanding of the genetic basis of disease."

The researchers said it was important to keep in mind that they only found associations between factors like ancestry and partner selection, not evidence that one was influencing the other, and they warned that some of the factors they measured, like the genes known to be involved in facial development and genomic ancestry could be entangled with one another, or related to other factors they did not measure, like culture and religion.

Given their subjects' mixed European, Native American and African ancestry, the researchers said their participants' high genomic diversity is likely to have contributed to a wider array of facial characteristics and may have magnified the effect of their tendency to choose similar-looking partners. The same thing could be happening in more homogenous populations, like European Americans, they said, but it could be harder to detect.

"To the extent that people assort based on physical appearance and cultural background, both factors can be correlated with individuals' genomic ancestries," said James Zou, PhD, a postdoctoral researcher with Microsoft Research in Cambridge, Mass. "In Mexican and Puerto Rican communities, there is greater diversity in individuals' genomic ancestries, compared to European Americans. If this is reflected in a greater diversity of physical appearances, this can contribute to stronger assortment."

The tendency to find a mate with a similar genetic background, a form of assortative mating, could also help perpetuate genetic diseases. In Puerto Ricans, who have founder mutations from both the Spaniards who colonized the island and the Native American women who bore their children, the researchers estimated that assortative mating could increase the prevalence of recessive diseases by 2 to 14 percent after 10 generations of mixing. And the researchers

said it may help explain the high prevalence of certain diseases like asthma and Hermansky Pudlak Syndrome among Puerto Ricans.

The researchers did not genotype the parents of the 2,757 trios they studied - about 1,246 of which were Mexican trios and 1,511 Puerto Rican trios - but rather inferred their relatedness through their children, who were genotyped. They also used a smaller study of 489 trios, in which both parents and children were genotyped, to validate their findings.

The researchers said more analyses should be done in other groups, to flesh out the implications of what they found.

"We need to understand how these patterns of assortment vary across diverse populations, as well, with finer geographic sampling of individuals," said Sriram Sankararaman, PhD, a postdoctoral fellow at Harvard Medical School.

Other authors of the study include Danny Park, MS, Esteban Burchard, MD, MPH, and Maria Pino-Yanes, PhD, of UCSF; Dara Torgerson, PhD, and Yun Song, PhD, of UC Berkeley; Sriram Sankararaman, PhD, of Harvard; and Eran Halperin, PhD, of Tel Aviv University, who were co-senior authors, along Zaitlen.

The study was funded by the National Institutes of Health and a Packard Fellowship for Science and Engineering.

http://www.eurekalert.org/pub_releases/2015-10/uoc--loe101915.php

Life on Earth likely started 4.1 billion years ago -- much earlier than scientists thought

UCLA-led research team finds evidence that early Earth was not dry and desolate

UCLA geochemists have found evidence that life likely existed on Earth at least 4.1 billion years ago -- 300 million years earlier than previous research suggested. The discovery indicates that life may have begun shortly after the planet formed 4.54 billion years ago. The research is published today in the online early edition of the journal Proceedings of the National Academy of Sciences.

"Twenty years ago, this would have been heretical; finding evidence of life 3.8 billion years ago was shocking," said Mark Harrison, co-author of the research and a professor of geochemistry at UCLA. "Life on Earth may have started almost instantaneously," added Harrison, a member of the National Academy of Sciences. "With the right ingredients, life seems to form very quickly."

The new research suggests that life existed prior to the massive bombardment of the inner solar system that formed the moon's large craters 3.9 billion years ago.

"If all life on Earth died during this bombardment, which some scientists have argued, then life must have restarted quickly," said Patrick Boehnke, a co-author of the research and a graduate student in Harrison's laboratory.

Scientists had long believed the Earth was dry and desolate during that time period. Harrison's research -- including a 2008 study in Nature he co-authored with Craig Manning, a professor of geology and geochemistry at UCLA, and former UCLA graduate student Michelle Hopkins -- is proving otherwise.

"The early Earth certainly wasn't a hellish, dry, boiling planet; we see absolutely no evidence for that," Harrison said. "The planet was probably much more like it is today than previously thought."

The researchers, led by Elizabeth Bell -- a postdoctoral scholar in Harrison's laboratory -- studied more than 10,000 zircons originally formed from molten rocks, or magmas, from Western Australia. Zircons are heavy, durable minerals related to the synthetic cubic zirconium used for imitation diamonds. They capture and preserve their immediate environment, meaning they can serve as time capsules. The scientists identified 656 zircons containing dark specks that could be revealing and closely analyzed 79 of them with Raman spectroscopy, a technique that shows the molecular and chemical structure of ancient microorganisms in three dimensions.

Bell and Boehnke, who have pioneered chemical and mineralogical tests to determine the condition of ancient zircons, were searching for carbon, the key component for life. One of the 79 zircons contained graphite -- pure carbon -- in two locations.

"The first time that the graphite ever got exposed in the last 4.1 billion years is when Beth Ann and Patrick made the measurements this year," Harrison said.

How confident are they that their zircon represents 4.1 billion-year-old graphite?

"Very confident," Harrison said. "There is no better case of a primary inclusion in a mineral ever documented, and nobody has offered a plausible alternative explanation for graphite of non-biological origin into a zircon."

The graphite is older than the zircon containing it, the researchers said. They know the zircon is 4.1 billion years old, based on its ratio of uranium to lead; they don't know how much older the graphite is.

The research suggests life in the universe could be abundant, Harrison said. On Earth, simple life appears to have formed quickly, but it likely took many millions of years for very simple life to evolve the ability to photosynthesize.

The carbon contained in the zircon has a characteristic signature -- a specific ratio of carbon-12 to carbon-13 -- that indicates the presence of photosynthetic life.

"We need to think differently about the early Earth," Bell said.

Wendy Mao, an associate professor of geological sciences and photon science at Stanford University, is the other co-author of the research.

The research was funded by the National Science Foundation and a Simons Collaboration on the Origin of Life Postdoctoral Fellowship granted to Bell.

http://www.eurekalert.org/pub_releases/2015-10/uob-spi101515.php

Some patients in a vegetative state retain awareness, despite being unable to move

New insight into a vital cerebral pathway has explained how some patients in a vegetative state are aware despite appearing to be unconscious and being behaviourally unresponsive.

The findings, published in JAMA Neurology, identify structural damage between the thalamus and primary motor cortex as the obstacle between covert awareness and intentional movement.

The team of researchers hope that their study, the first to understand the phenomenon, will pave the way for the development of restorative therapies for thousands of patients.

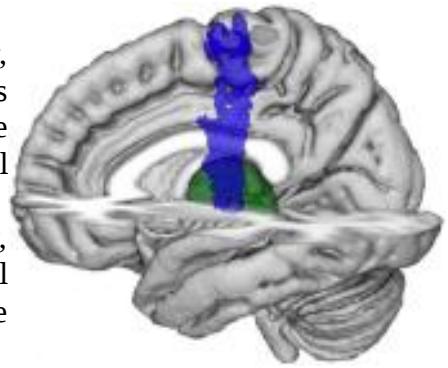


Image of brain showing the location of the thalamus (green) and primary motor cortex (blue). **University of Birmingham/Dr. Davinia Fernández-Espejo**

Dr Davinia Fernández-Espejo, from the University of Birmingham, explained, "A number of patients who appear to be in a vegetative state are actually aware of themselves and their surroundings, able to comprehend the world around them, create memories and imagine events as with any other person."

"However, before we take the crucial step of developing targeted therapies to help these patients, we needed to identify the reason for the dissociation between their retained awareness and their inability to respond with intentional movement."

"In highlighting damage to the pathways that physically connect the thalamus, one of the hubs of consciousness if you will, and the motor cortex, which drives our voluntary muscular activity, as the reason behind the dissociation we have provided an important explanation".

A patient who produced repeated evidence of covert awareness across multiple examinations, despite being in a vegetative state for over 12 years, was observed in a case study at the imaging centre at the Brain and Mind Institute, at Western University, Canada.

A fellow patient with similar clinical variables, but capable of intentional movement, and 15 healthy control volunteers were also monitored using functional magnetic resonance imaging (fMRI) and fiber tractography.

Participants were asked to respond to commands, for example, asking them to imagine moving their hand in response to the keyword "move", while their brain activity was measured. Additionally, the researchers assessed the integrity of the structural pathways that were revealed as essential for successful motor execution (those connecting the thalamus with the motor cortex).

Dr Fernández-Espejo added, "The ultimate aim is to use this information in targeted therapies that can drastically improve the quality of life of patients. For example, with the advances being made in assistive technology, if we can help a patient to regain even limited movement in one finger it opens up so many possibilities for communication and control of their environment."

Though it may be a number of years before an effective therapy is developed, the team believe that a significant milestone has been reached with the discovery.

http://www.eurekalert.org/pub_releases/2015-10/ehs-ola101615.php

Orange lichens are potential source for anticancer drugs

Parietin pigment kills leukemia cells, combats Warburg effect

An orange pigment found in lichens and rhubarb called parietin may have potential as an anti-cancer drug, scientists at Winship Cancer Institute of Emory University have discovered.

The results are scheduled for publication on October 19 in Nature Cell Biology.

Parietin, also known as physcion, could slow the growth of and kill human leukemia cells obtained directly from patients, without obvious toxicity to human blood cells, the authors report. The pigment could also inhibit the growth of human cancer cell lines derived from lung and head and neck tumors when grafted into mice.

A team of researchers led by Jing Chen, PhD, discovered the properties of parietin because they were looking for inhibitors for the metabolic enzyme 6PGD (6-phosphogluconate dehydrogenase). 6PGD is part of the pentose phosphate pathway, which supplies cellular building blocks for rapid growth. Researchers have already found 6PGD enzyme activity increased in several types of cancer cells.

"This is part of the Warburg effect, the distortion of cancer cells' metabolism," says Chen, professor of hematology and medical oncology at Emory University School of Medicine and Winship Cancer Institute. "We found that 6PGD is an important metabolic branch point in several types of cancer cells."

This work represents a collaboration among three laboratories at Winship led by Chen, Sumin Kang, PhD, assistant professor of hematology and medical oncology, and Jun Fan, PhD, assistant professor of radiation oncology. Co-first authors are postdoctoral fellows Ruiting Lin, PhD, and Changliang Shan, PhD, and former graduate student Shannon Elf, PhD, now at Harvard.

The Winship team obtained cancer cells from a patient with acute lymphoblastic leukemia, and found doses of physcion/parietin that could kill half the leukemia

cells in culture within 48 hours, while the same doses left healthy blood cells unscathed. A more potent derivative of the pigment called S3 could cut the growth of a lung cancer cell line by a factor of three over 11 days, when the cells were implanted into mice.

Although 6PGD inhibitors appear to be nontoxic to healthy cells, more toxicology studies are needed, both to assess potential side effects and to see whether people with inherited conditions would be more sensitive to the drugs. Parietin is present in some natural food pigments, but has not been tested as a drug in humans.

http://www.eurekalert.org/pub_releases/2015-10/acoc-nyy101915.php

Namaste, yogis: Yoga as effective as traditional pulmonary rehab in patients with COPD

Improvements are just as effective as traditional pulmonary rehabilitation methods

MONTRÉAL - Researchers from the Department of Pulmonary Medicine and Sleep Disorders and All India Institute of Medical Sciences, New Delhi, India, studied the effects of yoga as a form of pulmonary rehabilitation on markers of inflammation in the body. Results from this study showed yoga exercises provide improvements that are just as effective as traditional pulmonary rehabilitation methods in improving pulmonary function, exercise capacity, and indices of systemic inflammation.

Sixty patients with COPD were randomly divided into two groups, one of which was taught yoga exercises while the other underwent a structured pulmonary rehabilitation program. These groups were tested on shortness of breath, serum inflammation, and lung function tests.

Each group participated in 1 hour of training twice a week for the first 4 weeks, then training every 2 weeks for 8 weeks, and the remaining weeks were at home. Results showed that yoga and pulmonary rehabilitation exercises resulted in similar improvements in pulmonary function, 6-minute walk distance, Borg scale, severity of dyspnea, quality of life, and levels of C-reactive protein after 12 weeks of training.

"This study suggests yoga may be a cost-effective form of rehabilitation that is more convenient for patients," said Mark J. Rosen, MD, Master FCCP, CHEST Medical Director. "The authors recommended adoption of yoga programs as an option as part of long-term management of COPD. These findings should be confirmed in new studies and the potential mechanisms explored."

Further results will be shared during CHEST 2015 on Monday, October 26, 2015, at 8:30 AM at Palais des congrès de Montréal, room 513ef. The study abstract can be viewed on the CHEST website.

http://nyti.ms/1LIqC6P

A Touch-Source Disconnect for Babies

Babies do not link the sensation of touch with the object or person touching them until they are about 6 months old, a new study suggests.

By SINDYA N. BHANOO

At 4 months of age, “the sense of touch is still disconnected from other senses,” said Jannath Begum Ali, a psychologist at the University of London. “It is disconnected from visual information and auditory information.”

She and her colleagues published their findings in the journal Current Biology.

The researchers tickled babies and evaluated their responses. When 6-month-old infants were tickled on their feet with legs crossed, they were often confused about which foot was receiving the sensation.

“If we tickled their right foot, they would perhaps move their left foot,” Dr. Ali said. This sort of mistake indicates the babies are trying to process the sensation as well as the source of the tickle, she added.

Four-month-old infants, however, were less likely to be confused when their legs were crossed. They were also faster to respond, a sign that their brains may be processing less information.

Adults also make mistakes when identifying the origin of a sensation when their legs are crossed.

Earlier studies have found that congenitally blind adults are able to accurately identify touches whether their limbs are crossed or uncrossed. Adults who lost their sight after birth, however, do not have the same ability.

http://bit.ly/20hR345

First domestication of dogs took place in Asia, not Europe

First domestication of dogs took place in Asia, not Europe

Dogs became man’s best friends somewhere in central Asia close to Nepal and Mongolia, according to the largest genetic study yet. The work looked at DNA from thousands of living dogs to piece together their ancestry and geographical origins.

“This is the first global study of genomic patterns of dog diversity,” says Adam Boyko of Cornell University in Ithaca, New York, who led the team. “We find a clear pattern of genetic diversity focused on central Asia, suggesting the first domesticated dogs came from this region.”

That departs from earlier studies that pinpointed Europe as where dogs were domesticated, although more recent work puts the location in southern China, just 1000 kilometres from the area Boyko’s team proposes.

The team broke new ground by analysing DNA samples from so-called “village dogs”, which have lived alongside humans throughout the world since dogs first

evolved from wolves and were domesticated around 15,000 years ago. “Although they associate with humans, village dogs are more or less expected to make it on their own,” says Boyko.

Authentic signature

“They are very different from pure-bred dogs genetically because they are free-breeding, so in a genetic sense, they are a natural population.” Village dogs therefore carry a more authentic genetic signature of original dog populations than the modern-day breeds created in the past 200 years, mainly in Europe.

Boyko’s team took DNA samples from 549 village dogs in 38 countries all over the globe. They also took samples from 4676 pure-bred “modern” dogs of 161 breeds, many of European origin.

To further improve the reliability of the analysis, the team broadened the amount of DNA examined to include chromosomes inherited from both parents. Previous studies had relied mainly on mitochondrial DNA transmitted through the female line, or DNA from male sex chromosomes.

By analysing 185,805 genetic markers, Boyko’s team traced how all the animals were related, and from that how they had spread around the world. This essentially gave them a trail back to “founder” dogs in Nepal and Mongolia.

The analysis also revealed that following domestication, village dogs rapidly fanned out to other areas of Asia, particularly India and south-west and east Asia.

Scavenging

Boyko’s team speculates that hunter-gatherers in central Asia domesticated dogs from grey wolves. A combination of increasing human population density, better hunting methods and climate change may have reduced the availability of prey and pushed some wolves towards scavenging, which favoured tameness and smaller size. This would in turn have reduced their hunting prowess further, setting them on the path to domestication.

Other researchers have welcomed the tracing of domestication to the neighbourhood of central Asia, although some dispute the precise site.

“They are actually putting the origin very close to where we put it, just 1000 kilometres away in parts of Asia south of the Yangtze river,” says Peter Savolainen of the Royal Institute of Technology in Solna, Sweden. “So I would say the consensus pointing to south and east rather than central Asia is quite clear.”

Savolainen compliments the thoroughness of the study, but says that what is lacking is DNA from southern China, where he thinks dogs originated. “Since they don’t have a single sample from south China, they haven’t falsified [my] theory,” he says.

Olaf Thalmann at Uppsala University in Sweden praises the scale of the study, and says its conclusion is reasonable. “We know that this region was pivotal for ancient trade, and it seems plausible that animals followed the trading routes and thus increased the local diversity,” he says.

But Thalmann doubts that the study is the final word on where dogs were tamed, because the DNA comes only from animals living today. “I’m convinced the only way to shed further light on the topic is by analysing ancient remains,” he says. A consortium led by Greger Larson of the University of Oxford is now looking to doing just that.

Larson says Boyko’s result is important because it reaches a clear conclusion that can be tested further. “We are excited to be working with Boyko’s group and others,” he says.

“Having collected more than 1500 ancient dogs and wolves over the past few years, our lab has begun our next-generation sequencing effort.” The genetic data will then be compared with morphological data from more than 4000 specimens going right back into the late Pleistocene, he says.

Journal reference: PNAS, DOI: 10.1073/pnas.1516215112

http://bit.ly/1PbxntF

Traditional Healers Key to Stamping Out Ebola in Guinea

Guinea is the last country in West Africa where people are still getting sick from Ebola, and health authorities are rallying traditional healers to help in the fight against the disease.

Chris Stein

CONAKRY - Mory Kourouma says he will cure what ails you from the van he parks along a busy roadside in Guinea’s capital Conakry. He offers traditional medicines to treat common ailments, even if the ailment is fever, one of the first symptoms of the Ebola virus. "For those who are complaining of having fever, and they come to my place, what we normally give them is this one and that one over there in the bottle," Kourouma said.

Ebola outbreak

Guinea was the first country in West Africa in which Ebola broke out, and the last country in the region where people are still getting the virus. The virus has killed more than 11,300 people, mostly in Guinea and in nearby Sierra Leone and Liberia. While its neighbors have managed to get rid of the disease, two new Ebola cases were reported last week in Guinea.

After the virus broke out in 2013, Dr. Sakoba Keita, the national coordinator of Guinea’s fight against Ebola, said the government realized if it was going to beat the disease, it needed to get traditional healers on board. "More of them had already died because of their treating of Ebola cases. Mainstream science doesn't support that traditional healers can, as far as I know, treat Ebola. So we met with

the traditional healers, and we trained around 1,500 of them in measures of prevention and detection in Ebola cases," Keita said.

Weren't prepared

Mamady Nabe, president of Guinea's Union of Traditional Healers, said before the government intervened, most traditional doctors did not have the equipment to protect themselves from a disease that is transmitted through infected bodily fluids. "Before we were sensitized, we didn't have the hygiene kits, we didn't have infrared thermometers, we didn't have gloves," Nabe said.

Thanks to the sensitization efforts, this Ebola treatment center in Conakry is nearly empty. But as the recent cases show, the country still has much to do to defeat the disease entirely.

http://www.bbc.com/news/magazine-34572482

Why are placebos getting more effective?

Over the last 25 years the difference in effectiveness between real drugs and placebos has narrowed

By William Kremer BBC World Service

When new drugs are put on the market, clinical trials determine whether they perform better than inactive pills known as "placebos".

Research shows that over the last 25 years the difference in effectiveness between real drugs and these fake ones has narrowed - but more in the US than elsewhere. Are Americans really more susceptible to placebo effects, or is something else going on?

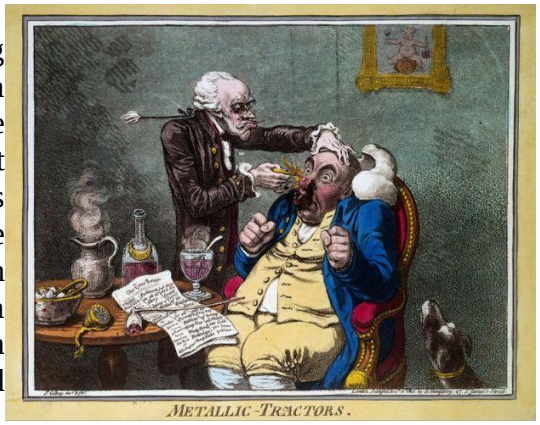
If you were a sick Londoner in the late 18th Century several treatment options were open to you. By no means the cheapest of these was to go along to a little shop on Leicester Square, hand over five guineas and receive a pair of pointy metal rods that would suck the disease from your body.

These instruments were called Perkins Tractors, after their American inventor Elisha Perkins, who claimed George Washington as a customer. They worked, it was said, because they were made of special alloys.

But in 1799 the renowned physician John Haygarth decided to test whether they really worked, and at the same time perform a scientific examination of "that faculty of the mind, that is denominated the Imagination".

He organised a trial at a hospital in which five people suffering chronic rheumatism were treated with replica wooden tractors. "All five patients, except one, assured us that their pain was relieved," he reported. "One felt his knee warmer, and he could walk much better, as he shewed us with great satisfaction. One was easier for nine hours, and till he went to bed, when the pain returned. One had a tingling sensation for two hours."

When the "real" metal tractors were used on the second day, they had much the same effect as the fake ones. "Such is the wonderful force of the Imagination!" mused Haygarth.



A print by James Gillray showing the use of Elisha Perkins's tractors **Wellcome Library, London**

The phenomenon of patients feeling better simply because they believe a treatment will help them has come to be known as the placebo effect (find out why at the bottom of the page). It comes into play most often when people are experiencing pain, fatigue, depression and nausea. Scans of patients taking a placebo show their brains switching on parts that can help control stress and pain.

When new drugs are being trialled in the US, the Food and Drug Administration (FDA) demands that the researchers factor in the placebo effect. They do this by engaging in controlled trials in which some participants are given the real drug and some are given a placebo - participants are generally not told whether their treatment contains the drug being tested or not.

The drug's effectiveness is then determined by subtracting the placebo response - the extent to which patients in the placebo group get better - from the drug response. Before allowing a drug to go on the market, the FDA demands that it has been shown to outperform a placebo by a significant margin.

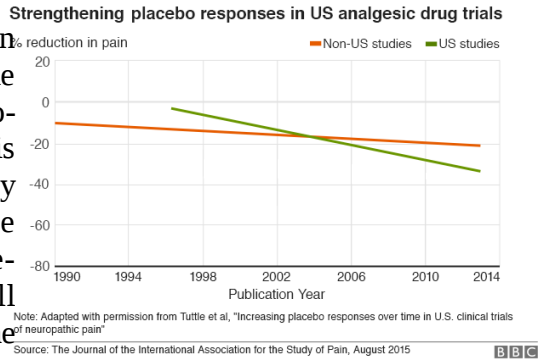
It seems, though, that this is happening less and less, because the placebo response has been steadily strengthening. Tests reveal that some well-known drugs for depression and anxiety would struggle to pass their clinical trials if they were re-tested in 2015.

This trend has become a huge concern for the pharmaceutical industry. A slew of drugs have flopped at these final clinical trials, by which time drugs companies have typically spent more than $1bn in research and development.

No-one knows why the placebo response is rising but a fascinating new study in the journal Pain might help experts pin it down.

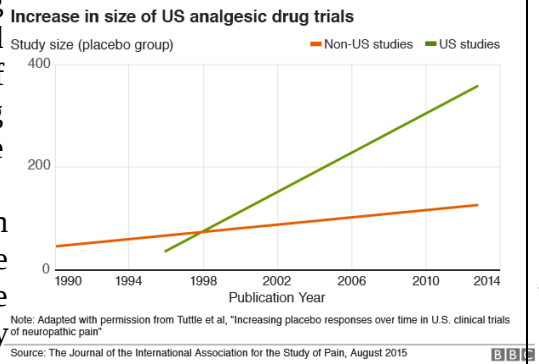
Drawing on data from 80 trials for drugs to treat neuropathic pain, the researchers led by Dr Jeffrey Mogil at McGill University in Montreal found that the trend was being driven by studies conducted in the US. Americans seem to be getting better merely by taking part in studies these days, regardless of whether they have been given real drugs or not.

Why? What could it be about Americans that might make them particularly susceptible to the placebo effect?



Top of the list of possibilities is that in the US, unlike every other country in the world except New Zealand, direct-to-consumer advertising of drugs is permitted. The placebo effect is strongly linked to patient expectations, and maybe all those adverts showing virile middle-aged men shooting hoops on a basketball court have had a drip-drip effect on the minds of patients taking drugs, even as part of a trial.

Mogil jokes that he and his co-writers disagree vehemently about the causes of the effect they have uncovered. His own favourite hypothesis does not relate to advertising but the fact that US trials have become larger and tend to go on longer than non-US trials.



Drug companies were probably hoping that larger, more ambitious trials would be better at showing the real effect of drugs, Mogil thinks, but in fact the big budgets may have made things worse, he suggests.

A well-funded trial would be reflected in lots of small ways that might come together to increase patients' confidence that they were engaged in a clinically beneficial process. Just adding a snazzy logo to a research trial could make people feel more optimistic.

Mogil believes that US companies are more likely than others to use contract research organisations (CROs) to conduct trials (though since the companies don't have to declare this, it is hard to know for sure). It may be that the staff who work at these service organisations are friendlier than the busy researchers who conduct academic trials. That in itself could make people feel better.

"There's been a push to gather data, not have missing data," says Dr John Farrar, a neurologist and epidemiologist at the University of Pennsylvania. "So a lot more attention has been paid to patients, there's a lot more contact with patients to make sure they fill out the forms in the right way, and a general increase in knowledge about the potential activity of the drug - talking about the science of it, how it might work etc. And one can assume that all of that leads to potentially a higher expectation in patients."

But Farrar adds that the profit motive of CROs might also be driving them to recruit people who shouldn't really be in the trial in the first place. A physician looking for participants may encourage them to classify their symptoms as more severe than they really are so that they become eligible to take part.

"The other thing is there has been a growth of what we would call 'professional patients' - patients who enrol in clinical trials because they find they can make money off that," says Farrar.

A lot of information about upcoming trials - including eligibility criteria - is now available online **National Institutes of Health**

In both those scenarios, after being admitted to a trial the patients may start to give a truer account of their symptoms, which may get chalked up as a positive placebo response.

Farrar advocates changing the design of trials in order to reduce the placebo effect. This includes things like:

more stringent controls on patient recruitment

being less specific about eligibility criteria, so that it's harder for people to claim they are eligible when they are not

adding a third group to the controlled trial set-up, which takes an existing drug that is known to work - if both that group and the group given the new drug fail to beat the placebo, researchers know that their trial design is flawed

There is also a drive to lower, through discussions with patients, their expectations of taking part in a trial. What is the best way to do that? "We tell them the truth," says Dr Nathaniel Katz, the president of Analgesic Solutions, a consultancy that helps drug companies avoid trial failures.

"Telling the truth" means reminding patients that they are part of a trial for a drug that may not work, and which they may not even be given. "Even if it works," Katz says, "it only works for about a third to a half of patients - that's as good as it gets these days."

His company also trains trial researchers to avoid "inappropriately optimistic body language" like putting an arm around the patient, shaking their hand or looking them in the eye. "These are all the things that enhance expectations," says Katz. But he adds that if you lower patient expectations too far you will certainly

minimise the placebo effect, but you are also likely to lower the effect of the drug being tested.

This was demonstrated in an experiment last year by Ted Kaptchuk at Harvard Medical School. He gave some migraine sufferers either the drug Maxalt or a placebo. But both those cohorts were divided into three further groups. The groups were given their drugs in envelopes with one of three labels: "Maxalt", "Placebo" or "Maxalt or placebo".

"When we gave them the placebo and the envelope said Maxalt, it had a good positive response," Kaptchuk told the BBC. "When we gave them Maxalt and told them it was a placebo, the response was no different, meaning that by just changing the word on the envelopes we could make the placebo as effective as the medication."

The challenge, in Kaptchuk's view, is to find a way of translating the remarkable power of the placebo into everyday clinical practice. While researchers in drug trials are keen to minimise patient expectations, maybe doctors outside the lab owe it to their patients to boost them as much as possible, harnessing John Haygarth's "wonderful force of the imagination".

"Doctors, every time they prescribe a medication - shall they say, 'This is going to help you, this will be really good because of trials'?" asked Kaptchuk. "Or shall they say, 'Shall we try and see if it works?'"

Placebo - the origin of the word, if you please

Placebo is Latin for "I will please"

It comes from the Psalm 116:9 of the Bible - "placebo Domino in regione vivorum" or "I will please the Lord in the land of the living"

It was the first response of mourners to a priest's recitation at a funeral

Hired mourners and people who came to a funeral to get free food and drink came to be known as "placebos"

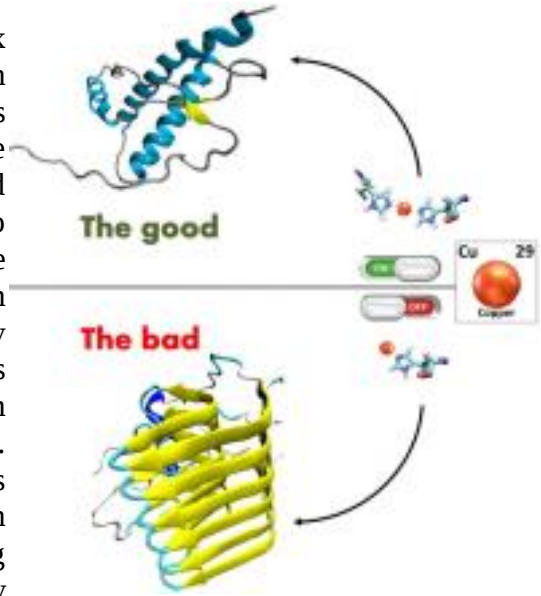
They were seen as insincere, their feelings not authentic

http://www.eurekalert.org/pub_releases/2015-10/isoa-fqt101915.php

From good to bad with a copper switch

Here's the mechanism that creates prions, the 'bad' proteins

At the molecular level, the difference between Doctor Jekyll and Mr Hyde lies in a metal, copper. In its physiological form, the prion protein (PrPC) is 'good' and is involved in normal body processes. It can happen, however, that because of some as yet unknown mechanism, it changes form and turns into a threat for the health of humans and animals (it is responsible for neurodegenerative diseases such as spongiform encephalopathies). According to a new SISSA study, the mechanism underlying this change is a metal, copper, or rather a particular region of the protein to which the metal binds, which acts as a sort of 'switch' that turns PrPC into its terrible alter ego.



Here's the mechanism that creates prions, the 'bad' proteins **International School of Advanced Studies (SISSA)**

"We still don't know what complex molecular mechanisms cause the prion protein to become bad," explains Giuseppe Legname, professor at the International School for Advanced Studies (SISSA) in Trieste who coordinated the new study, "nor do we know any treatments to cure prion diseases. Our research has finally uncovered a critical cofactor, which is capable of triggering the transformation of prions proteins from good to bad. And this cofactor is copper which binds to an amino acid sequence of the prion protein, known as 'fifth copper binding site', which has so far been poorly studied".

"In physiological conditions, copper is tightly bound to two histidine amino acids", continues Legname. "When copper is bound in this way it seems to protect the prion protein. When instead copper is missing or is bound to one rather than two histidines, that's when problems arise: the prion protein becomes unstable and turns into a bad and infectious prion".

To reach this conclusion, the researchers used multidisciplinary experimental approaches, ranging from structural to cellular biology. "It all started with an intuition we published in the journal Biochemistry in 2012", explains Gabriele Giachin, first author of the study and former SISSA PhD student (today at the European Synchrotron Radiation Facility, ESRF, in Grenoble, France). "On that occasion, we hypothesized that the pathological genetic mutations present in the prion protein could affect copper coordination". Starting from this intuition, Giachin and colleagues went on to conduct in-depth experiments using XAFS (X-ray absorption fine structure) spectroscopy, exploiting the powerful X-rays available at the Grenoble synchrotron. Then, drawing on the consolidated expertise in molecular and cellular biology available at the SISSA Laboratory of Prion Biology coordinated by Legname, the group confirmed the hypothesis in living cell systems.

"These results finally answer a fundamental question: what mechanism underlies the appearance of prions?", concludes Legname. "We have been the first to provide a detailed description of the role of copper in prion conversion, opening the way for the development of new drugs targeting this copper binding site, and thus for new potential treatments".

The study was conducted through the collaboration of a group of SISSA scientists (in addition to Giachin and Legname, the group includes Thao Mai, Thanh Hoa Tran, Giulia Salzano and Federico Benetti) and a group coordinated by the University of Rome "La Sapienza", led by Paola D'Angelo.

Prion proteins and prions Prions are proteins that have undergone a change in structure from a physiological "good" form normally present in our brain to an aberrant (or "bad") form capable of causing degeneration of nervous tissue and diseases, some of which very severe. Among the diseases are Creutzfeld Jakob disease in humans and "mad cow" disease in cattle. Unique in nature, prions can also be infectious, like viruses and bacteria, in that they can be transmitted between individuals of the same or even different species.

http://read.bi/1RETI1z

Hints of life on what was thought to be desolate early Earth

Fossil-like rock found in Australia contains hints of life from 4.1 billion years ago

Seth Borenstein, Associated Press

WASHINGTON (AP) - Scientists have found fossil-like hints that some kind of life existed on Earth 4.1 billion years ago — when the planet was a mere volcanic toddler. That's 300 million years earlier for life to pop up than previously thought.

Not only does that change the way scientists thought Earth was like soon after it formed 4.5 billion years ago, but gives them reason to theorize that life itself is more plentiful throughout the universe because it seemed to start up so quickly.

Researchers examined tiny grains of the mineral zircon from western Australia's Jack Hills and chemically dated them to when Earth was barely 400 million years old. Inside one of the 160 some grains they found what they call a "chemo-fossil" or a certain mix of carbon isotopes, according to a study published Monday in the journal Proceedings of the National Academy of Sciences.

Think of it as "the gooey remains of biotic life or anything more complicated," said study co-author Mark Harrison, a UCLA geochemistry professor.

There are different types of carbon with different weights. This carbon residue had a higher percentage of the lighter type of carbon, which is what scientists usually find in remnants of life, the same as if your finger decayed, Harrison said.

There are rare cases where this particular carbon signature wouldn't be from life, but they are exceedingly unusual and only in certain situations.

Harrison theorizes that the carbon is from a colony of tiny organisms of some unknown type. Life existing 300 million years earlier than science thought is the most logical and simplest explanation, but "this is not smoking gun evidence," Harrison said.

The common thinking of early volcanic Earth is that it was too molten and there was not enough liquid water for life to take hold this early. But, Harrison said, there's no physical evidence for this theory. What the zircon shows is "the Earth by 4.1, 4.2 billion years ago was basically behaving like it is today."

"This is what transformative science is all about," said Stephen Mojzsis, a University of Colorado scientist who wasn't part of the research. ""If life is responsible for these signatures, it arrives fast and early."

S. Blair Hedges of Temple University, who also wasn't part of the study, said Harrison's findings makes sense and the accelerated timeline of life fits with his genetic tracking work.

"If life arose relatively quickly on Earth," Hedges wrote in an email, "then it could be common in the universe."

http://www.pnas.org/content/early/2015/10/14/1517557112.abstract?sid=4b14154d-f242-4f6a-a401-2d596b67023d

http://www.eurekalert.org/pub_releases/2015-10/uoq-usp102015.php

UGR scientists patent an effective drug for treating breast, colon, and skin cancers

Reduced the tumor activity by 50 percent following 41 days of treatment

Scientists from the University of Granada (UGR) have patented an effective drug for treating cancer stem cells (CSCs) in breast, colon, and skin cancers. The researchers have proved the anti-tumor effects of the drug on immunodeficient mice.

The new compound and its derivatives enabled the researchers to reduce tumor activity by 50 percent after 41 days of treatment with the drug, administered twice a week, to mice with induced tumors. They have also managed to successfully describe the mechanisms by which the drug acts on the cancer stem cells (CSCs).

This crucial scientific breakthrough has been made by the UGR research groups "Research and Development of Pharmaceutical Drugs", directed by Professor Joaquín Campos Rosa, and "Advanced Therapies: Differentiation, Regeneration and Cancer", directedby Professor Juan Antonio Marchal Corrales. The Córdoba-based company Canvax Biotech has also participated in the development of the patent.

A non-toxic drug

One of the major advantages of the drug is that it is non-toxic. Despite being administered to the mice in high concentrations (150 milligrams per kilo), no

adverse effects were observed in the healthy cells. Moreover, from a pharmaceutical perspective this anti-tumor drug can be successfully produced in large quantities. The researchers were able to obtain the required amount of the synthesis in just five days.

In the initial phases of their research, the scientists had already managed to create an effective drug (called Bozepinib) for treating cancer stem cells, but the process involved in its chemical synthesis was lengthy and required a great deal of time to produce very small quantities of the drug.

Having completed structural modifications of the drug – Bozepinib (by making changes to its molecular architecture), they have successfully created a compound which maintains the biological activity of its predecessor as an effective anti-tumor drug, but which can also be synthesized and produced on a grand scale -- a fundamental condition for the drug's commercial development.

22 years of research

The two UGR groups behind this key scientific breakthrough have been working in this line of research since 1993. In order to be able to test the new drug on mice and gauge its effectiveness on human tumors, first of all they had to inject human tumor cells into immunodeficient mice (to ensure they did not reject these cancerous cells).

Following the treatment, they discovered that some of the compounds effectively inhibited the growth of the tumor cells and the migration ability of these cells to other healthy tissues, considerably diminishing the likelihood of metastasis.

The drug directly targets CSCs without affecting the healthy cells, a huge advantage when compared to other cancer treatments such as chemotherapy. Although CSCs are only found in small quantities in tumors, from a clinical perspective the ability to target them directly is of fundamental importance, given that they are responsible for originally causing the tumor, relapses and resistance to anticancer treatments.

The next step: Lungs and pancreas

Having proved the pre-clinical effectiveness of the new drug in treating cancer stem cells in breast, colon, and skin cancers, the scientists will now proceed to study the drug's effect on lung and pancreas cancers, two of the most aggressive types.

They must also complete further ADME-Tox ("absorption, distribution, metabolism, excretion and toxicity") studies of the compound's behavior within the organism, a necessary step before carrying out clinical trials.

In the last two months, the research project has received funding of over €124,930 from the public sector from the Ministry of Economy and Finance and the firm Canvax Biotech SL and €20,000 from the private sector.

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http://www.eurekalert.org/pub_releases/2015-10/nsfc-mew102015.php

Most earth-like worlds have yet to be born, according to theoretical study

Earth came early to the party in the evolving universe.

According to a new theoretical study, when our solar system was born 4.6 billion years ago only eight percent of the potentially habitable planets that will ever form in the universe existed. And, the party won't be over when the sun burns out in another 6 billion years. The bulk of those planets -- 92 percent -- have yet to be born.

This conclusion is based on an assessment of data collected by NASA's Hubble Space Telescope and the prolific planet-hunting Kepler space observatory.

"Our main motivation was understanding the Earth's place in the context of the rest of the universe," said study author Peter Behroozi of the Space Telescope Science Institute (STScI) in Baltimore, Maryland, "Compared to all the planets that will ever form in the universe, the Earth is actually quite early."

Looking far away and far back in time, Hubble has given astronomers a "family album" of galaxy observations that chronicle the universe's star formation history as galaxies grew. The data show that the universe was making stars at a fast rate 10 billion years ago, but the fraction of the universe's hydrogen and helium gas that was involved was very low. Today, star birth is happening at a much slower rate than long ago, but there is so much leftover gas available that the universe will keep cooking up stars and planets for a very long time to come.

"There is enough remaining material [after the big bang] to produce even more planets in the future, in the Milky Way and beyond," added co-investigator Molly Peeples of STScI.

Kepler's planet survey indicates that Earth-sized planets in a star's habitable zone, the perfect distance that could allow water to pool on the surface, are ubiquitous in our galaxy. Based on the survey, scientists predict that there should be 1 billion Earth-sized worlds in the Milky Way galaxy at present, a good portion of them presumed to be rocky. That estimate skyrockets when you include the other 100 billion galaxies in the observable universe.

This leaves plenty of opportunity for untold more Earth-sized planets in the habitable zone to arise in the future. The last star isn't expected to burn out until 100 trillion years from now. That's plenty of time for literally anything to happen on the planet landscape.

The researchers say that future Earths are more likely to appear inside giant galaxy clusters and also in dwarf galaxies, which have yet to use up all their gas for building stars and accompanying planetary systems. By contrast, our Milky Way galaxy has used up much more of the gas available for future star formation.

A big advantage to our civilization arising early in the evolution of the universe is our being able to use powerful telescopes like Hubble to trace our lineage from the big bang through the early evolution of galaxies. The observational evidence for the big bang and cosmic evolution, encoded in light and other electromagnetic radiation, will be all but erased away 1 trillion years from now due to the runaway expansion of space. Any far-future civilizations that might arise will be largely clueless as to how or if the universe began and evolved.

The results will appear in the Oct. 20 Monthly Notices of the Royal Astronomical Society.

http://www.eurekalert.org/pub_releases/2015-10/nyu-sfl102015.php

Scientists find link between comet and asteroid showers and mass extinctions

Mass extinctions occurring over the past 260 million years were likely caused by comet and asteroid showers, scientists conclude in a new study published in Monthly Notices of the Royal Astronomical Society.

For more than 30 years, scientists have argued about a controversial hypothesis relating to periodic mass extinctions and impact craters--caused by comet and asteroid showers--on Earth.

In their MNRAS paper, Michael Rampino, a New York University geologist, and Ken Caldeira, a scientist in the Carnegie Institution's Department of Global Ecology, offer new support linking the age of these craters with recurring mass extinctions of life, including the demise of dinosaurs. Specifically, they show a cyclical pattern over the studied period, with both impact craters and extinction events taking place every 26 million years.

This cycle has been linked to periodic motion of the sun and planets through the dense mid-plane of our galaxy. Scientists have theorized that gravitational perturbations of the distant Oort comet cloud that surrounds the sun lead to periodic comet showers in the inner solar system, where some comets strike the Earth.

To test their hypothesis, Rampino and Caldeira performed time-series analyses of impacts and extinctions using newly available data offering more accurate age estimates. "The correlation between the formation of these impacts and extinction events over the past 260 million years is striking and suggests a cause-and-effect relationship," says Rampino.

Specifically, he and Caldeira found that six mass extinctions of life during the studied period correlate with times of enhanced impact cratering on Earth. One of the craters considered in the study is the large (180 km diameter) Chicxulub impact structure in the Yucatan, which dates at about 65 million years ago--the time of a great mass extinction that included the dinosaurs.

Moreover, they add, five out of the six largest impact craters of the last 260 million years on earth correlate with mass extinction events.

"This cosmic cycle of death and destruction has without a doubt affected the history of life on our planet," Rampino observes.

http://www.eurekalert.org/pub_releases/2015-10/ki-tws101915.php

Transfusion with stored blood safe in heart surgery

Researchers have shown that stored blood does not influence patient outcomes after heart surgery

A large registry study led from Sweden's Karolinska Institutet shed new light on the much debated issue of transfusions with stored blood. The study, which is published in the journal JAMA, shows that the use of stored blood units does not influence patient outcomes after heart surgery.

In Sweden and most other western countries, blood units can be stored for as long as 6 weeks before being transfused. However, a high-profile publication in 2008, which claimed that storage for a mere 14 days or more was unsafe for heart surgery, has caused confusion and anxiety at hospital clinics worldwide.

"There have literally been hundreds of studies conducted on this topic the past five or six years, none of which have been able to provide a definitive answer", says senior author Gustaf Edgren, MD, Associate Professor at the Department of Medical Epidemiology and Biostatistics.

To tackle the problem at its roots, Dr. Gustaf Edgren and his research team performed a large-scale study of almost 50,000 patients in Sweden over a 16-year period. The study was made possible by linking a number of high-quality health registries, which allowed researchers to include all heart surgery patients in

Sweden during the study period, with complete information about all blood transfusions administered together with clinical details about the patients. The cohort included patients receiving transfusions with blood that had been stored between 14 and 42 days.

"This study is by far the largest investigation focusing on the issue of blood storage in this very sensitive patient group, and we find absolutely no hint of negative health effects associated with stored blood", says lead study-author Ulrik Sartipy, a Cardiac Surgeon and Associate Professor at the Department of Molecular Medicine and Surgery.

"Thanks to these unique health registers we have been able to provide very firm reassurance that the current blood storage practices are safe," says Gustaf Edgren.

Funding was provided by the Swedish Medical Society, Karolinska Institutet Foundations and Funds, the Mats Kleberg Foundation, the Swedish Research Council, the Swedish Heart-Lung Foundation, and the Swedish Society for Medical Research. Co-authors of the study are also affiliated to Karolinska University Hospital, Sweden, and Statens Serum Institut in Denmark. Registries used in the study were amongst others the SWEDEHEART registry, which records information on patients who undergo heart surgery in Sweden, and the SCANDAT2 database, a nationwide register of blood transfusions.

Publication: 'Red Cell Concentrate Storage and Survival after Cardiac Surgery', Ulrik Sartipy, Martin J. Holzmann, Henrik Hjalgrim, Gustaf Edgren, JAMA, online 20 October 2015.

http://www.eurekalert.org/pub_releases/2015-10/jcu-cpm102015.php

Cancer-causing parasite may accelerate wound healing

Cancer-causing, parasitic worm could help patients recover from their wounds

It's short, ugly and deadly. But James Cook University scientists have found a cancer-causing, parasitic worm could help patients recover from their wounds.

JCU scientists at the Australian Institute of Tropical Health and Medicine (AITHM) have discovered that the parasitic worm that kills tens of thousands of people every year may also supercharge recovery from wounds.

The oriental liver fluke, Opisthorchis viverrini is caught by eating raw fish. It infects millions of people in south-east Asia and kills 26,000 people each year due to a parasite-induced bile duct cancer it causes, known as cholangiocarcinoma (CCA).

JCU scientists, Dr Michael Smout and Professor Alex Loukas found that a growth factor secreted by the one centimetre-long worm drives wound healing and blood vessel growth. However an unfortunate consequence of this accelerated wound repair over many years is an increased risk of developing liver cancer.

Dr Smout said the discovery means it's possible the growth factor could be used to accelerate the healing of chronic wounds such as diabetic ulcers and to develop a vaccine against the worm-induced cancer.

He said the vaccine would obviously benefit the people directly at risk of cancer, but the growth factor would also benefit the developed world as a possible wound healing agent.

"Diabetes is a big problem as we live longer and get heavier," he said. "There are increasing numbers of inflammatory diseases such as diabetes and associated non-healing wounds. A powerful wound healing agent designed by millennia of host-parasite co-evolution may accelerate the impaired healing processes that plague diabetic and elderly patients"

Dr Smout said the parasite could live for decades in the human body before CCA developed and it had an incentive to keep its host healthy while chewing away at its cells. He said scientists are still learning how this growth factor controls healing, and ultimate development of the discovery as a healing agent or vaccine was still a number of years away.

http://bit.ly/1N1qB56

World Health Organization may approve first malaria vaccine

Experts advising the World Health Organization look set to recommend the use of the world's first malaria vaccine.

Original story:

Malaria kills half a million African children under 5 every year. In April, a massive trial of the vaccine RTS,S, made by GlaxoSmithKline, found that children over 5 who got three doses plus a booster 18 months later had 36 per cent fewer cases of malaria over the subsequent four years. Cases fell 26 per cent in young babies vaccinated in the same way – enough to avert one or two cases of malaria per child.

The trial was carried out in seven African countries. Communities hosting the trial also received other measures to combat the disease, such as insecticide-treated bed nets and prompt diagnosis and treatment.

Although the vaccine offers only modest protection, Marcel Tanner of the Swiss Tropical and Public Health Institute in Basel, one of the WHO's advisers, says its benefits should be even greater in African communities with less access to these measures.

Complementary effect

In any case, he says, "a partially effective vaccine should be used where it will complement other anti-malaria measures". This would include areas with especially high rates of malaria transmission, areas where mosquitoes are hard to control and bed nets cannot totally prevent exposure.

In July, the European Medicines Agency advised that the vaccine would be cost-effective, especially in high-transmission zones. A map of these areas will be published next month.

African countries will then have to decide whether to adopt the vaccine. That may depend on whether they think they can keep giving children boosters.

The vaccine's effectiveness waned over the four-year trial, and children who didn't get a booster seemed more at risk of severe malaria after two years than children who got no vaccine at all. It is possible that the unvaccinated children had their immunity to malaria boosted by bouts of the disease. Vaccinated children who were free of the disease while the vaccine's effect lasted showed a decline in their antibodies if they didn't get a booster, leaving them less immune and prone to more intense malaria than children who had recently had either malaria or a second vaccination.

The WHO's advisers will present their evidence at a meeting in Geneva, Switzerland, this week, and their views will help shape its formal guidance for member states.

Update, 23 October 2015:

Scientists advising the WHO have now announced that they need more data before they can approve the vaccine for general release. "We need to know kids will come back for that fourth dose after 18 months," says committee member John Abramson of Wake Forest Baptist Medical Center in Winston-Salem, North Carolina.

The committee has called for up to five pilot projects in different areas of Africa with intense malaria transmission. Each study would involve about 200,000 children to see how reliably health systems can reliably administer all four doses. This decision could delay the approval of the vaccine by another five years.

http://nyti.ms/1Hiv7u9

American Cancer Society, in a Shift, Recommends Fewer Mammograms

One of the most respected and influential groups in the continuing breast-cancer screening debate said on Tuesday that women should begin mammograms later and have them less frequently than it had long advocated.

By DENISE GRADY OCT. 20, 2015

The American Cancer Society, which has for years taken the most aggressive approach to screening, issued new guidelines on Tuesday, recommending that women with an average risk of breast cancer start having mammograms at 45 and continue once a year until 54, then every other year for as long as they are healthy and likely to live another 10 years.

The organization also said it no longer recommended clinical breast exams, in which doctors or nurses feel for lumps, for women of any age who have had no symptoms of abnormality in the breasts.

Previously, the society recommended mammograms and clinical breast exams every year, starting at 40.

The changes reflect increasing evidence that mammography is imperfect, that it is less useful in younger women, and that it has serious drawbacks, like false-positive results that lead to additional testing, including biopsies.

But the organization's shift seems unlikely to settle the issue. Some other influential groups recommend earlier and more frequent screening than the cancer society now does, and some recommend less, leaving women and their doctors to sort through the conflicting messages and to figure out what makes the most sense for their circumstances.

In fact, although the new guidelines may seem to differ markedly from the old ones, the American Cancer Society carefully tempered its language to leave plenty of room for women's preferences. Though it no longer recommends mammograms for women ages 40 to 44, it said that those women should still "have the opportunity" to have the test if they choose to, and that women 55 and older should be able to keep having mammograms once a year.

This year, 231,840 new cases of invasive breast cancer and 40,290 deaths are expected in the United States.

The new guidelines were published on Tuesday in the Journal of the American Medical Association, along with an editorial and an article on the benefits and risks of screening, which provided evidence for the guidelines. A separate article and editorial on the subject were also published in another journal, JAMA Oncology.

http://bit.ly/1MyWnME

Did Life on Earth Really Start 4.1 Billion Years Ago? Not So Fast

Don't rewrite the Earth's history just yet

By Danny Lewis

Pinpointing the beginning of life on Earth is tricky. The fossil record only goes so far. While geologists have uncovered hints of life dating back 3.8 billion years, a controversial new study claims to have discovered evidence for the building blocks of life as old as 4.1 billion years. If true, this find suggests that organic compounds formed while the planet was still in its infancy.

While scientists know that our planet first formed about 4.5 billion years ago, the oldest evidence of life are fossil traces of 3.8 billion-year-old microbes called Archaea, Colin Barras writes for The New Scientist.

The intervening years between our planet's conception and evidence of Archea is coined the Hadean, after Hades, the Greek god of the underworld. During this time, the Earth's surface was likely molten. So scientists' only clues about this

period are hidden in tiny crystals called zircons, nearly indestructible baubles that form in magma, Julia Rosen writes for Science Magazine.

In the new study, published in the Proceedings of the National Academy of Sciences, scientists inspected 10,000 zircon crystals for clues about Earth's earliest days like insects sealed in amber. But they weren't looking for bugs, they were looking for other rocks, which is exactly what they found: One single 4.1 billion-year-old crystal containing graphite.

Graphite is made up entirely of carbon, and the isotopic pattern of this particular graphite resembled modern organic matter. "On Earth today, if you were looking at this carbon, you would say it was biogenic," lead author Elizabeth Bell tells Rosen. "Of course, that's more controversial for the Hadean."

Finding evidence of organics from the Hadean is a big deal, but it's a far cry from saying that Bell and her team discovered an ancient microbe. While a growing body of evidence suggests that early Earth wasn't as sterile as scientists once thought (and could have even had liquid water), some researchers are skeptical that this single piece of evidence is enough to suggest life existed during the Hadean.

"I know a lot of people want to use such data as evidence of life, but this is governed more by what they want the outcome to be rather than scientific principles," NASA astrobiologist Thomas McCollom tells Barras.

This skepticism in part comes from a study published in 2008 that claimed to have similarly found microscopic diamonds embedded in 4.25 billion-year-old zircon crystals. After their results were questioned, the scientists discovered the diamonds were merely contamination from grit used to polish the crystals.

While Bell and her team were careful to prevent similar issues, other researchers remain wary that graphite could have formed during the Hadean. Some suggest the graphite could have even been encapsulated at a later date by zircon melting and recrystallization.

"That one negative experience doesn't mean nobody should try again," California Institute of Technology geologist John Eiler tells Rosen. "But let's just say, I'm cautious."

While Bell and her colleagues are excited by their find, they aren't ruling out non-biological explanations for the graphite either. In the meantime, the best support for their theory would be replication—whether it is from other graphite-containing Hadean zircons or ancient Martain life, which has rocks even older than the Earth, Rosen writes.

"Hopefully we didn't just chance on the one freak zircon that had graphite in it," Bell tells Rosen. "Hopefully there is actually a fair amount of it."

http://www.eurekalert.org/pub_releases/2015-10/uow-mmp102115.php

Marker may predict risk of breast cancer spreading to the brain

New tumor marker test may help predict whether breast cancer is likely to spread or metastasize to the brain

MADISON, Wis. - A UW-Madison scientist working with an international team of researchers has developed a new tumor marker test that may help predict whether breast cancer is likely to spread or metastasize to the brain, a deadly complication with survival typically measured only in months after diagnosis.

The approach was based on prior laboratory experiments by Dr. Vincent Cryns, professor of medicine and study co-leader, on a cell stress protein called alpha B-crystallin. Working initially in mice, Cryns and colleagues found that alpha B-crystallin promoted brain metastasis in aggressive "triple-negative" breast cancers that lack expression of three different receptors, the estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER-2).

Based on these earlier findings, Cryns turned to an international team of scientists to examine whether levels of alpha B-crystallin in breast tumor samples could help identify those patients who would go on to develop metastasis to the brain. The team analyzed nearly 4,000 breast tumor samples from women with long-term clinical follow up, including sites of metastasis.

The researchers found that among women with metastatic disease, women whose breast tumors expressed alpha B-crystallin were nearly three times more likely to develop brain metastasis than women whose breast tumors did not express this protein. Alpha B-crystallin expression also predicted shorter survival after the initial breast cancer diagnosis and after the diagnosis of brain metastasis.

"The results were completely consistent with our predictions based on our prior laboratory studies," says Cryns.

"Our hope is that this test will become a useful biomarker to identify breast cancer patients at high risk for brain metastasis so that they could be monitored more closely or enrolled in trials of new agents to prevent brain metastasis. In addition, our lab is working on strategies to therapeutically target alpha B-crystallin as a strategy to treat or prevent brain metastasis in breast cancer," says Cryns. He cautions that these results need to be validated in additional studies before this test could be used in the clinic.

The research was funded by the Breast Cancer Research Foundation, the US National Cancer Institute, Cancer Research UK and the Canadian Breast Cancer Foundation. Additional scientists involved in the study include co-leader Maggie C. U. Cheang (The Institute of Cancer Research, London, UK), K. David Voduc, Torsten O. Nielsen, and Hagen Kennecke (University of British Columbia), Charles M. Perou and Cheng Fan (University of

North Carolina - Chapel Hill), J. Chuck Harrell (Virginia Commonwealth University), and Andy J. Minn (University of Pennsylvania). The study has been published in npj Breast Cancer.

http://www.eurekalert.org/pub_releases/2015-10/uon-nsa102115.php

New study: Algae virus can jump to mammalian cells

Verdict still out on whether virus causes slower cognition

Lincoln, Neb - New research led by the University of Nebraska-Lincoln has provided the first direct evidence that an algae-infecting virus can invade and potentially replicate within some mammalian cells.

Known as Acanthocystis turfacea chlorella virus 1, or ATCV-1, the pathogen is among a class of chloroviruses long believed to take up residence only in green algae. That thinking changed with a 2014 study from Johns Hopkins University and UNL that found gene sequences resembling those of ATCV-1 in throat swabs of human participants.

The new study, published in the Journal of Virology, introduced ATCV-1 to macrophage cells that serve critical functions in the immune responses of mice, humans and other mammals. By tagging the virus with fluorescent dye and assembling three-dimensional images of mouse cells, the authors determined that ATCV-1 successfully infiltrated them.

The authors also measured a three-fold increase in ATCV-1 within 24 hours of introducing the virus. The relatively modest spike nevertheless suggests that ATCV-1 can replicate within the macrophage cells, according to co-author David Dunigan.

Though a few studies have documented viruses jumping from one biological kingdom to another, chloroviruses were previously thought to have a limited "host range" that stopped well short of the animal kingdom, Dunigan said.

"A few years ago, no one I know would have made a prediction like this," said Dunigan, research professor of plant pathology and member of the Nebraska Center for Virology. "You probably would've been laughed out of the room. But we are now in the middle of something that is so very interesting."

The macrophage cells underwent multiple changes characteristic of those breached by a virus, Dunigan said. These changes eventually included a form of programmed death that virologists consider an innate "scorched earth" defense against the spread of viruses, which require living cells to survive and replicate.

Before dying, the cells exhibited multiple signs of stress that tentatively support links to mild cognitive impairments first reported in the 2014 paper, available at http://go.unl.edu/rfuo. The new study measured a post-viral rise in interleukin 6, a cellular protein that previous research has linked with diminished spatial learning and certain neurological diseases. The authors also reported an increase in nitric oxide, an important signaling molecule that has been associated with memory impairments when produced in excess.

The 2014 investigation, which was initially designed to test the cognitive functioning of human participants, found that those with the ATCV-1 DNA performed slightly worse on measures of visual processing and visual motor speed. Mice inoculated with the virus showed similar deficits in memory and attention while navigating mazes. The 2014 paper further suggested that ATCV-1 altered the expression of more than 1,000 genes in the rodent hippocampus, an area of the brain tied to memory and spatial navigation.

The new study's authors are continuing their collaboration with Johns Hopkins in the hope of ultimately confirming whether and how the virus contributes to any cognitive deficits suggested by the initial studies.

"It is still unclear whether the factors induced by the cell-based virus challenge could also be induced in the whole animal, and whether the induced factors cause cognitive impairments in the animal or the human," said co-author Tom Petro, professor of microbiology and immunology at the University of Nebraska Medical Center.

Dunigan said he and his colleagues are also searching for other cellular responses to ATCV-1 while investigating how these responses might drive systemic changes in mice. "These are pretty big, unexplored questions," Dunigan said. "There are so many very basic virological questions that we can and want to ask."

The study was co-authored by James Van Etten, a William Allington Distinguished Professor of plant pathology; Irina Agarkova, research assistant professor of plant pathology; You Zhou, research professor at the Morrison Microscopy Core Research Facility of the Center for Biotechnology; and Robert Yolken, director of the Stanley Neurovirology Laboratory at Johns Hopkins University.

The team's research was supported in part by the National Center for Research Resources, part of the National Institutes of Health, under grant number P30-RR031151.

http://www.eurekalert.org/pub_releases/2015-10/luhs-aaa102115.php

Antidepressants and Alzheimer's disease drugs might boost recovery in stroke patients

But more research needed before recommending their routine use

MAYWOOD, Ill. - Evidence is mounting that drugs used to treat depression and Alzheimer's disease also can help patients recover from strokes.

But there are conflicting findings from studies of these and other drugs given to recovering stroke patients. Large, well-designed studies are needed before any drug can be recommended routinely for stroke recovery, according to a study in the journal Drugs and Aging by neurologists Xabier Beristain, MD, and Esteban Golombievski, MD, of Loyola University Medical Center and Loyola University

Chicago Stritch School of Medicine. "These medications have not yet been clearly proven to be of benefit to patients recovering from strokes," Dr. Beristain said.

Speech and physical therapies traditionally have been the mainstays of stroke rehabilitation programs. But more than half of stroke survivors are left with some neurological impairment. "The limitations of these rehabilitation efforts have sparked an interest in finding other ways to enhance neurological recovery," Drs. Beristain and Golombievski write.

So far, the most promising drug treatments are antidepressants to improve motor recovery and Alzheimer's disease drugs to boost recovery from aphasia (impaired ability to speak, write and understand verbal and written language).

About one in three stroke patients suffers depression, which can limit a patient's ability to participate in rehabilitation. There is mounting evidence that the class of antidepressants known as selective serotonin reuptake inhibitors, or SSRIs (such as Prozac, Paxil and Celexa), may enhance neurological recovery beyond their effect on mood. Another type of antidepressant, norepinephrine reuptake inhibitor (NRI) also has shown benefit.

An analysis of 56 clinical trials of SSRIs found the drugs appeared to improve dependence, disability, neurological impairment, anxiety and depression after stroke. However, these findings should be taken with caution because the studies have different designs. Several additional clinical trials now underway are evaluating the use of antidepressants to enhance stroke recovery.

There is growing evidence that Alzheimer's disease drugs called acetylcholinesterase inhibitors (including Aricept, Exelon and Razadyne) can improve aphasia in stroke patients. A second type of Alzheimer's medication under study is memantine (Namenda). When used in combination with therapy, memantine has shown language benefits lasting at least one year when compared with a placebo. But clinical evidence of memantine for stroke recovery remains limited.

So far, most studies of these and other drugs used for stroke recovery have been small, employing different methodologies and time windows between the stroke and the clinical intervention. "We need well-designed, large clinical trials with enough power to establish the usefulness of medications as adjuvants to rehabilitation before we can routinely recommend the use of these agents to enhance neurological recovery after stroke," Drs. Beristain and Golombievski write.

Dr. Beristain is an associate professor in the Department of Neurology of Loyola University Chicago Stritch School of Medicine. Dr. Golombievski is a former neurology fellow at Loyola. The paper is titled "Pharmacotherapy to Enhance Cognitive and Motor Recovery Following Stroke."

http://bbc.in/1MyXtYI

The controversy over the chronic form of Lyme disease

Lyme disease is increasing in the UK. But there is huge controversy over the existence of a chronic form of the disease that resists treatment.

By Camila Ruz BBC News Magazine

Lyme disease is a bacterial infection that is spread to humans by a bite from an infected tick. The symptoms tend to start with a distinctive rash shaped like a bullseye. Not everyone gets one and this can make diagnosis tricky.

Early symptoms include tiredness and muscle aches. But if left untreated the disease can cause pain in the joints, paralysis of facial muscles, mental confusion and heart problems.

Cases of the bacteria quadrupled between 2000 and 2011, although some of that increase may be down to better reporting. But the NHS estimates there are now up to 3,000 cases of Lyme disease a year in England and Wales.

Recently, a number of high-profile people have been complaining that they have a chronic form of the disease that resists treatments and persists with severe symptoms - but such a condition is not widely accepted by doctors. Others have talked about Lyme disease being under-diagnosed or being the root cause of other illnesses.

It has been called the "most significant threat to human health" by billionaire Phones 4U founder John Caudwell who says his family has suffered with the disease for years.

The model Bella Hadid has also been revealed to have the disease. Her mother Yolanda Foster documents her struggle to find a cure for the "chronic" infection on Instagram, frequently posting pictures of herself taking alternative treatments.

But the idea of a Lyme infection that is not completely treated and lingers for years is controversial. Most doctors say that the vast majority of people with the disease, if caught early, can be treated completely with just a short course of antibiotics. "There is no consensus over whether chronic Lyme actually exists," says Matthew Dryden, a consultant microbiologist at Public Health England's Rare and Imported Pathogens Laboratory (RIPL).

The sceptical view is that "chronic Lyme disease" is a term that has sprung up in the US and is used inaccurately to cover a wide range of vague symptoms that are not all related to a Lyme infection. The other view is that it's a debilitating illness that is misunderstood and requires years of antibiotics to treat.

The real picture may be somewhere in between, says Dryden. In the UK, there has been a gradual recognition that a minority of Lyme disease patients do develop long-term symptoms, especially if there has been a delay in treating the infection. But the jury is still out on the cause and how best to treat them.

Helen Rowe is one such patient. She was a staff nurse with the NHS who was bitten in July 2008 and developed a circular rash. Rowe says she was given inadequate antibiotics at the time and that the "bacteria reared its ugly head" a year later. By then she had pages of neurological symptoms. "My brain just wouldn't work," she says. "I would say 'go and sit on the shed', instead of go and sit on the sofa."

Her blood test for Lyme disease came back positive but other diseases were also suspected and the result was not followed up. It took another five years before she was diagnosed by the NHS and could begin treatment. After three weeks of intravenous antibiotics she began to improve.

But now that her treatment has finished, Rowe says she still has symptoms. "I don't think you really get rid of it," she adds. "I don't know whether it's active or just dormant. I don't know if this is just the 'post' side of it."

The "post side" means Post-Treatment Lyme Disease Syndrome which is the medical term for describing lingering symptoms including fatigue and joint pain after treatment for confirmed Lyme disease. Its symptoms are seen by some as similar to those of Chronic Fatigue Syndrome, also known as Myalgic Encephalomyelitis (ME), and as little understood.

But some people do not like the term. "In including the word 'post' it implies this is a syndrome following Lyme disease - ie that the disease itself has been cured," says Stella Huyshe-Shires, director of Lyme Disease Action UK.

She argues that people can instead have a persistent infection. It took three years for her to get her diagnosis after being bitten by a tick in 1999. Her blood tests still show an immune response to Lyme disease. But it's not possible to use those tests to tell the difference between past exposure to the bacteria or a current illness.

It's hard to convince people that they have been fully treated when they are still feeling unwell, especially if the possibility of Lyme disease cannot be ruled out completely. The bacteria do have ways of evading the immune system and - albeit rarely - they can cause a low-grade local infection if the treatment was not good enough or was started too late, explains Tim Brooks, head of the Rare and Imported Pathogens Laboratory.

How to reduce the risk from Lyme disease

Keep to footpaths and avoid long grass when out walking

Wear appropriate clothing in tick-infested areas (a long-sleeved shirt and trousers tucked into your socks)

Wear light-coloured fabrics that may help you spot a tick on your clothes

Use insect repellent on exposed skin

Inspect your skin for ticks, particularly at the end of the day - remove any ticks you find promptly

Check your children's head and neck areas, including their scalp

Make sure ticks are not brought home on your clothes

Check that pets do not bring ticks into your home in their fur

Source: NHS Choices

There are also reports of various types of bacterial "persistor cells" that can survive antibiotic treatment, although whether they actually make someone ill is not known.

But long-term symptoms do not have to be from active Lyme disease. They could also be caused by tissue damage and problems with the immune system that were triggered by the previous infection.

There are plenty of diseases that can, rarely, lead to similar long-term symptoms from flu to glandular fever. "That's the mystery of these chronic symptoms that can be triggered by all sorts of infections," says Dryden. "They are very debilitating but nobody can find any pathological mechanism to explain them."

Ticks can also transmit more than one disease at a time. More research needs to be done to find out what diseases ticks are transmitting in the UK, says Dryden. "There could also be unknown viruses or toxins that are causing these symptoms," he adds. The question of co-infection has also been raised as a key uncertainty that needs to be resolved.

The uncertainty can be hard to deal with. Patients often end up being referred from specialist to specialist with no satisfying explanation for how they are feeling. This has led to protests from some groups who feel that their experiences are being ignored.

In the UK, some patients, fed up with negative results from the NHS, go overseas. But although some argue that the standard UK tests have limitations, they are done under the main internationally recognised standards. Some private clinics abroad are willing to use tests that are not verified for Lyme disease diagnosis, says Huyshe-Shires.

If you have been bitten:

Remove the tick as soon as possible - the safest way is to use a pair of fine-tipped tweezers, or a tick removal tool

Grasp the tick as close to the skin as possible, pull upwards slowly and firmly, as mouthparts left in the skin can cause a local infection

Once removed, apply antiseptic to the bite area, or wash with soap and water and keep an eye on it for several weeks for any changes

Contact your GP if you begin to feel unwell and remember to tell them you were bitten by a tick or have recently spent time outdoors

Source: Public Health England

"Desperate patients want a solution and you can quite understand that," she adds. But there are dangers that people could be persuaded to pay for long-term treatments that are not needed.

The best treatment for people with a clear history of Lyme disease and continued symptoms is not yet known. Some doctors - on both sides of the Atlantic - take a hard line on it and are reluctant to give more antibiotics without stronger evidence that they will help. This is especially true when faced with increased antibiotic drug resistance and when long-term intravenous treatment comes with a risk of blood poisoning.

Others argue that there should be more flexibility and that doctors have to discuss clinical judgements with their patients. "It's a very difficult decision," says Dryden. "There do seem to be some patients who respond to longer-term antibiotics but I'm very guarded in who I give them to."

It can be a frustrating position for doctors as well as patients. After spending 18 months out of work due to her illness, Helen Rowe is working again at a clinic in Weymouth and tries to advise GPs on cases that seem similar to hers. "I see the other side of it now as a nurse," she says. "You're damned if you do and damned if you don't."

http://www.bbc.com/news/uk-scotland-34583642

The woman who can smell Parkinson's disease

Meet the woman from Perth whose super sense of smell could change the way Parkinson's disease is diagnosed.

By Elizabeth Quigley BBC Scotland news

Joy Milne's husband, Les, died in June, aged 65. He worked as a consultant anaesthetist before being diagnosed with Parkinson's at the age of 45.

One in 500 people in the UK has Parkinson's - that is 127,000 across Britain. It can leave people struggling to walk, speak and sleep. There is no cure and no definitive diagnostic test.

Joy noticed something had changed with her husband long before he was diagnosed - six years before. She says: "His smell changed and it seemed difficult to describe. It wasn't all of a sudden. It was very subtle - a musky smell. "I got an occasional smell." Joy only linked this odour to Parkinson's after joining the charity Parkinson's UK and meeting people with the same distinct odour.

By complete chance she mentioned this to scientists at a talk. They were intrigued. Edinburgh University decided to test her - and she was very accurate.

Dr Tilo Kunath, a Parkinson's UK fellow at the school of biological sciences at Edinburgh University, was one of the first scientists Joy spoke to.

He says: "The first time we tested Joy we recruited six people with Parkinson's and six without.

"We had them wear a t-shirt for a day then retrieved the t-shirts, bagged them and coded them.

"Her job was to tell us who had Parkinson's and who didn't.

"Her accuracy was 11 out of 12. We were quite impressed."

Dr Kunath adds: "She got the six Parkinson's but then she was adamant one of the 'control' subjects had Parkinson's.

"But he was in our control group so he didn't have Parkinson's.

"According to him and according to us as well he didn't have Parkinson's.

"But eight months later he informed me that he had been diagnosed with Parkinson's.

"So Joy wasn't correct for 11 out of 12, she was actually 12 out of 12 correct at that time.

"That really impressed us and we had to dig further into this phenomenon."

And that is exactly what they are doing.

Scientists believe that changes in the skin of people with early Parkinson's produces a particular odour linked to the condition.

They hope to find the molecular signature responsible for the odour and then develop a simple test such as wiping a person's forehead with a swab.

The charity Parkinson's UK is now funding researchers at Manchester, Edinburgh and London to study about 200 people with and without Parkinson's.

Image caption Katherine Crawford, of Parkinson's UK, said it was an incredibly difficult disease to diagnose

A simple test for Parkinson's could be life-changing, according to Katherine Crawford, the Scotland director of Parkinson's UK.

"This study is potentially transformational for the lives of people living with Parkinson's," she says.

"Parkinson's is an incredibly difficult disease to diagnose.

"We still effectively diagnose it today the way that Dr James Parkinson diagnosed it in 1817, which is by observing people and their symptoms.

"A diagnostic test like this could cut through so much of that, enable people to go in and see a consultant, have a simple swab test and come out with a clear diagnosis of Parkinson's.

"It would be absolutely incredible and life-changing for them immediately."

Ms Crawford adds: "They and their professional colleagues would be able to discuss and arrange a treatment programme, be able to monitor the progression of the disease and treat it appropriately as it went on and it would potentially offer more opportunities for people living with Parkinson's to get involved in research."

It might have been an accidental discovery but Joy hopes it will make a real difference to people starting out on their own journey with Parkinson's.

http://www.bbc.com/news/health-34592242

Aspirin trial to examine if it can stop cancer returning

The world's largest clinical trial to examine whether aspirin can prevent cancers returning has begun in the UK.

By Smitha Mundasad Health reporter

About 11,000 people who have had early bowel, breast, prostate, stomach and oesophageal cancer will be involved.

Uncertainty about the drug's possible anti-cancer qualities has led to fierce medical debate in recent years.

If it is proven to work, scientists say it would be "game-changing", by providing a cheap and effective way to help more patients survive.

During the study, funded by the charity Cancer Research UK and the NIHR - the research arm of the NHS - patients will take a tablet every day for five years.

'Toughest experiences'

Researchers will compare groups of patients taking different doses of aspirin with people taking dummy (placebo) pills and check for any recurrences of cancer.

Dr Fiona Reddington from Cancer Research UK said: "The trial is especially exciting as cancers that recur are often harder to treat so finding a cheap and effective way to prevent this is potentially game-changing for patients."

The trial will run across 100 UK centres, involving patients who are having or have had treatment for early cancer, and will last up to 12 years.

But scientists warn that aspirin is not suitable for everyone and should not be used without medical advice.

Taking the drug every day comes with a serious health warning as it can cause side effects such as ulcers and bleeding from the stomach, or even the brain.

Clear proof sought

Prof Ruth Langley, lead investigator on the trial, said: "There's been some interesting research suggesting that aspirin could delay or stop early stage cancers coming back but there's been no randomised trial to give clear proof.

"The trial aims to answer this question once and for all.

"If we find that aspirin does stop these cancers returning, it could change future treatment - providing a cheap and simple way to help stop cancer coming back and helping more people survive."

Alex King, 51, who was diagnosed with breast cancer in December 2009 and has been given the all-clear, said: "Having cancer was one of the toughest experiences of my life.

"Any opportunity to reduce the chance of cancer coming back is incredibly important so patients can rest more easily."

Many people are already prescribed daily, low-dose aspirin as a heart drug.

http://www.eurekalert.org/pub_releases/2015-10/uoc-pih102115.php

Plague in humans 'twice as old' but didn't begin as flea-borne, ancient DNA reveals

Plague has been endemic in human populations for more than twice as long as previously thought

New research using ancient DNA has revealed that plague has been endemic in human populations for more than twice as long as previously thought, and that the ancestral plague would have been predominantly spread by human-to-human contact -- until genetic mutations allowed Yersinia pestis (Y. pestis), the bacteria that causes plague, to survive in the gut of fleas.

These mutations, which may have occurred near the turn of the 1st millennium BC, gave rise to the bubonic form of plague that spreads at terrifying speed through flea -- and consequently rat -- carriers. The bubonic plague caused the pandemics that decimated global populations, including the Black Death, which wiped out half the population of Europe in the 14th century.

Before its flea-borne evolution, however, researchers say that plague was in fact endemic in the human populations of Eurasia at least 3,000 years before the first plague pandemic in historical records (the Plague of Justinian in 541 AD).

They say the new evidence that Y. pestis bacterial infection in humans actually emerged around the beginning of the Bronze Age suggests that plague may have been responsible for major population declines believed to have occurred in the late 4th and early 3rd millennium BC.

The work was conducted by an international team including researchers from the universities of Copenhagen, Denmark, and Cambridge, UK, and the findings are published today in the journal Cell.

"We found that the Y. pestis lineage originated and was widespread much earlier than previously thought, and we narrowed the time window as to when and how it developed," said senior author Professor Eske Willerslev, who recently joined Cambridge University's Department of Zoology from the University of Copenhagen.

"The underlying mechanisms that facilitated the evolution of Y. pestis are present even today. Learning from the past may help us understand how future pathogens may arise and evolve," he said.

Researchers analysed ancient genomes extracted from the teeth of 101 adults dating from the Bronze Age and found across the Eurasian landmass from Siberia to Poland.

They found Y. pestis bacteria in the DNA of seven of the adults, the oldest of whom died 5,783 years ago -- the earliest evidence of plague. Previously, direct

molecular evidence for Y. pestis had not been obtained from skeletal material older than 1,500 years.

However, six of the seven plague samples were missing two key genetic components found in most modern strains of plague: a "virulence gene" called ymt, and a mutation in an "activator gene" called pla.

The ymt gene protects the bacteria from being destroyed by the toxins in flea guts, so that it multiplies, choking the flea's digestive tract. This causes the starving flea to frantically bite anything it can, and, in doing so, spread the plague.

The mutation in the pla gene allows Y. pestis bacteria to spread across different tissues, turning the localised lung infection of pneumonic plague into one of the blood and lymph nodes.

Researchers concluded these early strains of plague could not have been carried by fleas without ymt. Nor could they cause bubonic plague -- which affects the lymphatic immune system, and inflicts the infamous swollen buboes of the Black Death -- without the pla mutation.

Consequently, the plague that stalked populations for much of the Bronze Age must have been pneumonic, which directly affects the respiratory system and causes desperate, hacking coughing fits just before death. Breathing around infected people leads to inhalation of the bacteria, the crux of its human-to-human transmission.

Study co-author Dr Marta Mirazón-Lahr, from Cambridge's Leverhulme Centre for Human Evolutionary Studies (LCHES), points out that a study earlier this year from Willerslev's Copenhagen group showed the Bronze Age to be a highly active migratory period, which could have led to the spread of pneumonic plague.

"The Bronze Age was a period of major metal weapon production, and it is thought increased warfare, which is compatible with emerging evidence of large population movements at the time. If pneumonic plague was carried as part of these migrations, it would have had devastating effects on small groups they encountered," she said.

"Well-documented cases have shown the pneumonic plague's chain of infection can go from a single hunter or herder to ravaging an entire community in two to three days."

The most recent of the seven ancient genomes to reveal Y. pestis in the new study has both of the key genetic mutations, indicating an approximate timeline for the evolution that spawned flea-borne bubonic plague.

"Among our samples, the mutated plague strain is first observed in Armenia in 951 BC, yet is absent in the next most recent sample from 1686 BC -- suggesting bubonic strains evolve and become fixed in the late 2nd and very early 1st millennium BC," said Mirazón-Lahr.

"However, the 1686 BC sample is from the Altai mountains near Mongolia. Given the distance between Armenia and Altai, it's also possible that the Armenian strain of bubonic plague has a longer history in the Middle East, and that historical movements during the 1st millennium BC exported it elsewhere."

The Books of Samuel in the Bible describe an outbreak of plague among the Philistines in 1320 BC, complete with swellings in the groin, which the World Health Organization has argued fits the description of bubonic plague. Mirazón-Lahr suggests this may support the idea of a Middle Eastern origin for the plague's highly lethal genetic evolution.

Co-author Professor Robert Foley, also from Cambridge's LCHES, suggests that the lethality of bubonic plague may have required the right population demography before it could thrive.

"Every pathogen has a balance to maintain. If it kills a host before it can spread, it too reaches a 'dead end'. Highly lethal diseases require certain demographic intensity to sustain them.

"The endemic nature of pneumonic plague was perhaps more adapted for an earlier Bronze Age population. Then, as Eurasian societies grew in complexity and trading routes continued to open up, maybe the conditions started to favour the more lethal form of plague," Foley said.

"The Bronze Age is the edge of history, and ancient DNA is making what happened at this critical time more visible," he said.

Willerslev added: "These results show that the ancient DNA has the potential not only to map our history and prehistory, but also discover how disease may have shaped it."

http://www.eurekalert.org/pub_releases/2015-10/uom-gtt102215.php

Gene therapy treats all muscles in the body in muscular dystrophy dogs

Human clinical trials are next step

COLUMBIA, Mo. --- Muscular dystrophy, which affects approximately 250,000 people in the U.S., occurs when damaged muscle tissue is replaced with fibrous, fatty or bony tissue and loses function. For years, scientists have searched for a way to successfully treat the most common form of the disease, Duchenne Muscular Dystrophy (DMD), which primarily affects boys.

Now, a team of University of Missouri researchers have successfully treated dogs with DMD and say that human clinical trials are being planned in the next few years.

"This is the most common muscle disease in boys, and there is currently no effective therapy," said Dongsheng Duan, the study leader and the Margaret

Proctor Mulligan Professor in Medical Research at the MU School of Medicine. "This discovery took our research team more than 10 years, but we believe we are on the cusp of having a treatment for the disease."

Patients with Duchenne muscular dystrophy have a gene mutation that disrupts the production of a protein known as "dystrophin."

Absence of dystrophin starts a chain reaction that eventually leads to muscle cell degeneration and death. Affected boys lose their ability to walk and breathe as they get older. This places significant limitations on individuals afflicted with the disease. Dystrophin also is one of the largest genes in the human body.

"Due to its size, it is impossible to deliver the entire gene with a gene therapy vector, which is the vehicle that carries the therapeutic gene to the correct site in the body," Duan said.

"Through previous research, we were able to develop a miniature version of this gene called a microgene. This minimized dystrophin protected all muscles in the body of diseased mice."

However, it took the team more than 10 years to develop a strategy that can safely send the micro-dystrophin to every muscle in a dog that is afflicted by the disease. The dog has a body size similar to that of an affected boy. Success in the dog will set the foundation for human tests.

In this latest study, the MU team demonstrated for the first time that a common virus can deliver the microgene to all muscles in the body of a diseased dog. The dogs were injected with the virus when they were two to three months old and just starting to show signs of DMD. The dogs are now six to seven months old and continue to develop normally.

"The virus we are using is one of the most common viruses; it is also a virus that produces no symptoms in the human body, making this a safe way to spread the dystrophin gene throughout the body," Duan said.

"These dogs develop DMD naturally in a similar manner as humans. It's important to treat DMD early before the disease does a lot of damage as this therapy has the greatest impact at the early stages in life."

This study, "Safe and bodywide muscle transduction in young adult Duchenne muscular dystrophy dogs with adeno-associated virus," was published in Human Molecular Genetics and was supported by grants from the Department of Defense, Jesse's Journey-The Foundation for Cell and Gene Therapy, the National Institutes of Health, Hope for Javier, the Kansas City Area Life Sciences Institute and MU. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies

Duan also recently received a five-year, $3 million grant from the NIH to continue his research. The technology used to create the gene-therapy has been licensed by Solid Ventures, LLC.

http://bit.ly/1itHcGl

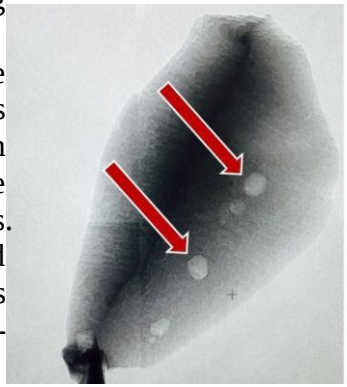
Earlier Origin of Life Raises Major Planetary Puzzles

Searching for clues to the earliest life on Earth is a tricky business.

By Caleb A. Scharf | October 22, 2015

Very little of the ancient planetary crust remains accessible, with the oldest recovered rock chunks clocking in at an age of somewhere around 3.8 billion years. To add to the problem, it seems unlikely that life consisted of anything but microscopic, single-celled, organisms for at least the first billion years - leaving the barest of geochemical or fossil remains.

However, even older geophysical samples do exist - in the form of tiny crystals of zircon (zirconium silicate) found inside some of the most ancient rocks. Some of these highly resilient grains have been dated to an age of approximately 4.4 billion years via their uranium, thorium, and lead contents. The isotopic ratios of oxygen in zircons also suggest that at least some of these grains interacted with a hydrosphere - evidence of liquid water on a very young Earth.



Carbon inclusions in a 4.1 Gya zircon crystal **(Credit: Stanford/UCLA)**

Now a new study, reported by Bell et al. in the Proceedings of the National Academy of Science, has trawled through over 10,000 tiny zircon crystals in search of the signs of early life. A total of 656 of these zircons were found to contain dark specks, or inclusions. 79 out of those zircons were subjected to more detailed analysis and one 4.1 billion year old zircon was discovered to contain two microscopic bits of graphite - pure carbon.

Critically, when the researchers measure the carbon isotope ratio of these graphite inclusions they find a significant enhancement of the abundance of the lighter carbon-12 isotope compared to carbon-13. This kind of isotopic bias is generally considered as a smoking gun for biological processes - which tend to preferentially sequester lighter isotopes. In fact the 13C/12C ratio seen in this 4.1 billion year old graphite is a near identical match to that of kerogen deposits across the Earth's rock record, and to the ratio in living microbial organisms.

The tentative conclusion is that these carbon specks could have been incorporated into the forming zircons from a biological source 4.1 billion years ago.

If further research supports this interpretation it'll be a stunning outcome - demonstrating that life existed on Earth barely 400 million years after the planet finished the majority of its hugely violent formative processes.

Except this now runs headlong into the generally accepted picture of what was happening to the Earth, and the solar system between 3.8 and 4.1 billion years ago. Evidence from lunar cratering and rocks retrieved by the Apollo missions, together with data from meteoritic compositions, have suggested that during this time the inner planets were experiencing what's now known as the Late Heavy Bombardment.

This is thought to have been a period of intense asteroid impacts on the Moon and, by extension, the Earth. In fact it's also been seen as a critical piece of the final touch-up to Earth's crust, adding a 'late veneer' of material. The cause of this bombardment has been hypothesized as the literal fallout (or fall-in) of material due to a dynamical reconfiguration of the outer, giant, planets.

Understanding that reconfiguration is in itself an entire field of research, but in essence this dynamical activity could help also explain the present distribution of Kuiper-belt objects and the orbital arrangement of the outer worlds in our solar system.

The problem is that the bombardment of Earth would have been intense, with some estimates suggesting that there were more than 20,000 impact events capable of making craters larger than 20 kilometers across, and several impacts producing 5,000 kilometer craters. In other words, big, bad stuff would have been taking place pretty much every 100 years for about 300 million years.

That could make the Earth's environment a very tough place for life. So finding evidence for life on Earth just prior to this bombardment, and right after, raises some very big questions.

Did this bombardment really happen when we think it did? Or did it take place before the first life? Could life on Earth have survived through those 300 million years of planetary pummeling? Or, did life just keep re-starting - re-originating - all through that period until finally the planet stopped killing it off?

We don't have answers to these questions yet, but these tiny carbon specks inside one ancient zircon crystal could prove to be a pivotal discovery in our efforts to understand life's intimate relationship to its cosmic cradle.

http://www.medscape.com/viewarticle/852655?src=rss

What Physicians and Other Healthcare Providers Need to Know Today About End-of-Life Care

End-of-Life Care: New CMS Reimbursement Rules

Robert Glatter, MD; Ferdinando L. Mirarchi, DO

Robert Glatter, MD: This past summer, the federal government announced a proposal to reimburse healthcare providers for talking to Medicare beneficiaries about end-of-life care.[1] This move comes after increasing calls for a better approach to conversations about dying, which can ultimately improve patient care and reduce healthcare expenditures. The proposal will be finalized in November 2015, with the goal to begin reimbursement for such discussions on January 1, 2016.

The rule, announced in July of 2015, would allow doctors, nurses, nurse practitioners (NPs), and physician assistants (PAs) to bill for discussions about end-of-life care, which was supported by a September 2014 report[2] by the Institute of Medicine (IOM) titled, *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*.

End-of-life care has changed considerably since the IOM last reported on this issue in 1998.[3] To begin with, palliative care is now well established in medicine, nursing, and social work. Yet there is considerable room for improvement. Americans have strong preferences and feelings about the type of care they would like to receive at the end of life. They generally prefer to die at home and with the ability to maintain control over healthcare decisions, according to the recent report.[2] As of now, however, there is minimal or no planning really put in place.

The report details findings about more than a quarter of adults, including those aged 75 years and older, who have not given thought to specifics regarding end-of-life care. Many more have not written down their preferences or spoken with their families about their true wishes, according to the report. Because our healthcare system is often focused on curative care rather than supportive and comfort care, such discussions are vital to support the preferences of dying patients and their families.

In 2009, efforts to reimburse medical providers for having such discussions ran into opposition after mostly Republican opponents of the Affordable Care Act (ACA) believed that the law would lead to death panels that aim to produce cost savings by rationing care. A provision to pay physicians for such end-of-life counseling was actually stripped from the final bill. Physicians who counsel *newly* enrolled Medicare beneficiaries, however, are currently reimbursed under the ACA, but this reimbursement does not apply to those patients who are currently enrolled in Medicare.

Many medical providers believe that we are not having these conversations often and soon enough. Family members, trying to do the right thing, may end up feeling guilty and uncertain without having had this kind of conversation. Also, the approach to a proper conversation regarding end-of-life care should not only focus on the existence of advance directives such as do-not-resuscitate (DNR) orders, or whether a living will exists, but more recently there is a significant push to generate a document known as a physician orders for life-sustaining treatment (POLST). Ideally, a POLST or a living will should be in place well before a catastrophic event occurs that may require care in an emergency department (ED).

A POLST clarifies and spells out instructions for medical providers to follow after a catastrophic event, such as a cardiac arrest, or when caring for patients who might be entering the last stages of a terminal disease. One expert who is well qualified to discuss aspects of end-of-life care and POLST documents is Dr Ferdinando Mirarchi, medical director in the department of emergency medicine at University of Pittsburgh Medical Center-Hamot in Erie, Pennsylvania. He is also the principal investigator of The Realistic Interpretation of Advanced Directives (TRIAD) studies.[4] Welcome back, Dr Mirarchi.

Can you explain what a POLST document is? How is it different from a living will or other advance directives?

What Makes A POLST Different

Ferdinando L. Mirarchi, DO: Great point! It is really important to clarify the difference between the POLST document and an advance directive. POLST is a medical order set that is supposed to go into place, just like any other physician order set, and that other medical professionals like nurses follow. The point of it is to create an order set that would encompass a patient's care spectrum when in cardiac arrest and when not in cardiac arrest, as well as to address other issues, etc. It is very important to clarify that POLST is an "immediately actionable document"—an order set—whereas a living will is not an immediately actionable order set. The POLST is a document that comes into play when a patient is frail, elderly, or expected to die within 6 months to 1 year. A living will comes into play when a patient cannot speak for themselves and has entered an end-stage medical condition or a persistent vegetative state. Although a living will can be helpful in creating a POLST document, the two are not the same. A living will declining treatment is not the same as a POLST specifying DNR with comfort measure only. Again, one is actionable (POLST), while the other one (living will) is not actionable.

Dr Glatter: To clarify, a DNR only refers to a condition when the patient has no pulse and is not breathing. Would you agree with that?

Dr Mirarchi: That is correct. A DNR does not equate with end-of-life care or do-not-treat orders. That is a misnomer that has developed over the years, which we in the healthcare community have allowed to happen. DNR orders only come into play when a patient is found in cardiac arrest.

Dr Glatter: In terms of a checklist or a resuscitation pause (what we would call an advance directive pause), where do you see this concept in terms of implementation into care? Do you see that happening in the near future?

Dr Mirarchi: I think it is imperative that it happens in the near future. In fact, the Joint Commission[5] recently came out with a statement about the whole issue of safety surrounding end-of-life care. We know from Atul Gawande's work[6] on surgical pauses that checklists have extreme benefit in preventing errors. At this point in time, I think a patient safety checklist is going to become imperative to making sure that we have safe, balanced discussions that will provide the patient with the ability to have informed consent. We have discussed the importance of checklists in previous conversations on Medscape.

Talking About End-of-Life

Dr Glatter: Getting to the discussions themselves, there have been several current procedural terminology (CPT) codes created for these types of discussions, though they have obviously not been activated. The codes are for coding of discussions of up to 30 minutes and even beyond. Certainly these discussions take time, and I think with the average amount of time that most medical physicians, PAs, and NPs have to care for patients, 30 minutes and even beyond is a significant amount of time. Do you see the time factor being an issue?

Dr Mirarchi: Yes and no. This is going to be new, so essentially physicians are going to have to figure out how they are going to go about having this discussion. If you are involved in a system today—and most of us are, because of all of the flux happening in medicine right now with increasing numbers of clinicians employed by big healthcare systems—that system is going to determine what resources clinicians will be utilizing to have these discussions based on the merits of compliance with the rule, so they can bill out for that first half-hour and second half-hour. There is going to be a lot of variable practice out there, ranging from the paternalistic approach of some organizations to the more patient-centered approaches of others. In order to ensure informed consent, it is important that these conversations be a balanced and not a leading discussion.

Dr Glatter: Another important question is whether the documents will be legally binding and official, assuming there is informed consent in these types of conversations.

Dr Mirarchi: I think they will be binding, and that is where the POLST is gaining ground as they are enacted into statutes across the states. There are states where there is physician or provider immunity. There are states where there is not provider immunity. If POLST documents are to really become embraced, there is going to have to be some immunity that comes with them. I think that when physicians do this, they are more than likely going to be creating POLST documents for people rather than attorneys. In contrast, patients might see their attorney to create a living will or go to a site like mydirectives.com and create a digitally created living will.

Dr Glatter: Anecdotally, I have seen social workers create these documents for patients in the throes of resuscitations. Nonmedical people are certainly informed, but they cannot give the type of advice a physician necessarily could give. Often a

group discussion takes place with the family member and the social worker, and then the document is created. We need to be aware of that.

Dr Mirarchi: That is a great point. And to expand on it, to date there are numerous healthcare payer systems out there that essentially incentivize the completion of forms with quality financial bonuses for the institutions. What is happening there, as you said, is that a social worker—who may not have as in-depth knowledge as we do—is essentially looking at a living will and then pulling out a POLST form, checking off a box that says, "DNR comfort measures only," and having the patient sign it. That is a very dangerous thing to do outside of an informed conversation because the end result is an *actionable order set*. As you have seen with the current DNR forms, we are getting very good at scanning documents into our electronic health records and setting up banner bars. It is not uncommon for patients to return to the hospital with a critical illness and for clinicians to look in the system to see that patient's code status, advance directive, or POLST information. If it is incorrect, it is a pretty serious patient safety risk.

A Call for Education

Dr Glatter: How can we educate all kinds of providers—from NPs to physicians to PAs—about how to read these documents and create them? How can we standardize this process? Where do we start?

Dr Mirarchi: My views might be skewed, but personally I think this has to become part of the curricula of all the professional schools—including medical, nursing, PA, and NP. Every facet of healthcare has to be educated and brought up to speed quickly. For those who are currently in practice, it needs to come back down to some degree of a continuing medical education (CME) activity—CME that is made mandatory by the institution or the state. As we go to the next American College of Emergency Physicians Assembly, it is very interesting that some states have requirements that physicians earn some number of CME credits on the topic of end of life. At this point in time, we are going to need to look at that education, standardize it, and then really begin to enforce the requirements for physicians and providers of all sorts to get that education because it is going to be vital.

Dr Glatter: Do you see this as one criterion to meet for renewing a medical license or even passing a 10-year exam, with the maintenance of certification (MOC) such a current issue?

Dr Mirarchi: That's my hope and dream—that eventually this kind of education becomes a medical licensure requirement. Remember, our TRIAD research showed that the existing education out there today is either ineffective or flawed because those who receive education perform *no differently* from those who did not receive the education. That was a very surprising finding to us.

Dr Glatter: It almost begs the question of whether physicians should have some sort of legal course in how to decipher these documents.

Dr Mirarchi: Yes, and remember, this is a new realm for physicians. These kind of documents are only maybe 20-30 years old at best. The POLST is a very effective document. It is good at limiting resources utilized at the end of life. However, if a clinician does not know what to do with it, it becomes a patient safety risk, just as has been previously shown with advance directives. Standardizing the approach to education about these documents and getting out ahead of their widespread use is going to be very important. But the horse is already out of the gate here: POLST documents are already approved—or in the process of being approved—in 46 states to at least some degree. We need physicians to become aware that they really need to question these documents and orders.

Dr Glatter: Do you think we should be educating the public as well about the POLST document? Is it something they should be aware of as much as we should?

Dr Mirarchi: I might have a skewed approach, but I think that there should be efforts geared towards educating the public about what a DNR order is, a living will is, and a POLST, and when it's appropriate to have each of those. At this point in time, this is all new to medicine, and we do not know who is actually going to receive reimbursement yet for end-of-life care counseling and at what point in time a patient's care becomes end-of-life care. In the situation of a critical illness, there are paternalistic providers who seem to think that is the time to essentially withdraw care, treatment, or life-supporting measures. Then there are others who are more patient-centered who feel that you give the treatment and then allow the family to make the decision. I do not know which one is going to win out there, but I have the feeling it is going to be financially based to some degree.

Timing an End-of-Life Talk

Dr Glatter: When should this discussion ideally take place? Should it be when someone is just 50 years old? Sixty years old? Or only when they are on the cusp, or the throes, of a terminal illness? Oftentimes it happens in the ED, right before resuscitation is to take place. If Medicare sees this as a process that requires 30 minutes for this discussion, it is certainly not going to happen in the ED. It's going to be somewhere in an office, well away from the frenetic pace of the ED.

Dr Mirarchi: Yes, that is correct. The ED is a disconnected setting. The primary care office is very disconnected from the hospital these days, and in an emergency, because of different on-call systems, ED clinicians may have no way to contact a physician who might know the patient. So, unfortunately, even though the patient

may have created these documents, we might not be able to talk to the physician who advised them or assisted with the creation of the document to get clarification as to what the patient's instructions mean and what we are supposed to be doing in terms of treatment. As far as *when* these discussions should occur, it would make sense that it would happen in the primary care physician's office and ideally as soon as possible. But in reality, I do not know if that is the most effective way to do it anymore because, with the birth of hospitalist physicians, primary care physicians are often not coming to the ED or hospitals anymore.

Dr Glatter: I think you bring up a good point about the separate nature of the office vs the hospital and the hospitalists because the hospitalist or intensivist is increasingly the provider who delivers medical care during a hospital stay—the time and place where there's a chance to intervene and really make clear changes in a patient's wishes and address these changes at that point.

Dr Mirarchi: I completely agree with you.

Dr Glatter: There was a recent article by Stub and colleagues[7] that looked at how resuscitation following out-of-hospital cardiac arrest occurs in hospitals and whether or not certain goals for resuscitation, including use of recommended interventions and amount of time per intervention, are met. I wonder if you could comment on this study and how it relates to our discussion.

Dr Mirarchi: In emergency medicine we are faced with this clinical scenario every day. Right now, with increased focus on public reporting, surgeons, emergency physicians, and interventional cardiologists are very concerned about the information, specifically mortality rates, that is publically reported. When you look at that study, it showed that our cardiac centers are actually following the guidelines on withdrawing life-sustaining treatment only 50% of the time.

The guidelines actually say that, for patients who have cardiac arrest either in or out of hospital (especially if there's hypothermia), healthcare professionals should wait at least 72 hours before withdrawing life-sustaining treatment. The most common reason for this decision is perceived neurologic damage that is expected to progress and be long term. In reality, we know that these patients need to be cooled, they need to go to the catheterization laboratory, and they need to have their artery opened up.

But what is happening, instead, is that centers and physicians are using these documents and orders to *bypass that 72-hour period* and withdrawing care too soon. We really need to look at this process and make sure that we are compliant with the guidelines for out-of-hospital cardiac arrest, whether it is a stroke or an intracerebral hemorrhage. There is a lot that we need to research still, and unfortunately this move towards payment for end-of-life care may precipitate some safety issues that we have not thought about.

Dr Glatter: I think that now that Medicare will be watching and possibly reporting on hospitals in terms of these issues, hospitals are going to be attentive to such data, assuming it does get incorporated into patient care.

I want to thank you so much for your time, and I appreciate your input into this important discussion about end-of-life care.

Dr Mirarchi: Thank you, Dr Glatter. Remember, above all else, just stick to a patient safety checklist and make the conversation balanced.

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Old rat brains rejuvenated and new neurons grown by asthma drug

Old rat brains rejuvenated and new neurons grown by asthma drug

It’s as good as new. An asthma drug has rejuvenated rat brains, making old rats perform as well as young rats in tests of memory and cognition. The drug also encouraged the birth of new brain cells.

As we get older, most of us will experience some kind of brain degeneration. Typically, we lose the ability to make new neurons. Another problem is chronic, low-grade inflammation in the brain, which is implicated in many age-related

brain disorders. To tackle both problems in one go, Ludwig Aigner at Paracelsus Medical University Salzburg in Austria and his colleagues targeted a set of receptors in the brain that, when activated, trigger inflammation.

High numbers of these receptors are found in areas of the brain where neurons are born, suggesting they might also be involved in this process, too.

A drug called montelukast (Singulair), regularly prescribed for asthma and allergic rhinitis, blocks these receptors, so Aigner and his colleagues tried it on young and old rats. The team used oral doses equivalent to those taken by people with asthma. The older animals were 20 months old – roughly equivalent to between 65 and 75 in human years. The younger rats were 4 months old – about 17 in human years. The animals were fed the drug daily for six weeks, while another set of young and old rats were left untreated. There were 20 young and 14 old rats in total.

Escape plan

The rats took part in a range of learning and memory tests. One of these, for example, involved the rats being placed in a pool of water with a hidden escape platform. At the start of the study, untreated young rats learned to recognise landmarks and quickly find their way to the platform, while the untreated older animals struggled at the task.

By the end of their six-week drug regime, though, old animals performed as well as their younger companions. “We’ve restored learning and memory 100 per cent, to a level comparable with youth,” says Aigner. He presented his findings last week at the Society for Neuroscience meeting in Chicago.

When the team studied the brains of the animals, they found that old rats that had been given montelukast had 80 per cent less inflammation. They also had an enhanced level of new neuron growth compared with untreated old rats – about 50 per cent of that seen in young rats, says Aigner.

The team also found that the blood-brain barrier – which stops infectious agents reaching the brain and which weakens in old age – was stronger in treated old rats. “Structurally, the brain had rejuvenated,” says Aigner.

No effect on the young

The drug had no effect on young animals, probably because it targets inflammation associated with age and disease, says Aigner. “We’ve identified a target that affects many different systems of the aged and degenerated brain,” he says. “I think the drug reverses the damage associated with ageing.”

Because montelukast is widely used, it should be relatively quick and easy to look for similar effects in clinical trials in people, says James Nicoll, a neuropathologist at the University of Southampton, UK.

Aigner says the results from the rat study are significant enough to warrant a clinical trial. He will start by testing the drug in people with Parkinson’s disease, he says.

“It’s a very promising approach,” says Arthur Roach, director of research and development at charity Parkinson’s UK. “They’ve reversed certain aspects of the aged brain.”

Real ageing

Although the results are in rats, they are exciting because the team used animals that had aged naturally, rather than young rodents with genetic mutations that make them age prematurely, or rodents bred to have age-related disease. “You don’t often see studies in old rats because they’re so expensive,” says Roach.

It is also a promising sign that montelukast can access the brain. “There are a lot of anti-inflammatory drugs out there, but they don’t tend to cross the blood-brain barrier,” says Gary Wenk at Ohio State University in Columbus.

Wenk isn’t surprised that a drug that targets inflammation in the brain should have such “restorative” effects. “It is now becoming accepted that inflammation does lead to neurodegeneration,” he says. Inflammation has also been linked to Alzheimer’s disease and Huntington’s disease, among other conditions.

Bryce Vissel at the Garvan Institute of Medical Research in Sydney, Australia, is cautious. “Millions of people are affected by Alzheimer’s and Parkinson’s worldwide… and hope that science will deliver a cure,” he says. “But so far no promising therapy in an animal model has translated to a therapy in people in neurodegenerative disease.”

http://bit.ly/1jZan5M

Sex: Seniors Find Answers Online

Older adults are seeking support and carnal knowledge from peers

By Melinda Wenner Moyer

Research suggests that a growing number of seniors continue to be sexually active, and in doing so, they stay healthier and happier. Although seniors are often hesitant to discuss intimate issues with their doctors, a new study suggests that older adults have been turning to online communities to get the answers and support they need from one another.

Sexual activity among older adults is commonplace—more than half of men and one third of women in their 70s, some married and some not, reported having sex at least twice a month in a 2015 study published in Archives of Sexual Behavior. (Scientific American Mind is part of Springer Nature.) But it can be complicated. Medical conditions that arise with advancing age, such as diabetes and heart disease, can affect sex drive and performance. Widows and widowers who start dating again later in life may not know how to protect themselves from sexually

transmitted diseases or how to approach a new partner. Making matters worse, ageist stereotypes—such as the idea that seniors are “too old for sex”—can make it difficult for older adults to get answers.

A 2011 review of the research literature concluded that not only do older adults seldom raise questions about sex with their physicians but that their doctors are hesitant to bring up the topic. “The findings, literature and current media suggest that health care providers and staff in seniors' residential facilities and nursing homes themselves often ignore their clients' and residents' sexual health, needs and rights,” explains Liza Berdychevsky, a social scientist at the University of Illinois at Urbana-Champaign.

In light of this concerning trend, Berdychevsky and her colleague Galit Nimrod, a communications researcher at Ben-Gurion University of the Negev in Israel, explored whether seniors get any sexual support from online forums. After reviewing nearly 700,000 messages posted in the span of a year to an international collection of online senior communities, they found approximately 2,500 posts dedicated to the discussion of sexual issues. Although that is less than 0.4 percent of all posts, some of these threads were hugely popular, with thousands of views, suggesting that a number of community members who were not participating in the discussions were nonetheless reading them. The researchers also saw evidence to suggest that these posts helped to answer users' questions and make them feel more comfortable about their evolving sexuality, according to a paper they published in June in the Journal of Leisure Research.

“The communities offer their members reassurance that they are not alone and that whatever they experience is faced by many others in their age group,” Berdychevsky says, and the online forums provide “a channel for sharing their difficulties, gaining firsthand knowledge and exchanging advice.” She and other investigators continue to emphasize the importance of better face-to-face communication about sex, especially in health care settings. Yet as more and more older adults around the world gain access to the Internet, their sex lives—and, it follows, general well-being—are better for it.

http://www.eurekalert.org/pub_releases/2015-10/sri-ssp102615.php

SwRI scientists predict that rocky planets formed from 'pebbles'

New process explains massive differences between Earth and Mars

Boulder, Colo - Using a new process in planetary formation modeling, where planets grow from tiny bodies called "pebbles," Southwest Research Institute scientists can explain why Mars is so much smaller than Earth. This same process also explains the rapid formation of the gas giants Jupiter and Saturn, as reported earlier this year.

"This numerical simulation actually reproduces the structure of the inner solar system, with Earth, Venus, and a smaller Mars," said Hal Levison, an Institute scientist at the SwRI Planetary Science Directorate. He is the first author of a new paper published in the Proceedings of the National Academy of Sciences of the United States (PNAS) Early Edition.

The fact that Mars has only 10 percent of the mass of the Earth has been a long-standing puzzle for solar system theorists. In the standard model of planet formation, similarly sized objects accumulate and assimilate through a process called accretion; rocks incorporated other rocks, creating mountains; then mountains merged to form city-size objects, and so on. While typical accretion models generate good analogs to Earth and Venus, they predict that Mars should be of similar-size, or even larger than Earth. Additionally, these models also overestimate the overall mass of the asteroid belt.

"Understanding why Mars is smaller than expected has been a major problem that has frustrated our modeling efforts for several decades," said Levison. "Here, we have a solution that arises directly from the planet formation process itself."

New calculations by Levison and co-authors Katherine Kretke, Kevin Walsh and Bill Bottke, all of SwRI's Planetary Science Directorate follow the growth and evolution of a system of planets. They demonstrate that the structure of the inner solar system is actually the natural outcome of a new mode of planetary growth known as Viscously Stirred Pebble Accretion (VSPA). With VSPA, dust readily grows to "pebbles" -- objects a few inches in diameter -- some of which gravitationally collapse to form asteroid-sized objects. Under the right conditions, these primordial asteroids can efficiently feed on the remaining pebbles, as aerodynamic drag pulls pebbles into orbit, where they spiral down and fuse with the growing planetary body. This allows certain asteroids to become planet-sized over relatively short time scales.

However, these new models find that not all of the primordial asteroids are equally well-positioned to accrete pebbles and grow. For example, an object the size of Ceres (about 600 miles across), which is the largest asteroid in the asteroid belt, would have grown very quickly near the current location of the Earth. But it would not have been able to grow effectively near the current location of Mars, or beyond, because aerodynamic drag is too weak for pebble capture to occur.

"This means that very few pebbles collide with objects near the current location of Mars. That provides a natural explanation for why it is so small," said Kretke. "Similarly, even fewer hit objects in the asteroid belt, keeping its net mass small as well. The only place that growth was efficient was near the current location of Earth and Venus."

"This model has huge implications for the history of the asteroid belt," said Bottke. Previous models have predicted that the belt originally contained a couple of Earth-masses' worth of material, meaning that planets began to grow there. The new model predicts that the asteroid belt never contained much mass in bodies like the currently observed asteroid.

"This presents the planetary science community with a testable prediction between this model and previous models that can be explored using data from meteorites, remote sensing, and spacecraft missions," said Bottke.

This work complements the recent study published in Nature by Levison, Kretke, and Martin Duncan (Queen's University), which demonstrated that pebbles can form the cores of the giant planets and explain the structure of the outer solar system. Combined, the two works present the means to produce the entire solar system from a single, unifying process.

"As far as I know, this is the first model to reproduce the structure of the solar system -- Earth and Venus, a small Mars, a low-mass asteroid belt, two gas giants, two ice giants (Uranus and Neptune), and a pristine Kuiper Belt," said Levison.

The article, "Growing the Terrestrial Planets from the Gradual Accumulation of Sub-meter Sized Objects," is published online by PNAS. Authors H.F. Levison, K.A. Kretke, K. Walsh, and W. Bottke are all of Southwest Research Institute's Space Science and Engineering Division. This work was supported by the NASA Solar System Exploration Research Virtual Institute (SSERVI) through institute grant number NNA14AB03A.

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What Everyone Needs to Know About Legionnaires Disease

Legionnaires Outbreaks

Preeta K. Kutty, MD, MPH

Legionnaires disease has been in the news lately, with outbreaks in New York City, New York; Quincy, Illinois; and San Quentin, California. Despite these outbreaks garnering media attention, Legionnaires disease continues to be underdiagnosed and underreported. Here is what you need to know.

Legionellosis

Legionellosis is a respiratory infection caused by *Legionella* bacteria; infection can manifest as either Legionnaires disease or Pontiac fever. Legionnaires disease is a common form of severe pneumonia requiring hospitalization, whereas Pontiac fever generally resolves on its own. Among those who develop Legionnaires disease, 5%-30% will die of their illness.

There are at least 60 different species of *Legionella*, and most are considered capable of causing disease. However, most disease is caused by *Legionella pneumophila*, particularly serogroup 1.

Transmission

Legionella are transmitted by aerosolized water containing the bacteria. Less commonly, these bacteria can be transmitted by aspiration of drinking water. *Legionella* are not transmitted from person to person, and most people exposed to the bacteria do not become ill.

Legionella can be found everywhere in natural, freshwater environments but generally are present in insufficient numbers to cause disease. In man-made water systems like the plumbing of large buildings (eg, hot water heaters, storage tanks, pipes), cooling towers, decorative fountains, or hot tubs, *Legionella* can amplify and be transmitted to susceptible hosts through aerosolization. Certain conditions (eg, temperature, the amount of nutrients, pH) allow for amplification of *Legionella*. Water systems that are not properly cleaned, maintained, or disinfected are at risk for *Legionella* amplification.

The majority of legionellosis outbreaks are associated with hotels, resorts, cruise ships, hospitals, and long-term care facilities. More than 20% of all persons with Legionnaires disease have traveled during their incubation periods (2-14 days after exposure). And 7% of those with Legionnaires disease stayed overnight in a healthcare facility during their incubation periods. Most people who develop Legionnaires disease have a medical condition that makes them more susceptible to developing the infection or are smokers.

Pontiac fever has a shorter incubation period (6-48 hours after exposure) and most commonly affects young, healthy adults.[1] The pathogenesis of Pontiac fever is poorly understood, and why exposure to *Legionella* may result in these two clinically and epidemiologically distinct syndromes is not known.

Risk Factors

Risk factors for developing Legionnaires disease include:

- ***Renal or hepatic failure;***
- ***Diabetes;***
- ***Chronic lung disease;***
- ***Systemic malignancy;***
- ***Smoking (current or historical);***
- ***Immune system disorders; and***
- ***Age ≥50 years.***

Risk factors for exposure to* Legionella *include:

- ***Recent travel with an overnight stay outside of the home, including a stay in a healthcare facility;***
- ***Exposure to hot tubs or other recreational water; and***
- ***Exposure to domestic plumbing that has had recent repairs or maintenance work.***

Burden of Disease

The number of legionellosis cases reported to Centers for Disease Control and Prevention (CDC) has been on the rise over the past decade.[2] This rise may reflect a true increase in the frequency of disease due to a number of factors (eg, older US population, more at-risk individuals, aging plumbing infrastructure, climate). It may also be a result of increased use of diagnostic testing or more reliable reporting to local and state health departments and to CDC.

Between 2008 and 2012, a total of 3000-4000 cases of Legionnaires disease were reported to CDC each year.[3] Yet, research studies with thorough diagnostic testing estimate that 8000-18,000 hospitalized cases of the disease may occur in the United States each year. Accurate data reflecting the true incidence of this disease are not available because of underutilization of diagnostic testing and underreporting.

More illness is usually found in the summer and early fall, but legionellosis can happen any time of year. Legionellosis is reported more commonly in the mid-Atlantic and nearby states than in other parts of the country.

Diagnosis and Testing

Clinical features of Legionnaires disease include cough, fever, and radiographic pneumonia. For Pontiac fever, clinical features include flu-like illness (ie, fever, chills, malaise) without pneumonia.

Indications that warrant testing for Legionnaires disease include (Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults can be found here):

- Patients who have failed outpatient antibiotic therapy for community-acquired pneumonia;
- Patients with severe pneumonia, in particular those requiring intensive care;
- Immunocompromised patients with pneumonia;
- Patients with pneumonia in the setting of a legionellosis outbreak;
- Patients with a travel history (patients who have traveled away from their home within 2 weeks before the onset of illness); and
- Patients suspected of having healthcare-associated pneumonia.

The preferred diagnostic tests for Legionnaires disease are culture of respiratory secretions on selective media *and* the *Legionella* urinary antigen assay. Isolation of *Legionella* from respiratory secretions or lung tissue is confirmatory and an important method for diagnosis, despite the convenience and specificity of urinary antigen testing. If your patient has pneumonia, and the urinary antigen test is positive for *Legionella*, then your patient is considered to have Legionnaires disease. This test is designed to detect the most common cause of legionellosis (*L pneumophila* serogroup 1). However, all species and serogroups of *Legionella* are potentially pathogenic, so a patient with a negative urinary antigen result may have legionellosis caused by some other member of the *Legionella* genus. In addition, if urinary antigen testing is negative, but Legionnaires disease is still suspected, then a respiratory culture is required.

Finally, molecular techniques can be used to compare clinical isolates to environmental isolates and confirm the source of an outbreak. Thus, best practice for detection of *Legionella* and for public health surveillance is to also obtain respiratory specimens for culture at the time urinary antigen testing is ordered, preferably before the administration of antibiotics.

Most cases of Pontiac fever are diagnosed in association with an outbreak, on the basis of clinical signs and symptoms, often along with cases of Legionnaires disease. The urinary antigen test as well as serology can be used to confirm the diagnosis; however, owing to the low sensitivity of these tests in the setting of Pontiac fever, they cannot be used to rule it out. Serologic confirmation requires a fourfold change between acute and convalescent sera collected 3-6 weeks apart.[4]

Treatment

If your patient has Legionnaires disease, see the most recent guidelines for treatment of community-acquired pneumonia. If your patient has Pontiac fever, antibiotic therapy should not be prescribed. It is a self-limited illness that does not benefit from antibiotic treatment. Recovery usually occurs within 1 week.

Reporting

Legionellosis is a nationally notifiable disease in the United States that is monitored through two surveillance systems at the national level. With improved diagnosis and reporting, public health experts can better understand the true burden of legionellosis.

Timely identification and reporting of legionellosis cases is important because this allows public health officials to quickly identify and stop potential clusters and outbreaks. Outbreaks among travelers can be difficult to detect because of the low attack rate, long incubation period, and the dispersal of people from the source of the outbreak, so collecting and reporting information about overnight travel in the 14 days prior to onset is important. Healthcare facility exposures can be difficult to ascertain if the patient has not been in the same facility for the entire incubation period or was discharged prior to onset and readmitted. Outpatient, employee, and visitor exposures should be reported because they can help determine the scope and source of an outbreak. Timely reporting of healthcare-associated cases ensures that steps can be taken to protect these highly susceptible populations.

Prevention

The key to preventing legionellosis is maintenance of the water systems in which *Legionella* may grow, including drinking water systems, hot tubs, decorative

fountains, and cooling towers. If *Legionella* bacteria are found, facilities should be prepared to eliminate them, especially if they serve people at higher risk for legionellosis. CDC encourages all building owners and especially healthcare facilities to develop comprehensive water safety management plans. Persons at increased risk for infection may choose to avoid high-risk exposures, such as being in or near a hot tub.

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