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1 in 7 colorectal cancer patients diagnosed before recommended screening age

Colorectal cancer in younger people linked to more advanced disease but better survival

ANN ARBOR, Mich. -- Nearly 15 percent of patients diagnosed with colorectal cancer were younger than 50, the age at which screening recommendations begin.

The study by researchers at the University of Michigan Comprehensive Cancer Center also found that younger patients were more likely to have advanced disease. The authors suggest this is in part because they are diagnosed only after their cancers have grown large enough to cause symptoms.

"Colorectal cancer has traditionally been thought of as a disease of the elderly. This study is really a wake-up call to the medical community that a relatively large number of colorectal cancers are occurring in people under 50," says study author Samantha Hendren, M.D., M.P.H., associate professor of surgery at the University of Michigan Medical School.

"To put this in context, breast cancer screening often begins at age 40, and less than 5 percent of invasive breast cancers occur in women under that age. Our study found that about 15 percent of colorectal cancers are diagnosed before the screening age of 50," she adds.

The study identified 258,024 patients diagnosed with colon or rectal cancer from the Surveillance, Epidemiology and End Results database, a national database of cancer incidence. Results appear in the journal Cancer.

The authors found that younger patients were more likely to receive aggressive surgery and radiation therapy. In addition, this group had better survival rates, both overall and by stage. Among patients whose cancer had spread to distant organs, 21 percent of younger patients survived beyond five years, compared to 14 percent of older patients.

The improved survival could be in part due to the more aggressive treatment, the authors suggest.

The findings suggest the need for more awareness of warning signs of colorectal cancer: anemia, a dramatic change in the size or frequency of bowel movements, and bleeding with bowel movements. The authors also say that more people need to consider family history of colorectal cancer, which is a significant risk factor.

Should guidelines change to begin screening at an earlier age? Hendren says not so fast. "This would be a big and costly change, and I don't know whether it would help more people than it would hurt," she says. "A lot of research would be required to understand this before any changes should be made."

Meanwhile, the more aggressive treatment and longer survival for younger patients suggest the need to improve long-term survivorship resources.

"The cancer community needs to prepare for the increasing number of very young colorectal cancer survivors who will need long-term support to cope with the physical and psychological consequences of their disease and treatments," Hendren says.

Additional authors: Zaid M. Abdelsattar, M.D., MSc; Sandra L. Wong, M.D., M.S.; Scott E. Regenbogen, M.D., M.P.H.; Diana M. Jomaa; Karin M. Hardiman, M.D., Ph.D.

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Unraveling the Ties of Altitude, Oxygen and Lung Cancer

Epidemiologists have long been puzzled by a strange pattern in their data: People living at higher altitudes appear less likely to get lung cancer.

George Johnson

Associations like these can be notoriously misleading. Slice and dice the profusion of data, and there is no end to the coincidences that can arise.

There is, for instance, a strong correlation between per-capita cheese consumption and the number of people strangled accidentally by their bedsheets. Slice and dice the profusion of data, and there is no end to the coincidences that can arise. Some were recently collected in a book called "Spurious Correlations." Year by year, it turns out, the number of letters making up the winning word for the Scripps National Spelling Bee closely tracks the number of people killed by venomous spiders.

These are probably not important clues about the nature of reality. But the evidence for an inverse relationship between lung cancer and elevation has been much harder to dismiss.

A paper published last year in the journal PeerJ plumbed the question to new depths and arrived at an intriguing explanation. The higher you live, the thinner the air, so maybe oxygen is a cause of lung cancer.

Oxygen cannot compete with cigarettes, of course, but the study suggests that if everyone in the United States moved to the alpine heights of San Juan County, Colo. (population: 700), there would be 65,496 fewer cases of lung cancer each year.

This idea didn't appear out of the blue. A connection between lung cancer and altitude was proposed as early as 1982. Five years later, other researchers suggested that oxygen might be the reason.

But the authors of the PeerJ paper — two doctoral students at the University of Pennsylvania and the University of California, San Francisco — have made the strongest case yet. At the University of Pennsylvania Medical School, the paper

won last year's Abramson Cancer Center prize for basic research. And in July it was chosen as one of PeerJ's best papers on cancer biology.

Skeptics were quick to strike back, though not very effectively. A would-be debunking on the Cancer Research UK website was quickly followed by a debunking of the debunking.

All of the usual caveats apply. Studies like this, which compare whole populations, can be used only to suggest possibilities to be explored in future research. But the hypothesis is not as crazy as it may sound. Oxygen is what energizes the cells of our bodies. Like any fuel, it inevitably spews out waste — a corrosive exhaust of substances called "free radicals," or "reactive oxygen species," that can mutate DNA and nudge a cell closer to malignancy.

That is not a good reason to consume antioxidant pills. While the logic may seem sound, there is no convincing evidence that these supplements add to nature's already formidable means of repairing oxidative damage — and they may even disrupt some delicate biological balance, increasing cancer risk and speeding tumor growth.

But there is no question that oxidation, so crucial to life, rusts our cells and can edge them closer to becoming cancerous.

In examining the possibility that breathing itself significantly increases the risk of lung cancer, the authors of the paper, Kamen P. Simeonov and Daniel S. Himmelstein, began by eliminating confounding variables. Maybe younger, healthier people tend to live at higher altitudes, with older and weaker ones, including smokers, retreating to lower lands. That could create the illusion of a protective altitude effect, but one that has nothing to do with oxygen.

The authors also took into account factors like income, education and race, which affect access to medical care. To reduce distortions caused by noisy data, the researchers excluded counties with large numbers of recent immigrants, who might have acquired cancer-causing mutations elsewhere. Also ruled out were places with a large number of Native Americans, whose cancer rates often go underreported.

Beyond the human variables were geophysical ones. Air at higher altitudes may be less polluted by carcinogens. And since sunlight exposure is more intense, maybe the increase in vitamin D helps stave off lung cancer — an idea previously suggested. Differences in precipitation and temperature might also have some effect.

These data, too, were added to the scales, along with the influence of radon gas and ultraviolet rays, which is greater at higher elevations. The frequency of obesity and diabetes, which are risks for many cancers, was adjusted for, along with alcohol use, meat consumption and other factors.

After an examination of all these numbers for the residents of 260 counties in the Western United States, situated from sea level to nearly 11,400 feet, one pattern stood out: a correlation between the concentration of oxygen in the air and the incidence of lung cancer. For each 1,000-meter rise in elevation, there were 7.23 fewer lung cancer cases per 100,000 people. (The study found no similar correlations for breast, colon and prostate cancer.)

That is not a good reason to inhale less deeply at sea level or to flee to the mountains. Wherever you live, smoking accounts for as much as 90 percent of lung cancer. Radon is considered a distant second cause. But the PeerJ study complicates things.

For various reasons, radon levels are generally higher at higher altitudes, while lung cancer rates are lower. Does that mean radon is not so dangerous after all? Or are its bad effects offset by the healthy deficit of carcinogenic oxygen?

Or maybe radon, like thinner air, protects against lung cancer. According to a long-debated hypothesis called hormesis, the earth's low levels of natural radiation actually might reduce cancer risk.

However this all shakes out, the study is a reminder that not all carcinogens are manufactured by chemical plants. And not all of them can be avoided. You can quit smoking and mitigate the radon in your basement. But you can't mitigate oxygen.

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Encapsulated human islet cells can normalize blood sugar levels in mice

In a first, encapsulated human insulin-producing cells have been implanted and maintained long-term control of blood sugar without immunosuppressants

For the first time ever, scientists studying a mouse model of diabetes have implanted encapsulated insulin-producing cells derived from human stem cells and maintained long-term control of blood sugar -- without administering immunosuppressant drugs.

The results of the multi-institutional effort are published in Nature Medicine.

People with type 1 diabetes have an overactive immune system that destroys the insulin-producing islet cells in the pancreas. Lacking that hormone, the body fails to convert sugars to usable energy, and glucose rises to harmful levels in the blood without daily insulin injections. Islet cells have been successfully transplanted to treat type 1 diabetes, but those patients must take immunosuppressant drugs to keep their immune system from destroying the transplanted cells.

Previous research had shown that rodent islet cells could normalize blood sugar levels in animal models without immunosuppression if the cells were encased in

hydrogel capsules. The semi-porous capsules allow insulin to escape into the blood, while preventing the host's immune system from attacking the foreign cells. Larger capsules, about 1.5 millimeters across, even seemed able to avoid the buildup of scar tissue, which can choke off the cells' supply of oxygen and nutrients.

The new study, a collaboration led by scientists at the Massachusetts Institute of Technology and Boston Children's Hospital, used islet cells derived from human stem cells and capsules made of chemically-tweaked gel that are even more resistant to the build-up of scar tissue.

Dr. Jose Oberholzer, chief of transplantation surgery and director of cell and pancreas transplantation at the University of Illinois Hospital & Health Sciences System, professor of bioengineering at the University of Illinois at Chicago, and an author on the paper, tested several varieties of chemically-modified alginate hydrogel spheres -- in various sizes -- to see if any excelled at resisting scar-tissue formation. Oberholzer and his coworkers at the University of Illinois at Chicago first tested the spheres to ensure they would allow the islet cells to function inside a host. Using a special microfluidic device developed at UIC under a grant from the National Institute of Diabetes and Digestive and Kidney Diseases, they delivered minute amounts of glucose into tiny wells containing encapsulated islet cells and measured the amount of insulin that seeped out. They implanted spheres that showed promise into rodents and non-human primates to look for the development of scar tissue.

They found (and reported in the journal Nature Biotechnology) that 1.5-millimeter spheres of triazole-thiomorphine dioxide (TMTD) alginate were best at allowing insulin to escape while resisting immune response and the buildup of scar tissue.

When implanted into a mouse model of diabetes, TMTD-alginate spheres containing human islet cells were able to maintain proper blood glucose control for 174 days -- decades, in terms relative to the human lifespan.

"When we stopped the experiment and took the spheres out, they were virtually free of scar tissue," Oberholzer said.

"While this is a very promising step towards an eventual cure for diabetes, a lot more testing is needed to ensure that the islet cells don't de-differentiate back toward their stem-cell states or become cancerous," said Oberholzer. If the cells did become cancerous, he said, they could easily break through the spheres. Oberholzer also cautioned that a cure for human diabetes would require scientists to develop techniques to grow large numbers of human islet cells from stem cells -- a worthy goal.

"In the United States, there are 30 million cases of type 2 diabetes and about 2 million patients with type 1 diabetes who could potentially benefit from such a procedure," he said. "But we need to grow billions of islet cells."

Co-authors on the papers are James McGarrigle, Meirigeng Qi and Matthew Bochenek of UIC; Daniel Anderson, Arturo Vegas, Omid Veiseh, Andrew Bader, Joshua Doloff, Jie Li, Michael Chen, Karsten Olejnik, Hok Hei-Tam, Siddharth Jhunjhunwala, Erin Langan, Stephanie Aresta-Dasilva, Srujan Grandham, Minglin Ma, Kaitlin Bratlie, Patrick Fenton, Alan Chiu, Sean Siebert, Katherine Tang, Nimit Dholakia, Raj Thakrar, Thema Vietti, Michael Chen, Jeon Woong Kang and Robert Langer of MIT and Boston Children's Hospital; Douglas Melton, Mads Gurtler, Jeffrey Millman and Felicia Pagliuca of Harvard University; Jennifer Hollister-Lock, Josh Cohen, Karolina Siniakowicz and Gordon Weir of the Joslin Diabetes Center; and Dale Greiner, Stephen Lyle and David Harlan of the University of Massachusetts Medical School.

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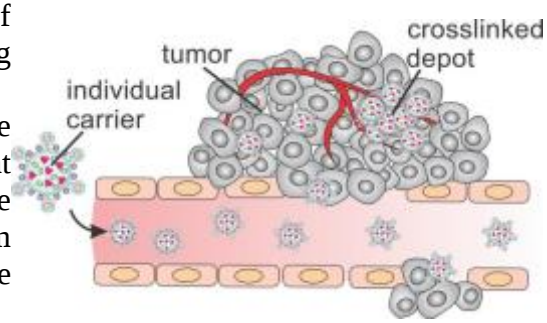
Microscopic drug 'depots' boost efficacy against tumors in animal model

Biomedical engineering researchers have developed a technique for creating microscopic "depots" for trapping drugs inside cancer tumors.

In an animal model, these drug depots were 10 times more effective at shrinking tumors than the use of the same drugs without the depots.

Some anti-cancer drugs are most effective outside of cancer cells. For example, the anti-cancer drug TRAIL attacks a cancer cell's cell membrane, while another drug, cilengitide, inhibits the growth of blood vessels around a tumor, starving it of nutrients.



To improve the effectiveness of these drugs, scientists want to both prevent them from being absorbed into the cancer cells and prevent them from being washed away from the tumor site by the circulatory system.

Biomedical engineering researchers have developed a technique for creating microscopic "depots" for trapping drugs inside cancer tumors. In an animal model, these drug depots were 10 times more effective at shrinking tumors than the use of the same drugs without the depots. **Quanyin Hu**

"We have now found a way to do both, by creating micro-scale depots of these drugs inside a tumor," says Zhen Gu, corresponding author of a paper on the work and an assistant professor in the joint department of biomedical engineering at North Carolina State University and the University of North Carolina at Chapel Hill.

The researchers begin by creating a drug cocktail of TRAIL and cilengitide, then wrap the cocktail in a "nanocarrier" that is 100 nanometers (nm) in diameter. The nanocarrier is then studded with human serum albumin (HSA), an abundant protein in human blood.

The 100-nm nanocarrier is also studded with smaller nanocapsules - only 10 nm in diameter - that are made of a hyaluronic acid gel and contain an enzyme called transglutaminase (TG). The nanocarriers are then injected into the blood stream.

Some cancer tumors produce large quantities of an enzyme called hyaluronidase, which breaks up hyaluronic acid. So, when the nanocarriers enter a cancer tumor, the hyaluronidase dissolves the small hyaluronic acid gel nanocapsules on their surface. This releases the TG enzymes, which help to connect the HSA proteins studding the surface of other nanocarriers, creating a cross-linked drug depot inside the tumor.

The size of the cross-linked depot largely prevents it from being absorbed by individual cancer cells or from being quickly swept away in the bloodstream. In addition, the TG can also help nanocarriers bind to other proteins in the tumor, helping to hold the depot in place.

The environment inside the tumor is also more acidic than its surroundings, and this acidity slowly breaks down the nanocarriers.

"This ensures a gradual, sustained release of the TRAIL and cilengitide into the tumor environment, maximizing the effectiveness of the drugs," Gu says.

The researchers evaluated this technique using breast cancer tumors in mice.

"We found that the use of cross-linked depots to deliver TRAIL and cilengitide shrunk tumors tenfold more than the use of the same dose of those drugs using conventional techniques," says Quanyin Hu, lead author of the paper and a Ph.D. student in the joint biomedical engineering department at NC State and UNC-Chapel Hill.

"This is a proof-of-concept study and additional work needs to be done to develop the technique," Gu says. "But it is promising, and we think this strategy could also be used for cancer immunotherapy. We would need to do more work in an animal model before pursuing clinical trials."

Gu also notes that it is too early to estimate costs associated with the technique.

"We're in the early stages of developing this technique, and we're trying to make the process simpler and more effective - which would drive down manufacturing costs," Gu says. "That makes it difficult to estimate what the potential cost might be.

"And while we don't foresee any significant health risks beyond those posed by whatever drugs are being delivered, one reason we do animal and clinical trials is to identify any unforeseen risks."

The paper, "Tumor Microenvironment-Mediated Construction and Deconstruction of Extracellular Drug-Delivery Depots," was published Jan. 19 in the journal NanoLetters. The paper was co-authored by Wujin Sun, Yue Lu, Hunter Bomba, and Yanqi Ye in the joint biomedical engineering department at NC State and UNC-Chapel Hill; Tianyue Jiang of Nanjing Tech University; and Ari Isaacson of UNC-Chapel Hill. The work was supported by NC TraCS, NIH's Clinical and Translational Science Awards at UNC-CH, grant number 1UL1TR001111.

http://www.eurekalert.org/pub_releases/2016-01/ez-heh012216.php

Highly efficient heavy metal ions filter

Almost completely removes heavy metal ions from water in just a single pass through the filter membrane

In November 2015, Brazil experienced an unparalleled environmental disaster. When two dams broke at an iron ore mine, a poisonous cocktail of heavy metals was sent pouring into the Rio Doce, reaching the Atlantic some days later. The consequences were devastating for nature and humans alike: countless fish, birds and animals died, and a quarter of a million people were left without drinking water.

This case demonstrates that water pollution is one of today's most serious global problems. No satisfactory technical solution has been found for the treatment of water contaminated with heavy metals or radioactive substances. Existing methods used to remove water from heavy metals, for example, have several disadvantages: either they are too targeted at a specific element or their filter capacity is too small; additionally, they are often too expensive.

Effective filtration of heavy metals

Now, a solution may have been found in a new type of hybrid filter membrane developed in the laboratory of Raffaele Mezzenga, Professor of Food and Soft Materials at ETH Zurich. This technology not only has an extremely simple structure, but also comprises low-cost raw materials, such as whey protein fibres and activated charcoal. Heavy metal ions can be almost completely removed from water in just a single pass through the filter membrane.

"The project is one of the most important things I might have ever done," says Mezzenga, enthusing about the new development. He and his researcher Sreenath Bolisetty were the only people to work on it, and their publication has just appeared in the journal Nature Nanotechnology.

Whey and activated charcoal required

At the heart of the filtration system is a new type of hybrid membrane made up of activated charcoal and tough, rigid whey protein fibres. The two components are cheap to obtain and simple to produce.

First of all, the whey proteins are denatured, which causes them to stretch, and ultimately come together in the form of amyloid fibrils. Together with activated carbon (which is also contained in medical charcoal tablets), these fibres are applied to a suitable substrate material, such as a cellulose filter paper. The carbon content is 98%, with a mere 2% made up by the protein.

Gold recovery thanks to the filter membrane

This hybrid membrane absorbs various heavy metals in a non-specific manner, including industrially relevant elements, such as lead, mercury, gold and palladium. However, it also absorbs radioactive substances, such as uranium or phosphorus-32, which are relevant in nuclear waste or certain cancer therapies, respectively.

Moreover, the membrane eliminates highly toxic metal cyanides from water. This class of materials includes gold cyanide, which is used commonly in the electronics industry to produce conductor tracks on circuit boards. The membrane provides a simple way of filtering out and recovering the gold, thus the filter system could one day play an important role in gold recycling as well. "The profit generated by the recovered gold is more than 200 times the cost of the hybrid membrane," says Mezzenga.

The filtration process is extremely simple: contaminated water is drawn through the membrane by vacuum. "A sufficiently strong vacuum could be produced with a simple hand pump," says Mezzenga, "which would allow the system to be operated without electricity." Furthermore, the system is almost infinitely scaleable, allowing even large volumes of water to be filtered cost effectively.

As they are drawn through the filter, the toxic substances 'stick' primarily to the protein fibres, which have numerous binding sites where individual metal ions can dock. However, the large surface area of the activated charcoal can also absorb large quantities of toxins, which allows delaying the saturation limits of the membranes. In addition, the protein fibres lend mechanical strength to the membrane and at high temperatures allow the trapped ions to be chemically converted into valuable metallic nanoparticles.

Unsurpassed absorptive capacity

Mezzenga is enthusiastic about the hybrid membrane's filter capacity: in tests with mercury chloride, for example, the mercury concentration present in the filtrate fell by more than 99.5%. The efficiency was even higher with a toxic potassium gold cyanide compound, where 99.98% of the compound was bound to the membrane, or with lead salts, where the efficiency was larger than 99.97%. And with radioactive uranium, 99.4% of the original concentration was bound during filtration. "We achieved these high values in just a single pass," emphasises Bolisetty, co-author of the invention.

Even over multiple passes, the hybrid membrane filters out toxic substances with a high degree of reliability. Although the mercury concentration in the filtrate increased by a factor of 10 from 0.4 ppm (parts per millions) to 4.2 ppm after 10 passes, the quantity of protein used was extremely low. To filter half a litre of contaminated water, the researchers used a membrane weighing just a 10th of a gram, of which seven percent by weight was made up of protein fibres. "One kilo of whey protein would be enough to purify 90'000 litres of water, more than the amount of water needed in a human life time," says the ETH professor. This also implies that the efficiency can be further increased to the desirable requirements, by simply increasing the protein content in the membrane, he adds, emphasizing the flexibility of this new approach.

Promising potential

Mezzenga is confident that his technology will find its way onto the market. "There are numerous applications for it, and water is one of the most pressing problems we face today," he says in light of the torrent of mud experienced in Brazil. The ETH professor has patented his technology and was nominated in March this year for ETH Zurich's Spark Award. However, because the scientific publication had to undergo a nine-month review process, only now can Bolisetty and Mezzenga make public their discovery.

Bolisetty S, Mezzenga R. Amyloid-carbon hybrid membranes for universal water purification. Nature Nanotechnology, published online Jan 25th 2016. doi: 10.1038/nnano.2015.310

http://www.eurekalert.org/pub_releases/2016-01/aha-awh012116.php

A woman's heart attack causes, symptoms may differ from a man's

American Heart Association Scientific Statement

DALLAS - A woman's heart attack may have different underlying causes, symptoms and outcomes compared to men, and differences in risk factors and outcomes are further pronounced in black and Hispanic women, according to a scientific statement published in the American Heart Association's journal Circulation.

The statement is the first scientific statement from the American Heart Association on heart attacks in women. It notes that there have been dramatic declines in cardiovascular deaths among women due to improved treatment and prevention of heart disease as well as increased public awareness.

"Despite stunning improvements in cardiovascular deaths over the last decade, women still fare worse than men and heart disease in women remains underdiagnosed, and undertreated, especially among African-American women," said writing group chair Laxmi Mehta, M.D., a noninvasive cardiologist and Director of the Women's Cardiovascular Health Program at The Ohio State University.

Causes:

Heart attacks caused by blockages in the main arteries leading to the heart can occur in both men and women. However, the way the blockages form a blood clot may differ. Compared to men, women can have less severe blockages that do not require any stents; yet the heart's coronary artery blood vessels are damaged which results in decreased blood flow to the heart muscle. The result is the same - when blood flow to the heart is decreased for any reason, a heart attack can occur. If doctors don't correctly diagnose the underlying cause of a woman' heart attack, they may not be prescribing the right type of treatments after the heart attack. Medical therapies are similar regardless of the cause of the heart attack or the severity of the blockages. However women are undertreated compared to men despite proven benefits of these medications.

Treatment:

Women face greater complications from attempts to restore blood flow because their blood vessels tend to be smaller, they are older and have increased rates of risk factors, such as diabetes and high blood pressure. Guideline recommended medications are consistently underutilized in women leading to worse outcomes. Also, cardiac rehabilitation is prescribed less frequently for women and even when it is prescribed, women are less likely to participate in it or complete it.

Symptoms:

While the most common heart attack symptom is chest pain or discomfort for both sexes, women are more likely to have atypical symptoms such as shortness of breath, nausea or vomiting, and back or jaw pain.

Risk factors:

Risk factors for heart attacks also differ in degree of risk in men compared to women. For example, high blood pressure is more strongly associated with heart attacks in women and if a young woman has diabetes her risk for heart disease is 4 to 5 times higher compared to young men.

Racial differences:

Compared to white women, black women have a higher incidence of heart attacks in all age categories and young black women have higher in-hospital death rates. Black and Hispanic women tend to have more heart- related risk factors such as diabetes, obesity and high blood pressure at the time of their heart attack compared to non-Hispanic white women. Compared to white women, black women are also less likely to be referred for important treatments such as cardiac catheterization..

Understanding gender differences can help improve prevention and treatment among women. "Women should not be afraid to ask questions - we advise all women to have more open and candid discussions with their doctor about both medication and interventional treatments to prevent and treat a heart attack," Mehta said.

"Coronary heart disease afflicts 6.6 million American women annually and remains the leading threat to the lives of women. Helping women prevent and survive heart attacks through increased research and improving ethnic and racial disparities in prevention and treatment is a public health priority," she said.

Statement co-authors are Theresa Beckie, Ph.D.; Holli DeVon, Ph.D., R.N.; Cindy Grines, M.D.; Harlan Krumholz, M.D., S.M.; Michelle Johnson, M.D., M.P.H.; Kathryn Lindley, M.D.; Viola Vaccarino, M.D., Ph.D.; Tracy Wang, M.D., M.H.S., M.Sc.; Karol Watson, M.D., Ph.D.; Nanette Wenger, M.D.

http://bit.ly/1PmZruB

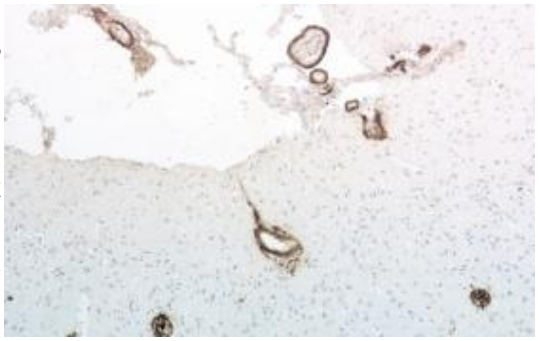
More Evidence Emerges for "Transmissible Alzheimer's" Theory

The disease is not normally infectious, but people who received grafts from cadavers did show telltale markers in their brains

By Alison Abbott, Nature magazine

For the second time in four months, researchers have reported autopsy results that suggest Alzheimer's disease might occasionally be transmitted to people during certain medical treatments—although scientists say that neither set of findings is conclusive.

The latest autopsies, described in the *Swiss Medical Weekly* on January 26, were conducted on the brains of seven people who died of the rare, brain-wasting Creutzfeldt–Jakob disease (CJD). Decades before their deaths, the individuals had all received surgical grafts of dura mater—the membrane that covers the brain and spinal cord. These grafts had been prepared from human cadavers and were contaminated with the prion protein that causes CJD.



Deposits of amyloid-β protein (brown) in the frontal cortex of patients who developed CJD after surgery. **Frontzek K, Lutz MI, Aguzzi A, Kovacs GG, Budka H. Amyloid-β pathology and cerebral amyloid angiopathy are frequent iniatrogenic Creutzfeldt-Jakob disease after dural grafting. Swiss Med Wkly. 2016;146:w14287.**

But in addition to the damage caused by the prions, five of the brains displayed some of the pathological signs that are associated with Alzheimer's disease, researchers from Switzerland and Austria report. Plaques formed from amyloid-β protein were discovered in the grey matter and blood vessels. The individuals, aged between 28 and 63, were unusually young to have developed such plaques. A set of 21 controls, who had not had surgical grafts of dura mater but died of sporadic CJD at similar ages, did not have this amyloid signature.

Transplant trouble

According to the authors, it is possible that the transplanted dura mater was contaminated with small 'seeds' of amyloid-β protein—which some scientists think could be a trigger for Alzheimer's—along with the prion protein that gave the recipients CJD.

Both diseases have long incubation periods. But whereas CJD progresses quickly once initiated, age-related Alzheimer's develops slowly. None of the individuals had displayed obvious Alzheimer's symptoms before their deaths.

The results follow a study published in *Nature* last September in which scientists from University College London reported that four of eight relatively young people, all of whom died of CJD decades after receiving contaminated batches of growth hormone prepared from cadavers, also displayed amyloid plaques in the blood vessels and grey matter of their brains.

"Our results are all consistent," says neurologist John Collinge, a co-author on the *Nature* paper. "The fact that the new study shows the same pathology emerging after a completely different procedure increases our concern."

Not infectious

Neither study implies that Alzheimer's disease could ever be transmitted through normal contact with caretakers or family members, the scientists emphasize. And no one uses cadaver-derived preparations in the clinic anymore. Synthetic growth hormone is used for growth disorders, and synthetic membranes are used for patching up in brain surgery.

But the scientists say that if the theory of amyloid seeding turns out to be true, it would have important clinical implications. In general surgery, for example, any amyloid-β proteins, which are very sticky, would not be routinely removed from surgical instruments; standard sterilization procedures cannot shift them.

"It is our job as doctors to see in advance what might become a problem in the clinic," says neuropathologist Herbert Budka of the University Hospital Zurich, Switzerland, who is a co-author of the latest paper.

"Nothing is proven yet," cautions Pierluigi Nicotera, head of the German Centre for Neurodegenerative Diseases in Bonn. He points out that amyloid-β has not been identified in the preparations that were transplanted in either the growth hormone or dura mater studies. Nor can researchers rule out the possibility that the underlying condition that led to the need for neurosurgery could have contributed to the observed amyloid pathology, as the authors of the latest paper note.

"We need more systematic studies in model organisms to work out if the seeding hypothesis of Alzheimer's is correct," Nicotera says.

http://bit.ly/1KKeauh

Did Zika's recent mutations let it explode as a global threat?

Don't get pregnant, at least for now. That is the chilling warning from governments battling the Zika pandemic, as evidence mounts that the mosquito-borne virus can cause severe birth defects.

As the scale of the impact starts to emerge, scientists are scrambling to learn more about the little-known virus. Is it evolving to be more severe and contagious in humans? Or has it taken off so aggressively simply because someone carried it to a new place with the right mosquitoes?

Zika virus got a foothold in the Americas, via Brazil, early last year. Since then it is estimated to have infected up to 1.3 million people there, and to have broken out in 25 countries where it was previously unknown, across Asia, Africa and the Pacific. This includes 12 countries in the Americas that have been infected since mid-December.

Travellers with Zika are turning up as far afield as New York and the UK. In places where the *Aedes* mosquitoes that carry the virus live, such infected people could spread it further.

Aedes mosquitoes occur throughout the tropics and into the temperate zone, including southern Europe and as far north in the US as Long Island. The World Health Organization announced today that in the Americas only Canada and continental Chile are free of *Aedes* – hence the virus could spread everywhere else.

More efficient virus?

What is worrying virologists, says Paolo Zanotto of the University of Sao Paulo in Brazil, is that before 2000, Zika wasn't known to spread widely among humans or cause the kind of complications we are seeing today, such as stunted brain development in fetuses and the potentially fatal neural disorder Guillain-Barré syndrome (see "Zika: symptoms and complications", below).

It evolved in Africa as an infection of forest animals – possibly primates – that occasionally infected people, but never spread. Decades ago it invaded some parts of South-East Asia, abandoning animals and spreading solely among humans, but went no further.

Now that Asian strain is exploding. It infected 75 per cent of Yap islanders in Polynesia in 2007 and caused a massive outbreak in French Polynesia in 2013.

That outbreak was followed by a rise in Guillain-Barré syndrome and brain damage in newborns. “I suspect the virus may have changed,” says Scott Weaver of the University of Texas in Galveston. It may be able to infect mosquitoes more easily, or multiply to higher levels in humans, so a mosquito is more likely to ingest some and infect her next victim.

In work awaiting peer review, Zanotto reports that Zika has recently acquired subtle changes to its genome, which may allow it to hijack human cells more efficiently.

Crowded cities

But both Zanotto and Weaver stress that the virus’s apparent leap in virulence and transmission might just be down to it invading virgin territory, where people have no previous exposure and therefore no immunity.

Other factors might have pushed it beyond its South-East Asian stronghold. Increasingly dense urban populations where humans and mosquitoes are crowded together will have led to more infections, making it more likely that someone with high levels of virus in their blood would carry Zika somewhere else with *Aedes* mosquitoes.

Several labs are gearing up to see if recent strains are better at infecting *Aedes* – and have the mutations to match. After discovering molecules on Zika that resemble some on dengue virus, Zanotto is starting a trial to see if exposure to one causes damaging immune reactions to the other. He is worried that getting Zika might leave people vulnerable to a more serious form of dengue, and vice versa.

“There are a lot of studies going on in Brazil,” says Maurício Nogueira of the Medical Faculty of São José in Rio Preto, Brazil, but results will take time, and the epidemic is growing. “We are trying to change the tyres with the car running.”

Meanwhile, virologists worry about which virus will next leap from obscurity. “This will not stop with Zika,” warns Ab Osterhaus of the University of Rotterdam in the Netherlands, who is looking at recent mutations in the virus. “We must get better at picking up these things earlier, and intervening.”

Zika: symptoms and complications

Some 80 per cent of people infected with the Zika virus don't have any symptoms. Those that do occur are mild: fever, rash, joint pain and eye inflammation for a week or less. The problem now emerging is its complications. Like many viruses including flu, Zika seems to trigger neural damage called Guillain-Barré syndrome in some people, which can lead to paralysis or death.

It also attacks unborn babies. Microcephaly - babies born with brain damage and abnormally small heads - has jumped 20-fold in Brazil since Zika arrived. Other malformations have also afflicted babies whose mothers had Zika symptoms during pregnancy.

Strengthening the link to the virus, the European Centre for Disease Control and Prevention in Stockholm, Sweden, reported last week that Zika has been found in tissues from five affected babies. Maurício Nogueira of the Medical Faculty of São José in Rio Preto, Brazil, says ultrasound studies to be published soon suggest it attacks the developing forebrain.

With no defence beyond anti-mosquito measures, affected countries are advising women to postpose pregnancy, while countries outside the outbreak zone are telling women to postpose travel to the area.

El Salvador, for example, has warned women not to get pregnant until 2018, although it is unclear how, in a country where birth control isn't always available, or what will have changed by 2018. Chikungunya, a similar virus, invaded the Americas in 2013 and is still raging.

http://www.eurekalert.org/pub_releases/2016-01/uoi-crs012616.php

Cancer riddle, solved

University of Iowa researchers reveal how cancer cells form tumors

Cancer is a mysterious disease for many reasons. Chief among the unknowns are how and why tumors form.

Two University of Iowa studies offer key insights by recording in real time, and in 3-D, the movements of cancerous human breast tissue cells. It's believed to be the first time cancer cells' motion and accretion into tumors has been continuously tracked. (See accompanying videos.)

The team discovered that cancerous cells actively recruit healthy cells into tumors by extending a cable of sorts to grab their neighbors--both cancerous and healthy--and reel them in. Moreover, the Iowa researchers report that as little as five percent of cancerous cells are needed to form the tumors, a ratio that heretofore had been unknown.

"It's not like things sticking to each other," said David Soll, biology professor at the UI and corresponding author on the paper, published in the American Journal of Cancer Research. "It's that these cells go out and actively recruit. It's complicated stuff, and it's not passive. No one had a clue that there were specialized cells in this process, and that it's a small number that pulls all the rest in."

The findings could lead to a more precise identification of tumorigenic cells (those that form tumors) and testing which antibodies would be best equipped to eliminate them. Soll's Monoclonal Antibody Research Institute and the Developmental Studies Hybridoma Bank, created by the National Institutes of Health as a national resource, directed by Soll and housed at the UI, together contain one of the world's largest collections of antibodies that could be used for the anti-cancer testing, based on the new findings.

In a paper published last spring in the journal PLOS One, Soll's team showed that only cancerous cells (from a variety of cancers, including lung, skin, and aggressive brain tumors known as glioblastomas) engaged in tumor formation by actively soliciting other cells. Like evil-minded envoys, individual cancer cells extend themselves outward from the original cluster, probing for other cells in the area, the researchers observed.

Once it detects one, the extended cell latches on and pulls it in, forming a larger mass. The activity continues, the cancerous extensions drawing in more and more cells--including healthy cells--as the tumor enlarges. "There's nothing but tumorigenic cells in the bridge (between cells)," Soll said, "and that's the discovery. The tumorigenic cells know what they're doing. They make tumors."

The question is how these cells know what to do. Soll hypothesizes they're reaching back to a primitive past, when these cells were programmed to form embryos. If true, perhaps the cancerous cells--masquerading as embryo-forming cells--recruit other cells to make tissue that then forms the layered, self-sustaining architecture needed for a tumor to form and thrive.

Think of a Death Star that's built up enough defenses to ward off repeated attacks. Or, less figuratively, how bacteria can conspire to create an impenetrable film on surfaces, from orthopedic implants to catheters.

"There must be a reason," Soll said. "You might want one big tumor capable of producing the tissue it needs to form a micro-environment. It's as if it's building its own defenses against the body's efforts to defeat them."

In the AJCR paper, the researchers compared the actions of human breast tissue cells (MoVi-10') to a weakly tumorigenic, parental breast cancer cell line (MCF-7). First, they found that over a 50-hour period, MoVi-10'-only cells grew more in density, primarily by joining together, than did MCF-7.

Also, in all instances, regardless of the ratio of MCF-7 to MoVi-10' cells in the cluster, only MoVi-10' cells reached out and drew in other cells--including healthy cells--to the growing mass.

"The results here extend our original observation that tumorigenic cell lines and fresh tumor cells possess the unique capacity to undergo coalescence through the active formation of cellular cables," the authors write. The finding lends more weight to the idea that tumors are created concurrently, in multiple locations, by individual clusters of cells that employ the cancer-cell cables to draw in more cells and enlarge themselves. Some have argued that tumors come about more by cellular changes within the masses, known as the "cancer stem cell theory."

Soll's team also discovered that the Mo-Vi10' cells move at 92 microns per hour, about twice the speed of healthy cells. That's important because it helps scientists better understand how quickly tumors can be created.

Contributing authors, all from the University of Iowa, include Joseph Ambrose, Michelle Livitz, Deborah Wessels, Spencer Kuhl, Daniel Lusche, and Edward Voss. Amanda Scherer, now at the University of Michigan, also contributed to the research while at the UI.

The Developmental Studies Hybridoma Bank funded the study.

http://bit.ly/1P1Mzqf

How Data Brokers Make Money Off Your Medical Records

Data brokers legally buy, sell and trade health information, but the practice risks undermining public confidence

By Adam Tanner on February 1, 2016

For decades researchers have run longitudinal studies to gain new insights into health and illness. By regularly recording information about the same individuals' medical history and care over many years, they have, for example, shown that lead from peeling paint damages children's brains and bodies and have demonstrated that high blood pressure and cholesterol levels contribute to heart disease and stroke. To this day, some of the original (and now at least 95-year-old) participants in the famous Framingham Heart Study, which began in 1948, still provide health information to study investigators.

Health researchers are not the only ones, however, who collect and analyze medical data over long periods. A growing number of companies specialize in gathering longitudinal information from hundreds of millions of hospitals' and doctors' records, as well as from prescription and insurance claims and laboratory tests. Pooling all these data turns them into a valuable commodity. Other businesses are willing to pay for the insights that they can glean from such collections to guide their investments in the pharmaceutical industry, for example, or more precisely tailor an advertising campaign promoting a new drug.

By law, the identities of everyone found in these commercial databases are supposed to be kept secret. Indeed, the organizations that sell medical information to data-mining companies strip their records of Social Security numbers, names and detailed addresses to protect people's privacy.

But the data brokers also add unique numbers to the records they collect that allow them to match disparate pieces of information to the same individual—even if they do not know that person's name. This matching of information makes the overall collection more valuable, but as data-mining technology becomes ubiquitous, it also makes it easier to learn a previously anonymous individual's identity.

At present, the system is so opaque that many doctors, nurses and patients are unaware that the information they record or divulge in an electronic health record or the results from lab tests they request or consent to may be anonymized and sold. But they will not remain in the dark about these practices forever. In

researching the medical-data-trading business for an upcoming book, I have found growing unease about the ever expanding sale of our medical information not just among privacy advocates but among health industry insiders as well.

The entire health care system depends on patients trusting that their information will be kept confidential. When they learn that others have insights into what happens between them and their medical providers, they may be less forthcoming in describing their conditions or in seeking help. More and more health care experts believe that it is time to adopt measures that give patients more control over their data.

Multibillion-Dollar Business

The dominant player in the medical-data-trading industry is IMS Health, which recorded $2.6 billion in revenue in 2014. Founded in 1954, the company was taken private in 2010 and relaunched as public in 2014. Since then, it has proved an investor favorite, with shares rising more than 50 percent above its initial price in little more than a year. At press time, IMS was a $9-billion company. Competitors include Symphony Health Solutions and smaller rivals in various countries.

Decades ago, before computers came into widespread use, IMS field agents photographed thousands of prescription records at pharmacies for hundreds of clerks to transcribe—a slow and costly process. Nowadays IMS automatically receives petabytes (10^{15} bytes or more) of data from the computerized records held by pharmacies, insurance companies and other medical organizations—including federal and many state health departments. Three quarters of all retail pharmacies in the U.S. send some portion of their electronic records to IMS. All told, the company says it has assembled half a billion dossiers on individual patients from the U.S. to Australia.

IMS and other data brokers are not restricted by medical privacy rules in the U.S., because their records are designed to be anonymous—containing only year of birth, gender, partial zip code and doctor's name. The Health Insurance Portability and Accountability Act (HIPAA) of 1996, for instance, governs only the transfer of medical information that is tied directly to an individual's identity.

Even anonymized, the data command premium prices. Every year, for example, Pfizer spends $12 million to buy health data from a variety of sources, including IMS, according to Marc Berger, who oversees the analysis of anonymized patient data at Pfizer. But companies engaged in the data trade tend to keep the practice below the general public's radar.

Case in point: In the 1990s IMS started selling data on what individual U.S. physicians prescribe to patients to help drug companies tailor sales pitches to specific care providers. (HIPAA protects the identity of patients, not health care workers.) For years doctors did not realize that outsiders had insights on their prescribing habits. “At the time, it was taboo. It was forbidden to ever mention that topic,” says Shahram Ahari, who used such data as a pharmaceutical representative visiting doctors for Eli Lilly from 1999 to 2000 and is now completing a residency at the University of Rochester. “It was the big secret.” Asked for a response, an Eli Lilly spokesperson replied in an e-mail, “We have always been up front that we receive data from IMS.”

Eventually physicians caught on and complained. Some considered such data gathering a privacy invasion; others objected to commercial firms profiting from details about their practices. A few states passed laws banning the collection of physician-prescribing habits. IMS challenged those rules all the way to the U.S. Supreme Court and—despite the arguments of 36 states, the Department of Justice, and numerous medical and consumer-advocacy groups supporting data limits—won its case in 2011 on corporate “free speech” grounds. The practice continues to this day, much of the time beyond public notice.

What Could Go Wrong?

Once upon a time, simply removing a person's name, address and Social Security number from a medical record may well have protected anonymity. Not so today. Straightforward data-mining tools can rummage through multiple databases containing anonymized and nonanonymized data to reidentify the individuals from their ostensibly private medical records.

Indeed, computer scientists have repeatedly shown how easy it can be to crack seemingly anonymous data sets. For example, Harvard University professor Latanya Sweeney used such methods when she was a graduate student at the Massachusetts Institute of Technology in 1997 to identify then Massachusetts governor William Weld in publicly available hospital records. All she had to do was compare the supposedly anonymous hospital data about state employees to voter registration rolls for the city of Cambridge, where she knew the governor lived.

Soon she was able to zero in on certain records based on age and gender that could have only belonged to Weld and that detailed a recent visit he made to a hospital, including his diagnosis and the prescriptions he took home with him.

“It is getting easier and easier to identify people from anonymized data,” says Chesley Richards, director of the Office of Public Health Scientific Services at the Centers for Disease Control and Prevention. “You may not be identifiable from a particular data set that an entity has collected, but if you are a broker that is assembling a number of sets and looking for ways to link those data, that's where, potentially, the risk becomes greater for identification.”

IMS officials say they have no interest in identifying patients and take careful steps to preserve anonymity. Moreover, there are no publicly recorded instances of someone taking anonymized patient data from IMS or a rival company and reidentifying individuals.

Yet IMS does not want to talk too much about the gathering and selling of longitudinal data. At IMS, the CEO, the head of its Institute for Healthcare Informatics, the vice president of industry relations and the chief privacy officer declined to be interviewed for this article, but a company spokesperson did assist with fact-checking.

Where to Draw the Line?

Apart from making money selling information to other businesses, IMS also shares some data with academic and other researchers for free or at a discount. The company has published a long list of medical articles that relied on its longitudinal data. For example, researchers learned that newer cardiovascular drugs reduce the length of hospital stays but do not prolong lives. In contrast, newer chemotherapy drugs are probably responsible for some of the recent decline in death rates from cancer in France.

Such benefits demonstrate that amassing medical data from multiple sources can have societal benefits. There is, however, a difference, says Jerry Avorn, a professor of medicine at Harvard Medical School, between “conscious, responsible researchers who only want to learn about medications' good and bad effects in a university medical school setting versus somebody sitting in the backroom [of a superstore] trying to figure out how can they sell more of product X by invading someone's privacy.”

One small step toward reestablishing trust in the confidentiality of medical information is to give individuals the chance to forbid collection of their information for commercial use—an option the Framingham study now offers its participants, as does the state of Rhode Island in its sharing of anonymized insurance claims. “I personally believe that at the end of the day, individuals own their data,” says Pfizer's Berger. “If somebody is using [their] data, they should know.” And if the collection is “only for commercial purposes, I think patients should have the ability to opt out.”

Seeking more detailed consent cannot, by itself, stem the erosion of patient privacy, but it will raise awareness—without which no further action is possible. Trust in the medical system is too vital to be sacrificed to uncontrolled market forces.

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http://www.eurekalert.org/pub_releases/2016-01/uobc-amc012516.php

Ancient medicinal clay shows promise against today's worst bacterial infections

Rare mineral clay recommended for study as a clinical treatment for serious infections caused by ESKAPE strains of bacteria

Naturally occurring clay from British Columbia, Canada -- long used by the region's Heiltsuk First Nation for its healing potential -- exhibits potent antibacterial activity against multidrug-resistant pathogens, according to new research from the University of British Columbia.

The researchers recommend the rare mineral clay be studied as a clinical treatment for serious infections caused by ESKAPE strains of bacteria.

The so-called ESKAPE pathogens -- Enterococcus faecium, , Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species -- cause the majority of U.S. hospital infections and effectively 'escape' the effects of antibacterial drugs.

"Infections caused by ESKAPE bacteria are essentially untreatable and contribute to increasing mortality in hospitals," says UBC microbiologist Julian Davies, co-author of the paper published today in the American Society for Microbiology's mBio journal. "After 50 years of over-using and misusing antibiotics, ancient medicinals and other natural mineral-based agents may provide new weapons in the battle against multidrug-resistant pathogens."

The clay deposit is situated on Heiltsuk First Nation's traditional territory, 400 kilometres (250 miles) north of Vancouver, Canada, in a shallow five-acre granite basin. The 400-million kilogram (400,000 tonne) deposit was formed near the end of the last Ice Age, approximately 10,000 years ago.

Local First Nations people have used the clay for centuries for its therapeutic properties -- anecdotal reports cite its effectiveness for ulcerative colitis, duodenal ulcer, arthritis, neuritis, phlebitis, skin irritation, and burns.

"We're fortunate to be able to partner with UBC on this significant research program" says Lawrence Lund, president of Kisameet Glacial Clay, a business formed to market cosmetic and medicinal products derived from the clay. "We hope it will lead to the development of a novel and safe antimicrobial that can be added to the diminished arsenal for the fight against the ESKAPE pathogens and other infection-related health issues plaguing the planet."

In the in vitro testing conducted by Davies and UBC researcher Shekooh Behroozian, clay suspended in water killed 16 strains of ESKAPE bacteria samples from sources including Vancouver General Hospital, St. Paul's Hospital, and the University of British Columbia's wastewater treatment pilot plant.

No toxic side effects have been reported in the human use of the clay, and the next stage in clinical evaluation would involve detailed clinical studies and toxicity testing. Loretta Li, with UBC's Department of Civil Engineering, is conducting mineralogical and chemical analyses of the clay as well. MITACS, Kisameet Glacial Clay Inc. and the Tally Fund supported the work.

http://www.eurekalert.org/pub_releases/2016-01/bifr-tcb012116.php

The connection between excess iron and Parkinson's disease

Excess iron impairs cellular recycling resulting in toxic oxidative stress

Credit: Subramanian Rajagopalan, MSc. Buck Institute for Research on Aging

It's long been known that excess iron is found in the brains of patients with Parkinson's disease (PD), an incurable neurodegenerative condition that affects motor function. The mechanism by which the iron wreaks damage on neurons involved in PD has not been clear. Research from the Andersen lab at the Buck Institute suggests that the damage stems from an impairment in the lysosome, the organelle that acts as a cellular recycling center for damaged proteins. Scientists report the impairment allows excess iron to escape into the neurons where it causes toxic oxidative stress. The research will be published online in The Journal of Neuroscience on Jan. 27, 2016.

Lysosomes are key to a process called autophagy, whereby damaged proteins are broken down into building blocks that are used to make newly-built proteins to take their place. It's the cellular equivalent of recycling. With age, the ability of the lysosome to participate in autophagy becomes slower, resulting in the build-up of non-protein "garbage" within the cells. Less-than-optimal autophagy has been associated with several age-related diseases, including PD.

"It's recently been realized that one of the most important functions of the lysosome is to store iron in a place in the cell where it is not accessible to participate in toxic oxidative stress-producing reactions," said Julie K. Andersen, PhD, senior scientist and Buck Institute faculty. "Now we have demonstrated that a mutation in a lysosomal gene results in the toxic release of iron into the cell resulting in neuronal cell death."

Spearheaded by staff scientist Shankar J. Chinta, PhD, the work (done in both mice and cultured human dopaminergic cells) involved a mutation in a gene (ATP13A2) associated with a rare early onset form of PD called Kufor-Rakeb syndrome. When researchers knocked out ATP13A2 the lysosome was unable to maintain the balance of iron within the cell.

The mutation responsible for Kufor-Rakeb was identified in 2010. Those suffering from the condition, which is named for the village in Jordan where the syndrome was first described, experience disease onset in adolescence. "Mutations in this same gene have also been recently linked to sporadic forms of PD," said Andersen. "This suggests that age-related impairments in lysosomal function that impact the ability of neurons to maintain a healthy balance of iron are part of what underlies the presentation of PD in the general population."

Andersen has a long-standing interest in the role of excess iron in PD and this current work provides an example of the value of basic research in drug discovery. In 2003 her lab showed that tying up excess iron with a metal chelator (derived from the Greek word for claw) protected mice from the ravaging effects of the well-known Parkinson's inducing toxin, MPTP. The study provided an important link between the observed excessive iron in the brains of PD patients and oxidative stress associated with neurodegeneration. "The issue with iron chelation is that it's a sledge hammer -- it pulls iron from the cells indiscriminately and iron is needed throughout the body for many biological functions," said Andersen. "Now we have a more specific target that we can hit with a smaller hammer, which could allow us to selectively impact iron toxicity within the affected neurons."

Citation: "Regulation of ATP13A2 via PHD2-HIF1a Signaling is Critical for Cellular Iron Homeostasis: Implications for Parkinson's Disease" DOI: 10.1523/JNEUROSCI.3117-15.2016

Other Buck scientists involved in the study include Subramanian Rajagopalan and Anand Rane. This work was supported by the National Institutes of Health (RO1 NS047198, NS047198, NS041264, and AG012141).

http://www.eurekalert.org/pub_releases/2016-01/uoo-tmm012216.php

Too many minions spoil the plot

Equation shows that large-scale conspiracies would quickly reveal themselves

If you're thinking of creating a massive conspiracy, you may be better scaling back your plans, according to an Oxford University researcher.

While we can all keep a secret, a study by Dr David Robert Grimes suggests that large groups of people sharing in a conspiracy will very quickly give themselves away. The study is published online by journal PLOS ONE.

Dr Grimes, a physicist working in cancer research, is also a science writer and broadcaster. His profile means that he receives many communications from people who believe in science-related conspiracies. Those messages prompted him to look at whether large-scale collusions were actually tenable.

He explained: 'A number of conspiracy theories revolve around science. While believing the moon landings were faked may not be harmful, believing misinformation about vaccines can be fatal. However, not every belief in a conspiracy is necessarily wrong - for example, the Snowden revelations confirmed some theories about the activities of the US National Security Agency.

'It is common to dismiss conspiracy theories and their proponents out of hand but I wanted to take the opposite approach, to see how these conspiracies might be possible. To do that, I looked at the vital requirement for a viable conspiracy - secrecy.'

Dr Grimes initially created an equation to express the probability of a conspiracy being either deliberately uncovered by a whistle-blower or inadvertently revealed by a bungler. This factors in the number of conspirators, the length of time, and even the effects of conspirators dying, whether of old age or more nefarious means, for those conspiracies that do not require active maintenance.

However, the equation required a realistic estimation of the chances of any one individual revealing a conspiracy. Three genuine conspiracies were used to provide this - including the NSA Prism project revealed by Edward Snowden.

In each case, the number of conspirators and the time before the conspiracy was revealed were over-estimated to ensure that the odds of a leak happening were a 'best case scenario' for the conspirators - around a four in one million chance of deliberate or accidental exposure.

Dr Grimes then looked at four alleged plots, estimating the maximum number of people required to be in on the conspiracy, in order to see how viable these conspiracies could be. These include: the theory that the US moon landings were a hoax (411,000 people); that Climate Change is a fraud (405,000 people); that unsafe vaccinations are being covered up (22,000 people assuming that only the World Health Organisation and the US Centers for Disease Control are conspirators and that others involved in advocating, producing, distributing and using vaccines are dupes. 736,000 people if, as would be more likely, pharmaceutical companies were included); that the cure for Cancer is being supressed by the world's leading pharmaceutical firms (714,000 people).

Using the equation, Dr Grimes calculated that hoax moon landings would have been revealed in 3 years 8 months, a climate change fraud in 3 years 9 months, a vaccination conspiracy in 3 years 2 months, and a suppressed Cancer cure in 3 years 3 months. In simple terms, any one of the four conspiracies would have been exposed long before now.

He then looked at the maximum number of people who could take part in an intrigue in order to maintain it. For a plot to last five years, the maximum was 2521 people. To keep a scheme operating undetected for more than a decade, fewer than 1000 people can be involved. A century-long deception should ideally include fewer than 125 collaborators. Even a straightforward cover-up of a single event, requiring no more complex machinations than everyone keeping their mouth shut, is likely to be blown if more than 650 people are accomplices.

Dr Grimes said: 'Not everyone who believes in a conspiracy is unreasonable or unthinking. I hope that by showing how eye-wateringly unlikely some alleged conspiracies are, some people will reconsider their anti-science beliefs.

'This will of course not convince everyone; there's ample evidence that belief in conspiracy is often ideological rather than rational, and that conspiracy theories thrive in an echo chamber. This makes challenging the more odious narratives much more difficult. If we are to address the multitudinous difficulties facing us as a species, from climate change to geo-politics, then we need to embrace reality over ideologically motivated fictions. To this end, we need to better understand how and why some ideas are entrenched and persistent among certain groups despite the evidence, and how we might counteract this.'

The paper, On the viability of conspiratorial beliefs, is published online by PLOS ONE: http://dx.plos.org/10.1371/journal.pone.0147905

http://www.eurekalert.org/pub_releases/2016-01/niom-ssk012716.php

Schizophrenia's strongest known genetic risk deconstructed

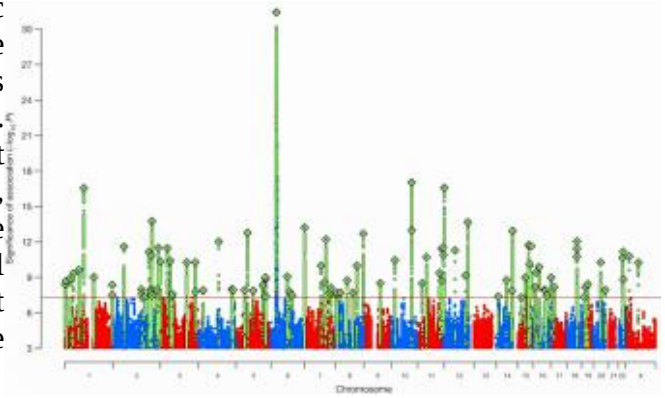
Suspect gene may trigger runaway synaptic pruning during adolescence -- NIH-funded study

Versions of a gene linked to schizophrenia may trigger runaway pruning of the teenage brain's still-maturing communications infrastructure, NIH-funded researchers have discovered. People with the illness show fewer such connections between neurons, or synapses. The gene switched on more in people with the suspect versions, who faced a higher risk of developing the disorder, characterized by hallucinations, delusions and impaired thinking and emotions.

"Normally, pruning gets rid of excess connections we no longer need, streamlining our brain for optimal performance, but too much pruning can impair mental function," explained Thomas Lehner, Ph.D., director of the Office of Genomics Research Coordination of the NIH's National Institute of Mental Health (NIMH), which co-funded the study along with the Stanley Center for Psychiatric Research at the Broad Institute and other NIH components. "It could help explain schizophrenia's delayed age-of-onset of symptoms in late adolescence/early adulthood and shrinkage of the brain's working tissue. Interventions that put the brakes on this pruning process-gone-awry could prove transformative."

The gene, called C4 (complement component 4), sits in by far the tallest tower on schizophrenia's genomic "skyline" (see graph below) of more than 100 chromosomal sites harboring known genetic risk for the disorder. Affecting about 1 percent of the population, schizophrenia is known to be as much as 90 percent heritable, yet discovering how specific genes work to confer risk has proven elusive, until now.

A team of scientists led by Steve McCarroll, Ph.D., of the Broad Institute and Harvard Medical School, Boston, leveraged the statistical power conferred by analyzing the genomes of 65,000 people, 700 postmortem brains, and the precision of mouse genetic engineering to discover the secrets of schizophrenia's strongest known genetic risk. C4's role represents the most compelling evidence, to date, linking specific gene versions to a biological process that could cause at least some cases of the illness.



The site in Chromosome 6 harboring the gene C4 towers far above other risk-associated areas on schizophrenia's genomic "skyline," marking its strongest known genetic influence. The new study is the first to explain how specific gene versions work biologically to confer schizophrenia risk. **Psychiatric Genomics Consortium**

"Since schizophrenia was first described over a century ago, its underlying biology has been a black box, in part because it has been virtually impossible to model the disorder in cells or animals," said McCarroll. "The human genome is providing a powerful new way in to this disease. Understanding these genetic effects on risk is a way of prying open that block box, peering inside and starting to see actual biological mechanisms." McCarroll's team, including Harvard colleagues Beth Stevens, Ph.D., Michael Carroll, Ph.D., and Aswin Sekar, report on their findings online Jan. 27, 2016 in the journal Nature.

A swath of chromosome 6 encompassing several genes known to be involved in immune function emerged as the strongest signal associated with schizophrenia risk in genome-wide analyses by the NIMH-funded Psychiatric Genomics Consortium over the past several years. Yet conventional genetics failed to turn up any specific gene versions there linked to schizophrenia.

To discover how the immune-related site confers risk for the mental disorder, McCarroll's team mounted a search for "cryptic genetic influences" that might generate "unconventional signals." C4, a gene with known roles in immunity, emerged as a prime suspect because it is unusually variable across individuals. It is not unusual for people to have different numbers of copies of the gene and distinct DNA sequences that result in the gene working differently.

The researchers dug deeply into the complexities of how such structural variation relates to the gene's level of expression and how that, in turn, might relate to schizophrenia. They discovered structurally distinct versions that affect expression of two main forms of the gene in the brain. The more a version resulted in expression of one of the forms, called C4A, the more it was associated with schizophrenia. The more a person had the suspect versions, the more C4 switched on and the higher their risk of developing schizophrenia. Moreover, in the human brain, the C4 protein turned out to be most prevalent in the cellular machinery that supports connections between neurons.

Adapting mouse molecular genetics techniques for studying synaptic pruning and C4's role in immune function, the researchers also discovered a previously unknown role for C4 in brain development. During critical periods of postnatal brain maturation, C4 tags a synapse for pruning by depositing a sister protein in it called C3. Again, the more C4 got switched on, the more synapses got eliminated.

In humans, such streamlining/pruning occurs as the brain develops to full maturity in the late teens/early adulthood - conspicuously corresponding to the age-of-onset of schizophrenia symptoms.

Future treatments designed to suppress excessive levels of pruning by counteracting runaway C4 in at risk individuals might nip in the bud a process that could otherwise develop into psychotic illness, suggest the researchers. And thanks to the head start gained in understanding the role of such complement proteins in immune function, such agents are already in development, they note.

"This study marks a crucial turning point in the fight against mental illness. It changes the game," added acting NIMH director Bruce Cuthbert, Ph.D. "Thanks to this genetic breakthrough, we can finally see the potential for clinical tests, early detection, new treatments and even prevention."

VIDEO: Opening Schizophrenia's Black Box https://youtu.be/s0y4equOTLg

Reference: Sekar A, Biala AR, de Rivera H, Davis A, Hammond TR, Kamitaki N, Tooley K Presumey J Baum M, Van Doren V, Genovese G, Rose SA, Handsaker RE, Schizophrenia Working Group of the Psychiatric Genomics Consortium, Daly MJ, Carroll MC, Stevens B, McCarroll SA. Schizophrenia risk from complex variation of complement component 4. Nature. Jan 27, 2016. DOI: 10.1038/nature16549.

http://bit.ly/2014e6I

Mass Shootings Are Contagious

A new analysis shows these incidents occur in clusters

By Kat Long, Victoria Stern

No one knows why mass murderers commit their appalling deeds. But new evidence reinforces the idea that mass shootings, publicized in the media, may have a contagious effect.

Researchers at Arizona State University analyzed news reports of gun-related incidents from 1997 to 2013. They hypothesized that the rampages did not occur

randomly over time but instead were clustered in patterns. The investigators applied a mathematical model and found that shootings that resulted in at least four deaths launched a period of contagion, marked by a heightened likelihood of more bloodshed, lasting an average of 13 days. Roughly 20 to 30 percent of all such violence took place in these windows.

Previous studies have shown that suicide can be similarly contagious. In one recent example, researchers found a correlation between celebrity suicides, like that of Robin Williams, and an increase in suicidal thoughts in an online Reddit suicide watch group for people battling depression.

"People are susceptible to information about these events, but the mechanism is less clear," says Andres Gomez-Lievano, a co-author of the mass-shooting study, published in July in *PLOS ONE*. Where and when the news reports were published could have an effect on incidence, says Dan Romer, director of the Adolescent Communication Institute at the University of Pennsylvania, who was not involved with the study. It is important to note, he says, that "suicides will trigger others, so it makes sense that people who want to commit suicide while killing others could be influenced in the same way." *—Kat Long*

Psychological Contagions

Many types of thoughts and behaviors can be socially contagious, according to a growing body of work.

- **Mass psychogenic illness.** ***When we see someone who is physically ill, we can manifest those symptoms simply by observing the person, leading to what looks like an outbreak.***
- **Emotions.** ***Altruism and happiness can spread within social groups. The flip side is true as well: bad moods, sadness, loneliness and depression can also spread in social groups or among individuals.***
- **Weight changes and disordered eating.** ***A 2007 study found that people are more likely to become obese when friends and relatives in their inner circle have gained a lot of weight. Some studies show that weight loss and disordered eating may be contagious, too. —Victoria Stern***

http://www.eurekalert.org/pub_releases/2016-01/asoh-ehd012216.php

Experts: High drug price trend has 'infected' generics

Authors highlight concern that pharmaceutical companies use strategies to delay patient access to affordable generic drugs

WASHINGTON - An article published online today in Blood, the Journal of the American Society of Hematology (ASH), suggests that pharmaceutical companies use several strategies to keep affordable generic drugs from the market, illustrating an emerging trend that authors say is becoming as harmful to consumers as high-cost brand-name drugs.

The market price of pharmaceuticals, some costing patients more than $100,000 per year, increases public health spending and sometimes forces patients to make life-or-death decisions when they cannot afford their medications. The authors write that approximately one in five Americans admit they do not fill their prescriptions because of cost. From an economic standpoint, in 2013 the United States spent nearly 40 percent more per capita on pharmaceuticals than the second highest spender, Canada.

Generic drugs, which by law may enter the market once the patent on a brand-name drug expires, are intended to offer an affordable option for patients without sacrificing the efficacy and safety of the original formula. From 2004-2013, generic drugs saved the U.S. health system nearly $1.5 trillion, according to the authors. However, for many patients generic drugs are inaccessible.

"The timely availability of affordable generic drugs is the difference between life or death for patients with cancer and other diseases who cannot afford brand-name pharmaceuticals, the majority of which are priced at monopoly levels and protected by 20-year patents," said lead author Hagop Kantarjian, MD, of The University of Texas MD Anderson Cancer Center. "Unfortunately, these sorely needed generics are increasingly out of reach. As we sought to understand what keeps these affordable drugs from the market, we identified several specific strategies that pharmaceutical companies use to extend their patents and eliminate competition."

In this Blood Forum article, a feature of the journal designed to present well-documented opinions on issues important to the science and practice of hematology, Dr. Kantarjian and colleagues assert that pharmaceutical companies use a variety of strategies to delay, prevent, and suppress the timely availability of affordable generic drugs. Among them, the authors detail "pay-for-delay," in which the company that owns the patent pays a generic company to delay entry into the market. The Federal Trade Commission estimates that the pay-for-delay settlements cost taxpayers, insurance companies, and consumers approximately $3.5 billion per year. In other cases detailed in the article, the patent-holder deters competition by creating its own version of drugs at generic prices. While this practice may reduce costs for consumers by 4-8 percent in the short-term, the authors suggest that companies often use the authorized generics as a bargaining chip in "pay-for-delay" deals, pledging not to release their own drugs in return for the true generic company promising to delay market entry.

Other strategies the authors discuss include investing heavily in advertising the brand-name drug (often spending more on marketing than on research and development) and lobbying for laws that prevent patients from importing cheaper generics from other countries, which the authors write can cost as little as 20-50

percent of U.S. prices. The authors also highlight some drug companies that they allege buy out competitors and then increase the price of a newly acquired generic drug by several fold overnight.

In addition, the authors also describe a strategy they call "product hopping," which involves switching the market for a drug to a reformulated "new and improved" version with a slightly different tablet or capsule dose that offers no therapeutic advantage over the original but has a later-expiring patent. The company then heavily advertises the new brand-name drug in an effort to convince patients and physicians to switch. As a result, when the generic version of the original becomes available, pharmacists cannot substitute it for the new branded version because state laws allow substitution only if certain characteristics, such as dosing, remain the same.

In recognition of the harm and expense that the authors suggest these strategies impart on both patients and the economy, they propose several solutions that would support timely access to affordable generic drugs, including allowing Medicare to negotiate drug prices, monitoring and penalizing pay-for-delay deals, allowing transportation of pharmaceuticals across borders for individual use, and challenging weak patents.

"Each day in my clinic I see leukemia patients who are harmed because they cannot afford their treatment, some risking death because they cannot pay for the medicine keeping them alive," said Dr. Kantarjian. "Overall, these strategies demonstrate that the trend of high brand-name drug prices has recently infected generic drugs, as companies value profit at the expense of long-term utility to society. We must be vigilant in recognizing these strategies and advocating for solutions that will allow companies to accomplish their dual mission: make reasonable profits and help save and/or improve patients' lives."

http://www.eurekalert.org/pub_releases/2016-01/tuhs-ssz012716.php

Study shows zinc supplement boosted serum zinc levels and immunity in older adults

Zinc supplementation is associated with enhancement of T-cell numbers and function

BOSTON -The immune system weakens as the body ages, making older adults more susceptible to infections. Low levels of zinc impair immunity, particularly in older adults. A research team set out to determine if it was feasible to increase serum zinc concentrations in older adults in nursing homes who were zinc-deficient. Their work appears today in The American Journal of Clinical Nutrition.

"Our previous work showed that 30 percent of nursing home residents have low serum zinc levels and those with low serum zinc levels had a significantly higher incidence of pneumonia and morbidity from it. Our new finding that serum zinc levels can be improved in older adults with zinc supplementation and that this is associated with enhancement of T-cell numbers and function strongly suggests that ensuring adequate zinc consumption by older adults could have a significant impact on reducing the incidence of and morbidity from infection, which is a major public health problem in older adults," said the study's lead author, Simin Nikbin Meydani, D.V.M., Ph.D., the director of the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University in Boston, and senior scientist and director of its Nutritional Immunology Laboratory.

The small double-blind, placebo-controlled trial involved adults age 65 or older from three Boston-area nursing homes. The study participants had baseline serum levels of zinc that ranged from moderately to very zinc-deficient. Participants were given zinc supplements or a placebo for three months. A total of 25 people completed the study, with 13 receiving the placebo (a daily multi-vitamin with only 5 mg of zinc), and 12 receiving a daily multi-vitamin with 30 mg of zinc. A serum-level of 70 micrograms per deciliter was used as the cut-off standard for adequate serum zinc level and measuring improvement from supplementation. The function of the immune response was assessed by determining the immune cell profile and function.

In addition to serum zinc concentrations, the researchers found that zinc supplementation improved the function of T-cells as determined by their ability to proliferate in response to stimuli that mimicked infection. Furthermore, they saw a positive correlation between serum zinc levels and the number and function of T-cells.

This effect of zinc was attributed to increasing the number of T-cells rather than enhancing the function of each T-cell. At the end of three months, researchers found that:

Zinc supplementation increased serum zinc concentrations in nursing home residents with low zinc levels.

Zinc supplementation increased both the number and effectiveness of T-cells in the treatment group at a much higher rate than the control group

The increase of serum zinc rose higher in the treatment group, at a rate of 16 percent, compared to those in the control group, which rose at a rate of 0.7 percent.

For those in the treatment group who were moderately zinc-sufficient at baseline, their serum zinc levels exceeded the cut-off standard.

Participants in the treatment group whose serum levels were measured as substantially zinc-deficient at baseline did not experience an increase to normal levels during the trial.

"Having a positive response to zinc supplementation may take some time in people who have been highly zinc deficient. We need to better understand how

much supplementation is needed for certain people, and for how long a period, so that more refined recommendations can be made," added first author Junaidah B. Barnett, M.C.H. (N), Ph.D., scientist in the Nutritional Immunology Laboratory at the HNRCA.

"It is worth noting that zinc deficiency is not just a problem in nursing home residents; it also exists in non-institutionalized older adults," Meydani continued. "On average, zinc supplementation measurably improved serum zinc levels in these older adults, with most participants achieving serum zinc levels considered to be adequate."

Zinc is found in a wide variety of foods, including oysters, pork, red meat, poultry, seafood, and fortified breakfast cereals. Zinc is also found in beans, nuts, whole grains, cucumber peel, and dairy products and is common in multi-vitamins. The Office of Dietary Supplements of the National Institutes of Health notes that zinc deficiency is rare in North America, but that some groups of people are more likely to have trouble getting enough zinc, including those with digestive disorders and vegetarians. Too much zinc (the upper limit for adults is 40 mg/day) can be harmful.

Some researchers suspect, however, the older adults do not absorb or use zinc as efficiently as others. In addition, while serum zinc levels are a commonly used measure to evaluate zinc deficiency, they might not accurately reflect cellular zinc status. Some cells might exhibit low zinc levels, which impacts their function, even when serum zinc levels are normal.

Meydani is also a professor at the Friedman School of Nutrition Science and Policy at Tufts and a member of the immunology program faculty at the Sackler School of Graduate Biomedical Sciences at Tufts.

Additional authors are Maria C. Dao, Ph.D., formerly of the HNRCA and now with Danone Research; Davidson H. Hamer, M.D., of the HNRCA, Boston University School of Medicine and Boston University School of Public Health; Ruth Kandel, M.D., of Hebrew SeniorLife and Harvard Medical School; Gary Brandeis, M.D., of Boston University School of Medicine; Dayong Wu, M.D., Ph.D., of the HNRCA; Gerard E. Dallal, Ph.D., formerly of the HNRCA; Paul F. Jacques, D.Sc., of the HNRCA; Robert Schreiber, M.D., of Hebrew SeniorLife and Harvard Medical School, and Eunhee Kong, M.D., Ph.D., formerly of the HNRCA.

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Barnett JB, Dao MC, Hamer DH, Kandel R, Brandeis G, Wu D, Dallal GE, Jacques PF, Schreiber R, Kong E, Meydani SN. Effect of zinc supplementation on serum zinc concentration and T cell proliferation in nursing home elderly: a randomized, double-blind, placebo-controlled trial. American Journal of Clinical Nutrition 2016 Jan 27 (Epub ahead of print; DOI: 10.3945/ajcn.115.115188).

http://www.eurekalert.org/pub_releases/2016-01/usmc-elt012716.php

Evidence lacking to support use of costlier biologic mesh for abdominal hernia repair

A UT Southwestern Medical Center study comparing two types of materials used in abdominal wall hernia repair surgery found no evidence to support the use of costlier biologic mesh versus synthetic mesh.

DALLAS - The findings, reported online today in JAMA Surgery, were based on a comprehensive review of published studies on patient outcomes following surgeries that used the two types of materials.

"In the absence of evidence demonstrating superiority of biological mesh materials, the expense associated with their use cannot be justified," said Dr. Sergio Huerta, Associate Professor of Surgery at UT Southwestern, staff physician at VA North Texas Health Care System, and first author of the study.

Abdominal hernia repair is one of the most common procedures performed by general surgeons. Recurrence of the hernia is common, and inserting a synthetic mesh at the time of the repair has been shown in a randomized clinical trial to substantially reduce the likelihood of recurrence. However, there is a risk of infection associated with synthetic mesh materials, and the mesh can erode into the bowel. In the 1990s, a new class of biologic mesh materials was introduced. The new biologically derived meshes were costlier, but it was hoped they might reduce infections and erosions.

The biologic mesh materials are derived from sources such as porcine skin and bovine pericardium derivatives. On average, biologic mesh costs 3½ times as much as synthetic mesh, the authors found.

In the study, researchers analyzed published results from the use of biologic mesh in abdominal wall hernia repair and reviewed the U.S. Food and Drug Administration approval history of these devices, a process known as 510(k) approval. This process included review of an FDA online database for 510(k) clearances for all commercially available biologic mesh materials.

The researchers screened 274 articles, and found three studies that compared biologics with synthetics. In total, outcomes were described for 1,033 patients. Studies varied widely in follow-up time, operative technique, meshes used, and patient selection criteria. The three comparative studies were not randomized clinical trials. Clinical outcomes, such as infection, were inconsistently reported across the studies. All of the biologic mesh devices were approved by the FDA based on "substantial equivalence" to synthetic devices, rather than in clinical trials, which is standard FDA practice for approval of medical devices. Taking all

these factors into account, the study found insufficient evidence to support the use of costlier biologic mesh materials.

Dr. Edward Livingston, Clinical Professor of Surgery at UT Southwestern and senior author of the study, said that new technologies are a key contributor to the rising cost of health care. "Greater application of evidence-based medicine will help control these increasing costs," said Dr. Livingston, who also serves as a deputy editor for JAMA. "The use of biological mesh materials for hernia repair is one of many examples in which significant costs could be avoided by tailoring clinical practice based on careful review of the evidence."

Other UT Southwestern researchers who contributed to this research were Prachi Patel, medical student, and Helen Mayo, faculty associate.

This study was supported by the Hudson-Penn Endowment fund at UT Southwestern.

http://www.eurekalert.org/pub_releases/2016-01/fhcr-fhe012716.php

Fred Hutch endorses HPV vaccination for cancer prevention

Researchers at Fred Hutch played pivotal role in development of vaccine

SEATTLE - In response to low national vaccination rates for the human papillomavirus, or HPV, Fred Hutchinson Cancer Research Center has joined with the 68 other U.S. National Cancer Institute-designated cancer centers in issuing a statement urging for increased vaccination in adolescent girls and boys for the prevention of many types of HPV-related cancers in adulthood. The virus, which is sexually transmitted, impacts nearly all men and women at some point in their lives and can lead to cervical, anal, vaginal, penile, vulvar, and head and neck cancers.

Fred Hutch and the other cancer centers named in the statement collectively recognize insufficient vaccination as a public health threat and call upon the nation's physicians, parents and adolescents to take advantage of this rare opportunity to prevent many types of cancer.

"The HPV vaccine is an amazing public health advance, but it doesn't guarantee eradication of HPV. It's important to remember that the vaccine works best in those who haven't been infected with the virus, which means, essentially, people who are not yet sexually active," said Dr. Gary Gilliland, president and director of Fred Hutch, whose researchers played a pivotal role in both discovering HPV's association with cancer and paving the way for the development of the vaccine.

The vaccine's roots lie in the laboratory of Dr. Denise Galloway, associate director and member of the Human Biology Division at Fred Hutch, as well as laboratories in Australia and the National Institutes of Health, where Galloway and fellow investigators accomplished the groundbreaking step of getting a key viral gene to assemble into particles that look like HPV, which became the basis of the vaccine.

Galloway and colleagues began studying HPV's utility as a tool for understanding how normal cells turn abnormal. Viruses disrupt cellular pathways in much the same way as cancers do, so studying them illuminates parallel cellular processes.

In 1992, Galloway made a breakthrough discovery when she and her colleagues found that they could use one viral gene, called L1, from the same type of HPV that causes plantar warts, and get it to self-assemble and form virus-like particles. This eventually led to the development of virus-like particles for the cancer-causing types of HPV, which then became the underpinning of the vaccine.

Despite the effectiveness of the vaccine in preventing HPV infection, vaccination rates remain low across the U.S., with under 40 percent of girls and just over 21 percent of boys receiving the recommended three doses. Research shows there are a number of barriers that must be overcome to improve vaccination rates, including a lack of strong recommendations from physicians and parents not understanding that this vaccine protects against several types of cancer.

"When I joined Fred Hutch in 1978, we didn't know what caused cervical cancer, and now we have a vaccine that can prevent HPV infections and the cancers they cause. It is incredibly gratifying to have been part of that discovery," Galloway said. "Wouldn't it be great if there was a high rate of vaccine usage to actually eliminate HPV-caused cancers?"

According to the Centers for Disease Control and Prevention, HPV infections are responsible for approximately 27,000 new cancer diagnoses each year in the U.S. Several vaccines are available that can prevent the majority of HPV-related cancers.

To discuss strategies for increasing HPV vaccination rates, experts from the NCI, CDC, American Cancer Society and more than half of the NCI-designated cancer centers met in a summit at MD Anderson Cancer Center last November. During this summit, cancer centers shared findings from 18 NCI-funded environmental scans, or detailed regional assessments, which sought to identify barriers to increasing immunization rates in pediatric settings across the country.

The published call to action was a major recommendation resulting from discussions at that summit, with the goal of sending a powerful message to parents, adolescents and health care providers about the importance of HPV vaccination for cancer prevention.

Fred Hutch and other National Cancer Institute-designated cancer centers joined in this effort in the spirit of President Barack Obama's recent State of the Union call for a national "moonshot" to cure cancer, a collaborative effort led by Vice President Joe Biden.

"We are on the threshold of incredible advances, such as harnessing the power of the immune system to fight cancer," Gilliland said. "At Fred Hutch, our mantra is

'Cures Start Here.' This is fitting, because the goal here is not merely to treat but to cure - and, ultimately, prevent - cancer. The HPV vaccine is a prime example of the power of prevention to save lives."

http://www.bbc.com/news/health-35427493

Zika virus: Up to four million Zika cases predicted

Three to four million people could be infected with Zika virus in the Americas this year, the World Health Organization (WHO) predicts.

By James Gallagher Health editor, BBC News website

Most will not develop symptoms, but the virus, spread by mosquitoes, has been linked to brain defects in babies. Meanwhile, the US says it hopes to begin human vaccine trials by the end of 2016. The head of the International Olympic Committee says steps are being taken to protect the Games in Rio de Janeiro.

Thomas Bach said the IOC would issue advice this week on how to keep athletes and visitors safe in Brazil, the worst affected country.

WHO director general Dr Margaret Chan said Zika had gone "from a mild threat to one of alarming proportions". She has set up a Zika "emergency team" after the "explosive" spread of the virus. It will meet on Monday to decide whether Zika should be treated as a global emergency.

The last time an international emergency was declared was for the Ebola outbreak in West Africa, which has killed more than 11,000 people.

Zika was first detected in Uganda in 1947, but has never caused an outbreak on this scale. Brazil reported the first cases of Zika in South America in May 2015.

Most cases result in no symptoms and it is hard to test for, but WHO officials said between 500,000 and 1.5 million people had been infected in the country.

The virus has since spread to more than 20 countries in the region. At the same time there has been a steep rise in levels of microcephaly - babies born with abnormally small heads - and the rare nervous system disorder Guillain-Barre syndrome. The link between the virus and these disorders has not been confirmed, but Dr Chan said it was "strongly suspected" and was "deeply alarming".

And she warned the situation could yet deteriorate as "this year's El Nino weather patterns are expected to increase mosquito populations greatly in many areas".

The BBC's David Shukman, reporting from Recife in north-east Brazil, said doctors were "overwhelmed" by cases of microcephaly.

One hospital in the city had gone from dealing with an average of five cases a year to 300 in the past six months.

Emergency team

Earlier, doctors writing in the Journal of the American Medical Association said Zika had "explosive pandemic potential" and said the WHO's failure to act swiftly on Ebola probably cost thousands of lives.

In a statement to the executive board meeting of the WHO, Dr Chan said: "The level of concern is high, as is the level of uncertainty. "Questions abound - we need to get some answers quickly. "For all these reasons, I have decided to convene an Emergency Committee. "I am asking the Committee for advice on the appropriate level of international concern and for recommended measures that should be undertaken in affected countries and elsewhere."

Vaccine

Officials from the US National Institute of Health said they had two potential Zika vaccines in development. One that is based on an experimental West Nile vaccine could be repurposed for Zika and enter clinical trials by the end of 2016, Dr Anthony Fauci from NIH said. He said talks were already taking place with pharmaceutical companies, but a vaccine would not be widely available for several years.

Meanwhile Dr Anne Schuchat, from the Centers for Disease Control confirmed there had been 31 cases of Zika in the country - all linked to travel to the affected areas. At a news conference, White House spokesman Josh Earnest said the country's response to the virus so far had been "consistent with the kind of threat that could be out there".

"At this point, here in the United States, the risk of a disease spread by mosquitoes is quite low, the January temperatures in North America are quite inhospitable to the mosquito populations." "But, obviously that's going to change," he added.

Dr Carissa Etienne, the regional-director for the WHO Pan American Health Organization, said the link between the abnormalities and Zika had not been confirmed. But she added: "We cannot tolerate the prospect of more babies being born with neurological and other malformations and more people facing the threat of paralysis."

http://www.eurekalert.org/pub_releases/2016-01/lm-nhc012816.php

Necroptosis: How crystals precipitate cell death

Crystal formation plays a defining role in the pathogenesis of a range of common diseases, such as gout and atherosclerosis.

Ludwig-Maximilians-Universitaet (LMU) in Munich researchers led by Hans-Joachim Anders have now elucidated how the insoluble deposits induce cell death. The formation of crystalline deposits in the extracellular medium is a defining feature of several widespread illnesses.

Examples of such 'crystallopathies' include gout, atherosclerosis and kidney disease, which are associated with the precipitation of urate, cholesterol and oxalate crystals, respectively. In these and other similar cases, exposure to crystalline microparticles not only provokes an immune reaction that initiates a chronic inflammatory process, but also results in cell death.

Now a team of researchers headed by LMU's Professor Hans-Joachim Anders at the Department of General Medicine and Nephrology (Medical Clinic IV, Downtown Medical Campus) has uncovered the mechanism by which such crystals set off the train of events that leads to cell death.

The new findings are of significance for many different disorders, including the conditions mentioned above. The study appears online in the journal Nature Communications.

Crystalline deposits provoke extensive tissue damage and can even lead to organ failure. Moreover, crystal-linked conditions exhibit common features, which suggest that they all share the same underlying mode of pathogenesis.

Up until now, researchers have regarded inflammation as the primary damage mechanism, and have therefore focused on the issue of how crystals trigger inflammatory reactions.

But Hans-Joachim Anders and his colleagues have now shown that the different types of crystals all initiate an active process that leads to cell necrosis. "Cell death in this context has hitherto been regarded mainly as a passive process of cell loss due to irreparable damage. But we have now demonstrated that it is the outcome of a regulated process, which actively eliminates cells," Anders explains.

New targets for therapies

In the study, a number of cell types, including kidney-tubule cells and the fibroblast cells responsible for the production of connective tissue, were exposed to a variety of crystals. In all cases, the researchers found that the crystals activated the same signal transduction pathway in the cells.

Strikingly, this signal relay is known to trigger a specific, injury-induced form of cell death, referred to as necroptosis. Furthermore, the observations strongly suggest that necroptosis is in turn responsible for inducing the inflammatory reaction, as inhibition of necrosis also prevents inflammation.

This last finding is important because therapeutic strategies employed in the treatment of such diseases have so far concentrated on inhibiting the inflammation reaction.

However, the discovery that the cytoxic effect of the crystals is itself actively regulated now offers a new target for drug therapy. "The components of the signal pathway could offer new targets for therapeutic drugs.

Pharmacological blockade of its action should prevent crystal-induced cell death," Anders says. And according to the new study, that should also be sufficient to impede the development of chronic inflammation. However, whether or not this innovative approach will actually result in practical improvements in the treatment of patients is a question that can only be answered by further research.

http://www.eurekalert.org/pub_releases/2016-01/ps-amn012816.php

Anticholinergics may not be best choice for rehab patients with dementia

During rehabilitation following an acute hospital stay, medications that block neurotransmitters may be overprescribed to older patients suffering from delirium superimposed on dementia, according to health researchers.

Specifically, strong anticholinergic medications may be prescribed to older adults when there are other suitable options. An anticholinergic medication blocks the neurotransmitter acetylcholine in the nervous system. These drugs are prescribed for a variety of symptoms, including incontinence, depression and insomnia. While their use can be very beneficial to some, they are also known to have significant adverse effects.

"In this study, people on anticholinergic medications had worse attention and physical function, and a longer stay (at the rehab facility) by four days, when compared to patients not on these medications," said Ann Kolanowski, professor of nursing, Penn State.

The researchers observed 99 patients for 30 days, or until they were released, beginning the day they entered rehabilitation. Upon entering the rehab facility, all of the participants had both delirium and dementia, were 65 or older and did not have any other neurological problems.

The participants' cognition and physical function were assessed daily by research staff. Physical function was measured by noting the amount of time and assistance patients needed to complete a task, such as feeding and dressing themselves and walking. Among other measures, patients' cognition was measured by being given increasingly longer sequences of numbers to repeat both forwards and backwards until they missed two sequences in a row. Kolanowski and colleagues report their findings in a recent issue of the American Journal of Geriatric Psychiatry.

Anticholinergic drugs are ranked in the study according to their effect on cognition as mild, moderate and severe. A quarter of the patients were taking a medication with a moderate or severe anticholinergic effect, while 15 percent of the patients were not taking any anticholinergic medications. The remaining patients were taking a medication with mild anticholinergic effects.

The researchers found that patients who had been taking a medication with moderate or severe anticholinergic effects performed more poorly on a test of attention than they had during the previous week and also had lower physical function than the previous week.

"For people with dementia, the loss of physical function is a major risk factor for permanent institutionalization, and contributes heavily to the national burden of

healthcare costs," said the researchers. "The goal of post-acute care is to optimize function. For people with dementia, appropriate anticholinergic medication management may help achieve rehabilitation goals and reduce the cost of care."

Jacqueline Mogle, assistant professor, Donna M. Fick, Distinguished Professor and director, Hartford Center of Geriatric Nursing Excellence, Nikki Hill, assistant professor, Paula Mulhall, research technologist, Liza Behrens, doctoral student, and Elise Colanecco, doctoral student, all College of Nursing, Penn State; Noll Campbell, research assistant professor, pharmacy, Purdue University; Malaz Boustani, professor, medicine, Indiana University; and Linda Clare, professor, clinical psychology, Washington Singer Laboratories, University of Exeter; all collaborated on this research as well.

http://www.eurekalert.org/pub_releases/2016-01/uowh-sdb012716.php

Scientists decode brain signals nearly at speed of perception

Electrodes in patients' temporal lobes carry information that, when analyzed, enables scientists to predict what object patients are seeing

Using electrodes implanted in the temporal lobes of awake patients, scientists have decoded brain signals at nearly the speed of perception. Further, analysis of patients' neural responses to two categories of visual stimuli - images of faces and houses - enabled the scientists to subsequently predict which images the patients were viewing, and when, with better than 95 percent accuracy.

The research is published today in PLOS Computational Biology.

University of Washington computational neuroscientist Rajesh Rao and UW Medicine neurosurgeon Jeff Ojemann, working their student Kai Miller and with colleagues in Southern California and New York, conducted the study.

"We were trying to understand, first, how the human brain perceives objects in the temporal lobe, and second, how one could use a computer to extract and predict what someone is seeing in real time?" explained Rao. He is a UW professor of computer science and engineering, and he directs the National Science Foundation's Center for Sensorimotor Engineering, headquartered at UW.

"Clinically, you could think of our result as a proof of concept toward building a communication mechanism for patients who are paralyzed or have had a stroke and are completely locked-in," he said.

The study involved seven epilepsy patients receiving care at Harborview Medical Center in Seattle. Each was experiencing epileptic seizures not relieved by medication, Ojemann said, so each had undergone surgery in which their brains' temporal lobes were implanted - temporarily, for about a week - with electrodes to try to locate the seizures' focal points.

"They were going to get the electrodes no matter what; we were just giving them additional tasks to do during their hospital stay while they are otherwise just waiting around," Ojemann said.

Temporal lobes process sensory input and are a common site of epileptic seizures. Situated behind mammals' eyes and ears, the lobes are also involved in Alzheimer's and dementias and appear somewhat more vulnerable than other brain structures to head traumas, he said.

In the experiment, the electrodes from multiple temporal-lobe locations were connected to powerful computational software that extracted two characteristic properties of the brain signal: "event-related potentials" and "broadband spectral changes."

Rao characterized the former as likely arising from "hundreds of thousands of neurons being co-activated when an image is first presented," and the latter as "continued processing after the initial wave of information."

The subjects, watching a computer monitor, were shown a random sequence of pictures - brief (400 millisecond) flashes of images of human faces and houses, interspersed with blank gray screens. Their task was to watch for an image of an upside-down house.

"We got different responses from different (electrode) locations; some were sensitive to faces and some were sensitive to houses," Rao said.

The computational software sampled and digitized the brain signals 1,000 times per second to extract their characteristics. The software also analyzed the data to determine which combination of electrode locations and signal types correlated best with what each subject actually saw.

In that way it yielded highly predictive information.

By training an algorithm on the subjects' responses to the (known) first two-thirds of the images, the researchers could examine the brain signals representing the final third of the images, whose labels were unknown to them, and predict with 96 percent accuracy whether and when (within 20 milliseconds) the subjects were seeing a house, a face or a gray screen.

This accuracy was attained only when event-related potentials and broadband changes were combined for prediction, which suggests they carry complementary information.

"Traditionally scientists have looked at single neurons," Rao said. "Our study gives a more global picture, at the level of very large networks of neurons, of how a person who is awake and paying attention perceives a complex visual object."

The scientists' technique, he said, is a steppingstone for brain mapping, in that it could be used to identify in real time which locations of the brain are sensitive to types of information.

Lead author of the study is Kai Miller, a neurosurgery resident and physicist at Stanford University who obtained his M.D. and Ph.D. at the UW. Other

collaborators were Dora Hermes, a Stanford postdoctoral fellow in neuroscience, and Gerwin Schalk, a neuroscientist at the Wadsworth Institute in New York.

"The computational tools that we developed can be applied to studies of motor function, studies of epilepsy, studies of memory. The math behind it, as applied to the biological, is fundamental to learning," Ojemann said.

http://www.eurekalert.org/pub_releases/2016-01/tu-snd012816.php

Study: New drug could be safer, non-addictive alternative to morphine

The peptide-based drugs, which mimic a natural brain chemical, target the same pain-relieving opioid receptor as morphine

Researchers at Tulane University and Southeast Louisiana Veterans Health Care System have developed a painkiller that is as strong as morphine but isn't likely to be addictive and with fewer side effects, according to a new study in the journal Neuropharmacology. Using rats, scientists compared several engineered variants of the neurochemical endomorphin, which is found naturally in the body, to morphine to measure their effectiveness and side effects. The peptide-based drugs target the same pain-relieving opioid receptor as morphine.

Opium-based drugs are the leading treatments for severe and chronic pain, but they can be highly addictive. Their abuse results in thousands of overdose deaths in the United States annually. They can cause motor impairment and potentially fatal respiratory depression. Patients also build up tolerance over time, increasing the risk for abuse and overdose.

"These side effects were absent or reduced with the new drug," said lead investigator James Zadina, VA senior research career scientist and professor of medicine, pharmacology and neuroscience at Tulane University School of Medicine. "It's unprecedented for a peptide to deliver such powerful pain relief with so few side effects."

In the study, the new endomorphin drug produced longer pain relief without substantially slowing breathing in rats; a similarly potent dosage of morphine produced significant respiratory depression. Impairment of motor coordination, which can be of particular importance to older adults, was significant after morphine but not with the endomorphin drug. The new drug produced far less tolerance than morphine and did not produce spinal glial cell activation, an inflammatory effect of morphine known to contribute to tolerance.

Scientists conducted several experiments to test whether the drug would be addictive. One showed that although rats would spend more time in a compartment where they had received morphine, the new drug did not affect this behavior. Another test showed that when the press of a bar produced an infusion of drug, the rats only increased efforts to obtain morphine and not the new drug. The tests are predictive of human drug abuse, Zadina said. Researchers hope to begin human clinical trials of the new drug within the next two years.

http://bit.ly/1JTjCA7

Earth Movements That Don't Shake Could Forecast Large Quakes

Temblors off northeastern Japan are often preceded by subtle slips along seafloor faults

By Sid Perkins on January 28, 2016

In a first-of-its-kind finding, researchers note that large quakes off Japan's northeastern coast are often presaged by subtle movements on submarine fault zones. Although these speedups in slippage along submarine faults, discernable by GPS equipment onshore, will not enable researchers to make a "We're gonna have a magnitude 7.3 quake next Thursday at 3:37 P.M." sort of prediction, they do provide insights into general patterns of seismic activity in the region and may ultimately give scientists a better understanding of what is happening along fault zones.

The researchers sorted through the listing of quakes that occurred before 2011 along the northeastern coast of Honshu and southeastern coast of Hokkaido, Japan's two largest islands, where tectonic forces slowly shove the western edge of the North American Plate beneath the Eurasian Plate and create a seafloor feature called the Japan Trench, linked to earthquakes and tsunamis in the region. From that list, which along the central stretch of coast includes data for quakes as far back as 1984, the team identified more than 1,500 sequences in which quakes seemed to repeat themselves over time, occurring at the same place with more or less the same magnitude, says the study's lead author Naoki Uchida, a geophysicist at Tohoku University in Japan. From the magnitude and frequency of those temblors, he and his colleagues were able to estimate the rates at which the tectonic plates were sliding past each other at each site. In some places the rates surged and stalled in three-year cycles, with speeds ranging from zero (when the faults were locked) to, at peak speed, nearly four times normal, the researchers report in this week's Science.

Then, the team looked at how those varying rates of slippage might be statistically correlated with other, nonrepeating quakes in the region whose magnitudes were magnitude 5 or larger. They found that in many instances the rates of inferred slippage accelerated in the days leading up to nearby quakes, Uchida says. Thus, the team's analysis suggests that gradual slippage along the tectonic interface shifts the seismic stress that is building up along the fault into nearby areas, where it eventually triggers a sudden slip—otherwise known as a quake.

Analyses of data gathered by onshore GPS stations, which over the long term reveal the movements of the tectonic plate on which they're mounted, show that their motions generally match the inferred rates of slippage along offshore faults. So, in a rough sense, the movements of the GPS equipment may presage impending quakes, Uchida says.

The team's research "is quite solid and presents some exciting conclusions," says Jeffrey Freymueller, a geophysicist at the University of Alaska, Fairbanks who was not part of the study. It stands to reason, he notes, that if the slippage along the tectonic interface offshore is periodic, then the seismic stress building up nearby where large quakes occur will be periodic as well. "Many people have speculated that this should be the case but this paper is the most convincing evidence yet," Freymueller says.

The findings "are potentially a powerful tool" to probe what's happening along the region's submarine faults, says Paul Segall, a geophysicist at Stanford University, also not involved with the research. He admits, however, "this is kind of a provocative result, in the realm of things that are suggestive." Whether the analysis offers anything that is relevant toward earthquake prediction is yet to be seen, he adds.

Although the statistical linkage discovered by Uchida and his colleagues suggests that an increase in tectonic slippage precedes nearby quakes, it is possible that another phenomenon entirely could be causing both, says Manoochehr Shirzaei, a geophysicist at Arizona State University in Tempe. For example, an increase in the fluid pressure within the rocks of the fault itself (a parameter known as pore pressure) could be decreasing friction within the fault and thus lubricating it, triggering both the accelerated slippage in one area and the quake nearby. He and his colleagues are now investigating that notion, and others, to see if they can discern what's going on in the faults off Japan and whether that might relate to what happens at similar tectonic interfaces elsewhere in the world.

"The answers may help scientists better understand how a subduction zone behaves," Shirzaei says. "No one really knows how the system works."

http://www.eurekalert.org/pub_releases/2016-01/uoc--mwp012816.php

Moon was produced by a head-on collision between Earth and a forming planet

UCLA-led research reconstructs massive crash, which took place 4.5 billion years ago

The moon was formed by a violent, head-on collision between the early Earth and a "planetary embryo" called Theia approximately 100 million years after the Earth formed, UCLA geochemists and colleagues report.

Scientists had already known about this high-speed crash, which occurred almost 4.5 billion years ago, but many thought the Earth collided with Theia (pronounced THAY-eh) at an angle of 45 degrees or more -- a powerful side-swipe (simulated in this 2012 YouTube video). New evidence reported Jan. 29 in the journal Science substantially strengthens the case for a head-on assault.

The researchers analyzed seven rocks brought to the Earth from the moon by the Apollo 12, 15 and 17 missions, as well as six volcanic rocks from the Earth's mantle -- five from Hawaii and one from Arizona.

The key to reconstructing the giant impact was a chemical signature revealed in the rocks' oxygen atoms. (Oxygen makes up 90 percent of rocks' volume and 50 percent of their weight.) More than 99.9 percent of Earth's oxygen is O-16, so called because each atom contains eight protons and eight neutrons. But there also are small quantities of heavier oxygen isotopes: O-17, which have one extra neutron, and O-18, which have two extra neutrons. Earth, Mars and other planetary bodies in our solar system each has a unique ratio of O-17 to O-16 -- each one a distinctive "fingerprint."

In 2014, a team of German scientists reported in Science that the moon also has its own unique ratio of oxygen isotopes, different from Earth's. The new research finds that is not the case.

"We don't see any difference between the Earth's and the moon's oxygen isotopes; they're indistinguishable," said Edward Young, lead author of the new study and a UCLA professor of geochemistry and cosmochemistry.

Young's research team used state-of-the-art technology and techniques to make extraordinarily precise and careful measurements, and verified them with UCLA's new mass spectrometer.

The fact that oxygen in rocks on the Earth and our moon share chemical signatures was very telling, Young said. Had Earth and Theia collided in a glancing side blow, the vast majority of the moon would have been made mainly of Theia, and the Earth and moon should have different oxygen isotopes. A head-on collision, however, likely would have resulted in similar chemical composition of both Earth and the moon.

"Theia was thoroughly mixed into both the Earth and the moon, and evenly dispersed between them," Young said. "This explains why we don't see a different signature of Theia in the moon versus the Earth."

Theia, which did not survive the collision (except that it now makes up large parts of Earth and the moon) was growing and probably would have become a planet if the crash had not occurred, Young said. Young and some other scientists believe the planet was approximately the same size as the Earth; others believe it was smaller, perhaps more similar in size to Mars.

Another interesting question is whether the collision with Theia removed any water that the early Earth may have contained. After the collision -- perhaps tens of millions of year later -- small asteroids likely hit the Earth, including ones that may have been rich in water, Young said. Collisions of growing bodies occurred very frequently back then, he said, although Mars avoided large collisions.

A head-on collision was initially proposed in 2012 by Matija ?uk, now a research scientist with the SETI Institute, and Sarah Stewart, now a professor at UC Davis; and, separately during the same year by Robin Canup of the Southwest Research Institute.

Co-authors of the Science paper are Issaku Kohl, a researcher in Young's laboratory; Paul Warren, a researcher in the UCLA department of Earth, planetary, and space sciences; David Rubie, a research professor at Germany's Bayerisches Geoinstitut, University of Bayreuth; and Seth Jacobson and Alessandro Morbidelli, planetary scientists at France's Laboratoire Lagrange, Université de Nice.

The research was funded by NASA, the Deep Carbon Observatory and a European Research Council advanced grant (ACCRETE).

http://www.eurekalert.org/pub_releases/2016-01/osu-nth012816.php

New therapy halts progression of Lou Gehrig's disease in mice

Researchers have essentially stopped the progression of ALS for nearly two years in one type of mouse model, allowing the mice to approach their normal lifespan

CORVALLIS, Ore. - Researchers at Oregon State University announced today that they have essentially stopped the progression of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, for nearly two years in one type of mouse model used to study the disease - allowing the mice to approach their normal lifespan.

The findings, scientists indicate, are some of the most compelling ever produced in the search for a therapy for ALS, a debilitating and fatal disease, and were just published in Neurobiology of Disease.

"We are shocked at how well this treatment can stop the progression of ALS," said Joseph Beckman, lead author on this study, a distinguished professor of biochemistry and biophysics in the College of Science at Oregon State University, and principal investigator and holder of the Burgess and Elizabeth Jamieson Chair in OSU's Linus Pauling Institute.

In decades of work, no treatment has been discovered for ALS that can do anything but prolong human survival less than a month. The mouse model used in this study is one that scientists believe may more closely resemble the human reaction to this treatment, which consists of a compound called copper-ATSM. It's not yet known if humans will have the same response, but researchers are moving as quickly as possible toward human clinical trials, testing first for safety and then efficacy of the new approach.

ALS was identified as a progressive and fatal neurodegenerative disease in the late 1800s, and gained international recognition in 1939 when it was diagnosed in American baseball legend Lou Gehrig. It's known to be caused by the death and deterioration of motor neurons in the spinal cord, which in turn has been linked to mutations in copper, zinc superoxide dismutase.

Copper-ATSM is a known compound that helps deliver copper specifically to cells with damaged mitochondria, and reaches the spinal cord where it's needed to treat ALS. This compound has low toxicity, easily penetrates the blood-brain barrier, is already used in human medicine at much lower doses for some purposes, and is well tolerated in laboratory animals at far higher levels. Any copper not needed after use of copper-ATSM is quickly flushed out of the body.

Experts caution, however, that this approach is not as simple as taking a nutritional supplement of copper, which can be toxic at even moderate doses. Such supplements would be of no value to people with ALS, they said.

The new findings were reported by scientists from OSU; the University of Melbourne in Australia; University of Texas Southwestern; University of Central Florida; and the Pasteur Institute of Montevideo in Uruguay. The study is available as open access in Neurobiology of Disease.

Using the new treatment, researchers were able to stop the progression of ALS in one type of transgenic mouse model, which ordinarily would die within two weeks without treatment. Some of these mice have survived for more than 650 days, 500 days longer than any previous research has been able to achieve.

In some experiments, the treatment was begun, and then withheld. In this circumstance the mice began to show ALS symptoms within two months after treatment was stopped, and would die within another month. But if treatment was resumed, the mice gained weight, progression of the disease once again was stopped, and the mice lived another 6-12 months.

In 2012, Beckman was recognized as the leading medical researcher in Oregon, with the Discovery Award from the Medical Research Foundation of Oregon. He is also director of OSU's Environmental Health Sciences Center, funded by the National Institutes of Health to support research on the role of the environment in causing disease.

"We have a solid understanding of why the treatment works in the mice, and we predict it should work in both familial and possibly sporadic human patients," Beckman said. "But we won't know until we try."

Familial ALS patients are those with more of a family history of the disease, while sporadic patients reflect the larger general population.

"We want people to understand that we are moving to human trials as quickly as we can," Beckman said. "In humans who develop ALS, the average time from onset to death is only three to four years."

The advances are based on substantial scientific progress in understanding the disease processes of ALS and basic research in biochemistry. The transgenic mice used in these studies have been engineered to carry the human gene for "copper chaperone for superoxide dismutase," or CCS gene. CCS inserts copper into superoxide dismustase, or SOD, and transgenic mice carrying these human genes die rapidly without treatment.

After years of research, scientists have developed an approach to treating ALS that's based on bringing copper into specific cells in the spinal cord and mitochondria weakened by copper deficiency. Copper is a metal that helps to stabilize SOD, an antioxidant protein whose proper function is essential to life. But when it lacks its metal co-factors, SOD can "unfold" and become toxic, leading to the death of motor neurons.

There's some evidence that this approach, which works in part by improving mitochondrial function, may also have value in Parkinson's disease and other conditions, researchers said. Research is progressing on those topics as well.

The treatment is unlikely to allow significant recovery from neuronal loss already caused by ALS, the scientists said, but could slow further disease progression when started after diagnosis. It could also potentially treat carriers of SOD mutant genes that cause ALS.

This work has been supported by the Department of Defense Congressionally Directed Medical Research Program, the U.S. National Institutes of Health, the Amyotrophic Lateral Sclerosis Association, the Australian National Health and Medical Research Association, and gifts by Michael Camillo and Burgess and Elizabeth Jamieson to the Linus Pauling Institute.

Editor's Notes: The study this story is based on is available online: http://bit.ly/1nqzRtY

http://www.eurekalert.org/pub_releases/2016-01/uoac-uoa012816.php

University of Arizona researchers identify food additive that may prevent skin cancer

Unlike sunscreen, the nutritional compound protects skin from the inside out

TUCSON, Ariz. - Researchers at the University of Arizona College of Pharmacy have discovered that a compound found in the natural food additive annatto prevents the formation of cancer cells and skin damage from UV radiation in mice. In the future the compound, bixin, may be valuable in the prevention and treatment of human skin cancers.

Georg Wondrak, PhD, associate professor, and Donna Zhang, PhD, professor, both members of the University of Arizona Cancer Center, recently published a study in Free Radical Biology and Medicine titled, "System Administration of the Apocarotenoid Bixin Protects Skin against Solar UV-Induced Damage through Activation of Nrf2."

Bixa orellana

Bixin is a bright reddish orange compound found in annatto, a natural condiment and food coloring derived from the seeds of the achiote fruit. Annatto, also known as achiote, has been a common ingredient in Latin American cooking since the pre-Columbian era.

Dr. Wondrak's lab works to find small molecules, often in edible plants, that can prevent skin cancer. Dr. Zhang is a leading expert on the Nrf2 transcription factor, which strengthens cells against exposure to carcinogens. Dr. Wondrak's investigations occasionally identify a compound that activates the Nrf2 pathway, and he calls on Dr. Zhang to collaborate in determining whether the compound has cancer-preventive properties.

In the recent study, mice injected with bixin and uninjected mice were exposed to UV radiation. The mice with the bixin injection experienced much less severe skin sun damage.

Dr. Wondrak says this discovery is unique because bixin is a nutritional factor, not a sunscreen applied to the skin. It prevents UV skin damage from the inside out by inducing cells to make protective antioxidants and repair factors. The compound does not kill skin cancer cells, but prevents their forming in the first place. Drs. Wondrak and Zhang find this research especially compelling because it involves a commonly consumed food substance.

The next steps for this line of research include finding out whether bixin prevents UV skin damage in humans as it does in mice. Because annatto is approved by the Food and Drug Administration asa safe food additive, its use in future clinical trials is expected to require fewer rounds of testing.

With continued research into bixin's effects, scientists soon may know if foods with annatto can help prevent sun damage, photo-aging and cancer in humans.

Research reported in this story was supported in part by grants from the National Institute of Environmental Health Sciences (2R01ES015010, ES007091 and ES006694) and the National Cancer Institute (R01CA154377, R03CA167580, R21CA166926, CA023074).

http://bit.ly/1OZEWTn

What Would It Take to Prove the Zika–Microcephaly Link

Public health officials are not yet ready to say the connection is causal

By Dina Fine Maron on January 28, 2016

Zika virus has been grabbing headlines because of its links to an alarming birth defect called microcephaly. The data to provide evidence linking the relatively mild mosquito-borne disease and babies born with small heads and potential brain damage, however, are not yet conclusive. World Health Organization and U.S. government officials today discussed this data gap today in a series of public comments and press briefings.

A top official from the U.S. Centers for Disease Control and Prevention told reporters today that to firm up the connections between the two conditions researchers must study the documented microcephaly cases, the case history of pregnant women and conduct case-control studies of babies born in affected areas such as Brazil to get further insights. Only then, following careful analyses, can scientists solidify the Zika–microcephaly links and the required preventative steps.

Although the Brazilian government has said there are almost 4,000 cases of microcephaly in the country, only six of the cases have been strongly linked to Zika virus via laboratory testing that confirms genetic material from the virus is present in the infant, Claudio Maierovitch, director of the Department of Communicable Disease Surveillance in Brazil's Ministry of Health told the WHO today in Geneva. Brazilian officials with assistance from the CDC and other groups are now trying to firm up that data. The director general of WHO, Margaret Chan, however, said that although that causal relationship has not been proved, it is "strongly suspected." That is due, in part, to other research that has shown the virus is capable of crossing the placental barrier and showing up in amniotic fluid. Retrospective analysis of an earlier outbreak of Zika in French Polynesia also separately suggests that there, too, was an increase in cases of neurological impairment, according to the CDC.

Microcephaly is defined as being born with an abnormally small head, established by measuring the circumference of a baby's head and comparing it with those of similarly aged babies of the same sex—a definition that is relatively loose, CDC Principal Deputy Director Anne Schuchat told reporters today. Developmental experts from the CDC, Brazil and elsewhere plan to scrutinize the records of individuals suspected of the abnormality to be certain their conditions were true microcephaly cases, she said.

Another key plank to proving the microcephaly link will be following women during their pregnancy to document what they are exposed to and their future health outcomes, she says. That type of work would require massive resources and logistical coordination and is not yet underway, she says.

Finally, proving these links would require case-control studies that compare microcephalic babies with those born around the same time and area. That type of information, Schuchat says, will provide much-needed nuance about other exposures and factors that could influence the health of these mothers and their offspring.

Even as researchers prepare to launch these further studies, however, families cannot wait to find out how to safeguard themselves and their future offspring. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, said today there will not be a vaccine ready to combat Zika for at least several years. So, in the absence of further answers, WHO is stressing that mosquito control in affected areas—helping eradicate mosquitoes and taking precautions to avoid their bites—is the safest course for people living in those regions.

http://bit.ly/1nXAMCB

Cats May Have Been Domesticated Twice

But only one ended up as the house cat

By Danny Lewis

Leopard cat **Roland Seitre/Minden Pictures/Corbis**

Whether they were being worshipped as gods or transformed into memes, the relationship between cats and humans goes back a long ways. There are more than 500 million domestic house cats around the world, all of which are descended from a single subspecies of wildcat. But according to new research, there might have been a second, more recent (and unrelated) instance of cats becoming domesticated in China.

Most archaeologists believe that cats probably domesticated themselves more than 10,000 years ago when the fluffy little murderbeasts realized they could get an easy meal by staking out Neolithic storerooms and farms for the rats and mice that were attracted to human settlements. More cats meant fewer rodents, which meant more crops for the hard-working humans. Over time, our ancestors started taking care of the felines, leading to the modern house cat, Grennan Milliken writes for Popular Science.

But this story of a second line began a few years ago, when researchers uncovered several cat bones near Quanhucun, an early farming village in central China. The bones were about 5,300 years old and analysis of their chemistry showed these felines likely survived on a diet of grain-fed rodents, suggesting they at least hunted for dinner near the town's millet stores.

The scientists found a few indications of domestication, according to the study recently published the journal PLOS One. First, based on the wear of its teeth, the remains of one of the cats seemed much older than the others, perhaps suggesting that someone took care of the cat as it got older, writes David Grimm for Science. These cats also were all slightly smaller than their wild counterparts, and one was even buried as a complete skeleton. "That's evidence of special treatment," study author Jean-Denis Vigne tells Grimm. "Even if what we're seeing here is not full domestication, it's an intensification of the relationship between cats and humans."

Further analysis showed that these cats did not descend from the same subspecies as the modern house cat, but actually belonged to a species known as "leopard cats," Grimm reports. This means that the leopard cat lineage is genetically distinct from our modern fuzz balls.

Aside from a breed called the Bengal cat, which was created in the 1960s by intentionally breeding leopard cats with house cats, the two cat species have never commingled. Quanhucun cats may have been partly domesticated at some point, but then backslid and stayed feral upon the introduction of other domesticated kitties.

If true, that would make cats only the second known species to have been domesticated twice (the first being pigs), Milliken reports. According to zooarchaeologist Fiona Marshall, who helped uncover the bones but was not involved in the study, this could indicate that it might have taken less intentional effort for our ancestors to domesticate all kinds of animals than researchers once thought. "This is very important work that should have a great impact," Marshall tells Grimm. "This is the leading edge in a shift in thinking about domestication processes."

http://www.eurekalert.org/pub_releases/2016-01/gumc-cbp012916.php

Could blood pressure drugs have a role in Alzheimer's disease treatment?

Drug used to treat high blood pressure reduced cell damage often linked to Alzheimer's disease

WASHINGTON - In laboratory neuronal cultures, an FDA-approved drug used to treat high blood pressure reduced cell damage often linked to Alzheimer's disease, say researchers at Georgetown University Medical Center (GUMC) and the National Institutes of Health. They say their work, published online Jan. 28 in the journal Alzheimer's Research and Therapy, provides information supporting the potential effect of the drug candesartan -- as well as other Angiotensin receptor blockers (ARBs) for the early treatment of Alzheimer's disease.

"Our findings make sense in many ways," says the study's senior author Juan M. Saavedra, MD, from GUMC's Department of Pharmacology and Physiology. "Hypertension reduces blood flow throughout the body and brain and is a risk factor of Alzheimer's disease. Previous epidemiological studies found that Alzheimer's progression is delayed in hypertensive patients treated with ARBs."

Using neuronal cultures, the researchers explored the action of candesartan on the neurotoxic effects of exposure to excessive glutamate, a demonstrated injury factor in the early stages of Alzheimer's disease.

The scientists found that candesartan prevented glutamate-induced neuronal death. They conducted in-depth gene analyses of the laboratory results, demonstrating that candesartan prevented neuronal inflammation and many other pathological processes, including alterations in amyloid metabolism, a hallmark of Alzheimer's disease.

The study's first author, Abdel G. Elkahloun, PhD, from the Comparative Genomics and Cancer Genetics Branch of the National Human Genome Research Institute, then compared gene expression in the neuronal cultures with published gene databases of autopsy samples from Alzheimer's disease patients.

"The correlations were impressive -- the expression of 471 genes that were altered by excess glutamate in our cultures were also altered in brain autopsy samples from patients who suffered from Alzheimer's disease. Candesartan normalized expression of these genes in our cultures," Elkahloun says.

"We hypothesize that candesartan, or other members of the ARB group, may not only slow progression of Alzheimer's but also prevent or delay its development," Saavedra says.

The researchers say this work has immediate translational value, supporting testing candesartan, or other ARBs, in controlled clinical studies on patients at early stages of Alzheimer's disease.

Roman Hafko, PhD, formerly of the National Institute of Mental Health, also contributed to this work and is an author of the paper.

The work was supported by grants from the National Institutes of Health including the National Human Genome Research Institute (MD 20892) and the National Institute of Mental Health (MH 002762-16). The authors report having no personal financial interests related to the study.

http://nyti.ms/1TwdOPc

New Weapon to Fight Zika: The Mosquito

Mosquitoes genetically engineered to pass a lethal gene to their offspring could become a weapon in the battle between humans and mosquitoes

By ANDREW POLLACK JAN. 30, 2016

Every weekday at 7 a.m., a van drives slowly through the southeastern Brazilian city of Piracicaba carrying a precious cargo — mosquitoes. More than 100,000 of them are dumped from plastic containers out the van's window, and they fly off to find mates.

But these are not ordinary mosquitoes. They have been genetically engineered to pass a lethal gene to their offspring, which die before they can reach adulthood. In small tests, this approach has lowered mosquito populations by 80 percent or more.

The biotech bugs could become one of the newest weapons in the perennial battle between humans and mosquitoes, which kill hundreds of thousands of people a year by transmitting malaria, dengue fever and other devastating diseases and have been called the deadliest animal in the world.

"When it comes to killing humans, no other animal even comes close," Bill Gates, whose foundation fights disease globally, has written.

The battle has abruptly become more pressing by what the World Health Organization has called the "explosive" spread of the mosquito-borne Zika virus through Brazil and other parts of Latin America. Experts say that new methods are needed because the standard practices — using insecticides and removing the standing water where mosquitoes breed — have not proved sufficient.

"After 30 years of this kind of fight, we had more than two million cases of dengue last year in Brazil," said Dr. Artur Timerman, an infectious disease expert in São Paulo. "New approaches are critically necessary."

But the new efforts have yet to be proved, and it would take some years to scale them up to a meaningful level. An alternative to mosquito control, a vaccine against Zika, is not expected to be available soon.

So for now, experts say, the best modes of prevention are to intensify use of the older methods of mosquito control and to lower the risk of being bitten using repellents and by wearing long sleeves.

Women are being advised to not get pregnant and to avoid infested areas if pregnant, since the virus is strongly suspected of causing babies to be born with abnormally small heads and damaged brains.

One old method that is not getting serious attention would be to use DDT, a powerful pesticide that is banned in many countries because of the ecological damage documented in the 1962 book "Silent Spring." Still, it is being mentioned a bit, and some experts defend its use for disease control.

"That concern about DDT has to be reconsidered in the public health context," said Dr. Lyle R. Petersen, director of the division of vector-borne diseases at the Centers for Disease Control and Prevention. He said the damage to fish and wildlife stemmed from widespread outdoor use of DDT in agriculture, not the use of small amounts on walls inside homes to kill mosquitoes.

Other experts say the old methods can work if applied diligently.

A determined American doctor named Fred L. Soper eradicated a malaria-carrying mosquito in Brazil in the 1930s, even before the widespread use of DDT. And dengue-carrying mosquitoes were eradicated in 18 Latin American countries from 1947 to 1962, Dr. Hotez said.

But Dr. Soper was a fanatic, making sure every house was thoroughly inspected and all standing water removed. In Brazil, he was backed by the government, which made it a crime to deny entry to an inspector. According to a profile of him in The New Yorker, Dr. Soper used to say that mosquito eradication was impossible in a democracy.

Such an autocratic approach might not be feasible in today's societies. Moreover, Latin American cities have grown tremendously since then, said Carlos Brisola Marcondes, a medical entomologist at the Federal University of Santa Catarina in Brazil.

"The situation is much worse than it was in the past," he said.

The main mosquito that transmits Zika virus — and also dengue, chikungunya and yellow fever — is Aedes aegypti, a particularly wily foe.

It prefers urban areas and bites mainly people, making it very efficient at spreading disease. It bites in the day, so bed nets, a common way to protect people against the night-biting malaria mosquitoes, have little effect. It breeds in small containers of water, such as flower pots, cans and tires that collect rainwater.

"I've seen Aedes aegypti merrily breeding in discarded soda caps," said Joseph M. Conlon, technical adviser to the American Mosquito Control Association.

Aedes aegypti is found in the southern part of the United States, so public health authorities say there will be some local transmission of Zika in this country, though it will be far less serious than in Latin America. Dr. Petersen of the C.D.C. said he envisioned "almost a SWAT team approach" in which resources would be rapidly deployed to areas of local transmission to control mosquitoes using conventional methods.

The genetically engineered Aedes aegypti mosquitoes were developed by Oxitec, a British company, to fight dengue, but would also work to curtail the spread of Zika.

Since last April, the mosquitoes have been released in one neighborhood of Piracicaba populated by about 5,000 people. By the end of 2015, there was a reduction in wild mosquito larvae — as opposed to larvae inheriting the lethal gene — of 82 percent, the company said.

Oxitec and the city said this month that they would extend the project for another year and expand it to cover an area of up to 60,000 people. Oxitec is building a new factory to rear enough mosquitoes to cover an area with 300,000 people.

The company, which was acquired last year by the American biotechnology firm Intrexon, calls its creation the "friendly Aedes aegypti" and notes that it releases only male mosquitoes, which do not bite. It says its solution is ecologically friendly because only the one species is targeted, whereas chemical spraying can affect many types of organisms. But critics worry about the long-term effects of releasing genetically modified organisms. Oxitec has run into public opposition to a proposed test in the Florida Keys.

A Brazilian commission that oversees genetically engineered organisms declared the Oxitec mosquitoes safe to release into the environment in 2014. But Oxitec still does not have a license from Brazil's health regulators that would allow it to actively market its approach to Brazilian cities.

Still, said Hadyn Parry, the company's chief executive, with the outbreak of Zika, "We've had a huge amount more interest from different municipalities."

Another approach, being tested in one Rio de Janeiro neighborhood, is to infect the mosquitoes with Wolbachia, a bacterium that does not infect them naturally. Once infected, the mosquitoes do not pick up and transmit viruses as easily.

The bacteria can be passed to the next generation through eggs, so they spread through the mosquito population.

"The beauty of it is it is a sustainable method — once you put it out it sustains itself in the environment and gives ongoing protection," said Scott O'Neill, dean of science at Monash University in Australia. He is the leader of Eliminate Dengue, a Wolbachia project supported by the Bill & Melinda Gates Foundation and others. Tests are now underway in Indonesia and Vietnam to see if the technique can reduce the number of people getting dengue fever.

Dr. Paulo Gadelha, president of the Oswaldo Cruz Foundation, a scientific institute under the Brazilian Ministry of Health, said initial results in his country were good and there were plans to try it on a larger scale, in Niterói, a municipality across Guanabara Bay from Rio.

"We are planning to scale this up," he said. "The mayor has already agreed."

A new and even more powerful tool may be gene drives, which are genetic mechanisms that rapidly propagate a trait through a wild population. Just in the last few months, scientists have made gene drives that work in mosquitoes in the laboratory.

Anthony A. James, a professor at the University of California, Irvine, said it would be straightforward to use a gene drive to spread something like a sterility trait through the Aedes aegypti population to kill them off.

"We have all the blueprints and have demonstrated proofs of principle," he said. "It's just public will to do this."

The public might not be ready to deploy gene drives outside the laboratory because once a new trait is let loose to spread through the population, it would be difficult to reverse it if something went wrong.

Dr. Petersen of the C.D.C. said of all the new approaches, "We don't know about the efficacy of any of them on a wide enough scale." He added, "For now, we've got to deal with what we have."

http://www.bbc.com/news/magazine-35410148

The country that supplies eyes

Sri Lanka, is doing its best to satisfy demand for corneas without seeking any reward

By Ross Velton BBC News, Colombo

To restore sight to damaged eyes, doctors often need to transplant the cornea - the transparent covering of the iris and the pupil - from a donor's dead body. There is a worldwide shortage, but one country, Sri Lanka, is doing its best to satisfy demand, without seeking any reward - at least in this life.

Bandages cover Paramon Malingam's right eye. A tear appears in the left one. It is the relief of a very lucky man. "I thought I was going to live the rest of my life with one eye," he says.

Thirteen years ago, Malingam, a shop owner from central Sri Lanka, cut his eye with steel wire. Last year, he injured the same eye with a piece of wood. After both accidents, a new cornea from a donor saved his sight.

The cornea is the clear front part of the eye, which lets in light and helps focus images on the retina. When it's damaged, as a result of injury or disease, a person's sight deteriorates, sometimes to the point of blindness.

Often the only solution is a transplant, but in many countries donated corneas are in short supply - a situation aggravated by the fact that they have a brief shelf-life.

Harvesting of the eye must happen within a few hours of death and the cornea itself must be used on a patient within about four weeks, depending on the storage method.

Malingam waited four days for his new cornea and is recovering at Sri Lanka's main eye hospital in the capital, Colombo. "After the surgery, I was reborn to the world," he says.

A few doors down from his ward, Viswani Pasadi, a student, is preparing for a different kind of rebirth, by filling out a form at the National Eye Bank pledging her eyes when she dies. Like most Sinhalese - who make up 75% of Sri Lanka's population - Pasadi is Buddhist. She believes in a cycle of birth, death and rebirth, and sees this donation as a sound investment in her future.

"If I donate my eyes in this life," she says, "I'll have better vision in my next life."

Another who has taken this step is bookkeeper Preethi Kahlewatte.

"Whatever good things we do in this birth, that will take into the next birth," she explains. "When the person needs something, we like to donate. Without hands, we can work. Without legs, we can work. Without eyes, what can we do?"

According to the Eye Donation Society - a non-profit organisation founded by a young doctor, Hudson Silva, in 1961 - one in five Sri Lankans have pledged to donate their corneas. This does not include those, like Pasadi, who have signed up with the National Eye Bank, a separate institution which opened five years ago.

"It seems like I've signed a certificate for every human being in Sri Lanka," says the Eye Donation Society's medical director, Dr Siri Cassim, whose job includes adding his name to the decorative papers given to donors' families.

The eagerness of Sri Lankans to offer their corneas to others means that the country has long harvested more than it needs and has been able to send the surplus to other countries.

The late Hudson Silva began this process in 1964, by packing a few eyes into an ice-filled thermos flask normally used for tea, and having them carried by hand on a flight to Singapore. In 2014, his Society exported 2,551 corneas, including 1,000 to China, 850 to Pakistan, 250 to Thailand, and 50 to Japan.

The country's emergence as a major donor of corneas is largely down to Silva's dynamism. He made his first appeal for eye donations as a student in 1958, in a newspaper article co-authored with his wife and mother, urging Sri Lankans to "give life to a dead eye". The first corneas he received, the following year, he stored in his own refrigerator "along with the eggs and butter". Then in 1960 his mother died and it's said that Silva won the nation's heart by grafting her corneas on to the eyes of a poor farmer, and restoring his sight.

Buddhist monks have also played a part in encouraging donations and teaching people to see them as an act of giving, or "dana", that will help them to be reincarnated into a better life. The venerable Kiribathgoda Gnanananda Thero, founder of the Mahamevnawa Buddhist Monastery in Sri Lanka, told me a story from the Jataka, an ancient book of poems about the Buddha's earlier lives.

"In Buddha's previous life, he became a king. A blind beggar came to the palace and met the king. And he requested, 'Oh king, give me your eyes'. So he [Buddha] decided to give," he said.

The Buddha's surgeon then removed the Buddha's eyes, and transferred them to the beggar, restoring his vision.

"Generation to generation, we are listening to those kind of stories. So we are very encouraged to give our body parts to others," Thero says.

He himself has already donated a kidney to a woman with kidney disease.

The certificates handed out by the Eye Donation Society to those who pledge their corneas, explicitly allude to Buddhist teaching by carrying the words, "Let the donor have a good rebirth", though people from other religions have both made donations and received donated corneas.

In Muslim countries it is generally forbidden to damage the human body, before or after death, so Pakistan and Egypt have been major recipients of Sri Lankan corneas. Malaysia, Nigeria, Sudan also feature on the list of more than 50 receiving countries.

The cornea is one of the easiest tissues to transplant as no matching is required between donor and recipient. It is bloodless tissue, taking oxygen directly from the air. It is also possible to take a cornea from an elderly person, and graft it on to the eyes of a much younger one. If a donor is more than 80 years old there is a higher chance that the cornea will not be suitable, but it's reported that in one case the cornea of an 86-year-old Buddhist monk was given to a nine-year-old Jordanian boy.

Despite this, in the UK at least, the cornea is the tissue donors are most likely to exclude from the list of organs they are prepared to donate - 11% of the total, compared with less than 1% who refuse to donate their kidneys.

"I literally get this image of someone scooping out my eyeballs and it makes me really think," says one Londoner, Cenay Said, a camera assistant in the movie business. "Some of the biggest connections we make with people are through the eyes. They feel really personal."

A cornea taken from Junius Jayewardene (president from 1978 to 1989) was split in two and grafted on to two Japanese patients - at least two former prime ministers also donated eyes **Image copyright Getty Images**

This may be one reason why, according to the National Eye Research Centre in Bristol, there is a shortage of corneas in the UK - though as there is no national waiting list for corneas, unlike some other body parts, experts are unable to say with certainty how big the shortfall is. When corneas are imported to the UK they

tend to come from other European countries or the US - another major exporter - because the similarity in quality and safety standards makes it easier.

"This is not to say that the eye bank in Sri Lanka doesn't apply appropriate standards," says John Armitage of the UK's Corneal Transplant Service Eye Bank. "Rather it's a question of an eye bank in the UK having to fully audit the exporting eye bank to ensure compliance with the UK's standards."

Surprisingly perhaps, the removal of a dead person's eyes is not a problem for families that want an open coffin at the funeral. Jayaratne Funerals in Colombo gets about six eyeless corpses a month. "The embalmers take two cotton balls about the size of the eyeballs," says director Hasanga Jayaratne. "They soak it in embalming fluid and put it inside the eyes and use a bit of glue to shut the eyes." Mourners are then able to see their loved-one one last time before the next life begins.

Corneas and blindness - facts and figures

According to the WHO, 4% of the world's 39 million blind people suffer from corneal opacity (the scarring or clouding over of the cornea) while another 3% suffer from trachoma, a bacterial infection that results in damage to the cornea

Cataracts and glaucoma cause more cases of blindness, but trachoma is described as the main cause of preventable blindness

The main reasons for cornea transplants (keratoplasty) in Sri Lanka are the damage to the cornea as the result of an infection - sometimes including ulcers (infective keratitis) - or keratoconus, where the cornea becomes too thin and its shape is distorted

Sri Lanka took corneas from executed prisoners until 1956, when the death penalty was temporarily abolished - it was reintroduced in 1959, but there have been no executions since 1976

In the UK, the main reason for cornea transplants is a condition that mainly affects older people called Fuchs' dystrophy, which causes the cornea to swell and become cloudy - keratoconus is also a problem, though, affecting younger patients

http://bbc.in/1OZLqBM

Microcephaly, Spotlighted by Zika Virus, Has Long Afflicted and Mystified

Microcephaly has pained families across the globe and mystified experts for decade

By CATHERINE SAINT LOUIS JAN. 31, 2016

The images pouring out of Brazil are haunting: struggling newborns with misshapen heads, cradled by mothers who desperately want to know whether their babies will ever walk or talk. There are thousands of these children in Brazil, and scientists fear thousands more might come as the Zika virus leaps across Latin America and the Caribbean. But the striking deformity at the center of the epidemic, microcephaly, is not new: It has pained families across the globe and mystified experts for decades.

For parents, having a child with microcephaly can mean a life of uncertainty. The diagnosis usually comes halfway through pregnancy, if at all; the cause may never be determined — Zika virus is only suspected in the Brazilian cases, while many other factors are well documented.

And no one can say what the future might hold for a particular child with microcephaly.

Dr. Hannah M. Tully, a neurologist at Seattle Children's Hospital, sees the pain regularly, particularly among expectant parents who have just been told that an ultrasound showed their child to be microcephalic: "a terrible situation with which to be confronted in a pregnancy," she said.

An estimated 25,000 babies receive a microcephaly diagnosis each year in the United States. Microcephaly simply means that the baby's head is abnormally small — sometimes just because the parents themselves have unusually small heads.

"By itself, it doesn't necessarily mean you have a neurological problem," said Dr. Marc C. Patterson, a pediatric neurologist at the Mayo Clinic Children's Center in Rochester, Minn.

But microcephaly can portend significant brain damage, as well. The most severe cases can be detected before birth with ultrasound scans, but usually only toward the end of the second trimester, at about 24 weeks.

Most expectant mothers have ultrasound exams at about 20 weeks, however, so the condition can be missed. Many parents learn their child is microcephalic only after birth, when the newborn's head is measured.

Even when it is made early, the diagnosis raises hard questions. Abortion is generally legal in the United States only until the fetus is viable outside the womb, which can range from 24 to 26 weeks.

That leaves parents little time for an enormously difficult decision, complicated by doctors' inability to say what the effects of microcephaly might be.

Prognoses for these children vary widely. At least 10 percent have no mental deficits at all.

Others are highly functional, albeit with intellectual disabilities. Still others are profoundly disabled, in wheelchairs with limited ability to communicate and fed through a gastric tube.

"Families have very little time to have the necessary studies, get the results, process their thoughts and make a decision before they reach the legal limits of termination," Dr. Tully said.

Melissa and Peter Therrien, of Brewster, Mass., faced that choice when they learned that their daughter had a very small skull, after an ultrasound during Mrs. Therrien's 24th week of pregnancy.

"I felt heartbroken," Mrs. Therrien, 21, said. "The doctor gave me the option to terminate the pregnancy." But, she said, "I couldn't do that."

Their daughter, Alainah, is now 15 months old, but her development is uncertain. She can walk, although doctors said she might not, and she is given to peals of laughter, Mrs. Therrien said.

Yet Alainah speaks just three words: Mama, Papa and "aba," which she uses to describe various objects. She can use sign language to say she is hungry. She has passed some standard milestones, but her parents do not know how far she will progress.

Doctors at Boston Children's Hospital will not know the extent of damage to her brain for nine months or so. She may still have seizures and profound disability.

"It's just tough," said Peter Therrien, 26. "There's nothing we can do to fix it. We'll pretty much be walking on eggshells for the rest of our lives."

If the cause of microcephaly is determined, it can give some clues to how children will fare.

Certain genetic conditions are linked to microcephaly, among them Down syndrome. Pregnant women who are badly malnourished, have diabetes or consume alcohol are also more likely to have children with microcephaly.

Microcephaly can develop after birth in children with some genetic disorders, and in some infants deprived of oxygen during labor whose injured brains stop growing in their first few years.

But of particular concern to researchers now is that microcephaly can be caused by infections, including toxoplasmosis, German measles and cytomegalovirus, a ubiquitous virus.

Zika virus may soon join the list. If it does cause microcephaly, it is a rare complication. No increases in microcephaly are conclusively linked to the virus outside Brazil, although French Polynesia is investigating a small number of neurological problems in babies after an outbreak there.

No such problems were seen in the first carefully studied Zika outbreak, which was on Yap Island in Micronesia in 2007. But Yap has fewer than 12,000 residents. The current outbreak is the first in which scientists have seen the virus invade a large continent where no one is immune.

Experts say it may be no surprise that a real but rare complication comes to light only when millions of adults are infected. There may have been surges in microcephaly when Zika reached Asia from Africa sometime in the last century, but genetic techniques to distinguish it from other illnesses did not exist then.

When caused by such an infection, microcephaly can lead to "a significant volume loss of brain tissue" and "complete loss of the use of their limbs," said Dr. Ganeshwaran H. Mochida, a neurologist at Boston Children's Hospital and Alainah's doctor.

In Brazil, researchers say they are seeing a disproportionate number of microcephalic infants with what appear to be severe deformities, many with four striking malformations at once: a large degree of brain tissue loss; unusually smooth, wrinkleless brains; many calcium deposits; and smaller cerebellums, which play a role in motor control.

"We can see many of these findings in other congenital infections," said Dr. Albert I. Ko, an infectious-diseases specialist at Yale School of Public Health who is helping Brazilian health officials put together a study of Zika infection and birth defects.

"It's the degree and pattern of findings that presumably make Zika different, and perhaps unique."

Dr. Ko, who is among the few American scientists to have reviewed brain scans of microcephalic infants in Brazil, fears that many have a "poor prognosis."

But Dr. Patterson cautioned that it is difficult to predict the future of any microcephalic child.

"It is premature to make predictions so early in the course of this apparent outbreak," he said. "I suspect that, as in other intrauterine infections, there will be a spectrum of outcomes."

There is no way to return a child's head to a normal size or shape. Specialists are left to draw clues to a child's prognosis from his or her early development.

"It's still very hard to tell people what to expect," said Dr. Constantine A. Stratakis, a pediatric geneticist and a scientific director at the National Institute of Child Health and Human Development. "You have to see whether the child meets the milestones, and you act accordingly."

Dr. Patterson noted, "I always want to emphasize the positive side. I tell them, 'We will monitor your child carefully, so that if it turns out the child is having physical difficulty or cognitive difficulty, we can ensure they get all the help they need.' "

The Therriens alternate between optimism and pessimism, waiting for the tests that will provide clues to Alainah's course.

"My biggest worry is her future," said Mrs. Therrien, who also has a 6-year-old daughter without microcephaly.

"Is she ever going to be able to live a life like her sister will?"

http://nyti.ms/1JTwpCP

New Plan to Treat Schizophrenia Is Worth Added Cost, Study Says

A new approach to treating early schizophrenia, which includes family counseling, results in improvements in quality of life that make it worth the added expense, researchers reported on Monday.

By BENEDICT CAREY FEB. 1, 2016

The study, published by the journal Schizophrenia Bulletin, is the first rigorous cost analysis of a federally backed treatment program that more than a dozen states have begun trying. In contrast to traditional outpatient care, which generally provides only services covered by insurance, like drugs and some psychotherapy, the new program offers other forms of support, such as help with jobs and school, as well as family counseling.

The program also tries to include the patients — people struggling with a first psychotic "break" from reality, most of them in their late teens and 20s — as equals in decisions about care, including drug dosage.

In a widely anticipated study last fall, called the Raise trial, researchers reported that after two years, people who got this more comprehensive care did better on a variety of measures than those who received the standard care. But the study found no evidence of related cost savings or differences in hospitalization rates, a prime driver of expense. As lawmakers in Washington are considering broad changes in mental health care, cost issues loom especially large.

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Outside experts said this analysis — which was based on the Raise trial data — was an important test of the new care program's value.

"This is the way cost analysis should be done," Sherry Glied, a professor of public service and the dean of New York University's graduate school of public service, said. "One way to think about it is to ask, if this program were a drug, would we pay for it? And the answer is yes."

Swaying policy makers will take far more work, others said.

"This study shows that the treatment is promising, in a research setting," said Thomas McGuire, a professor of health economics at Harvard Medical School. "We'll still need to see how it works in the real world, whether it makes sense for community mental health clinics."

The new research, led by Dr. Robert Rosenheck of the Yale School of Medicine, included 183 people who received typical care and 223 who got the more comprehensive services. The study aimed in part to assess whether investing more money in early treatment might forestall much higher costs later on.

The new analysis could not settle that question, because it compiled data from only two years. (Lifetime studies could estimate differences such as whether people stay in the workplace or off government assistance.) The researchers evaluated the costs of all added services, including the price for training and mounting the new program, and asked what differences in average quality of life that money yielded.

The treatment package cost about $3,600 a year more than traditional outpatient care, the researchers found, and resulted in an improvement of about 13 percent over the usual care. That measure included how patients were doing at home, in their primary relationships and in school or at work.

"We then had to ask, 'How do we put a precise value on improved quality of life?' " Dr. Rosenheck said.

Using standard scales applied to other health care, like medications and operations, the team found that the new approach delivered about the same value of health benefits as other widely accepted treatments, like statin drugs to prevent heart attacks, Dr. Rosenheck said, and was more cost effective than many cancer therapies.

The extra money spent, in short, "is at the low end of the range of services we already pay for," Dr. Glied said.

This cost-benefit ratio may improve in the coming years. Many medications used for schizophrenia are close to becoming generic, which would lower the average added expense of the new program to about $2,000 a year. But given the uncertainties of a chronic condition like schizophrenia, experts said the new study should be considered a good first-term report card, not a final rating.

"One thing that's incontrovertible is that when a child develops schizophrenia, your life's a mess. A truck has just run you over," Dr. Rosenheck said. "If nothing else, this intervention provides support for individuals and families at the worst times of their lives. It tells you that you will not be alone — there's people looking to make this better."

http://bit.ly/20Bibuk

Southeast Asia Braces for Zika Virus

The World Health Organization on Monday is convening a meeting in Geneva to determine whether a global health emergency should be declared for the Zika virus.

by Steve Herman

WHO is responding in a more pro-active manner to the relatively minor mosquito-borne virus in contrast to its slow response to the lethal 2013 outbreak of Ebola in West Africa, for which the U.N. agency faced heavy criticism.

Zika, suspected of causing a surge of birth defects in South Africa, is “spreading explosively” in the Americas, according to the WHO.

The U.N. agency also believes the disease has been more common in Southeast Asia than the smattering of cases reported in the region in the past several years.

Rarely fatal

Zika, usually mild and rarely fatal with symptoms often mistaken for other mosquito-borne viruses such as dengue and chikungunya, has “widespread distribution" across Thailand, according to an article last year in the *American Journal of Tropical Medicine and Hygiene*. But Thailand has only reported one case this year.

It is spread through the *Aedes aegypti* mosquito, responsible for dengue, yellow fever and other tropical diseases.

Thailand has seen a sharp increase in dengue in recent years.

A popular 37-year-old TV actor, Thrisadee “Por” Sahawong, died last month of complications related to dengue fever after more than two months in a coma, shining a fresh spotlight in the kingdom on the disease, which was first documented in the 1950s during epidemics in Thailand and the Philippines.

The Zika virus, first detected in a rhesus monkey in Uganda in 1947, had been limited to rare cases in human populations in Africa and Asia until an unprecedented outbreak on an island in the southwestern Pacific in 2007.

“It was something kind of unique, along with the fever and rash that we were starting to see, as well as patients having some kind of this typical rash around the earlobe,” said Dr. James Edilyong, the medical staff chief for the state of Yap in Micronesia. “That's when it kind of indicated to us that we need to more find about this kind of condition.”

Contracted virus

The general population on the island – which is home to little more than 10,000 people – was subsequently tested. It was discovered nearly three-fourths of those aged 3 and older had contracted the virus. But most did not realize it.

“A lot of them were basically sub-clinical. They didn't feel the need to come to the hospital. Maybe some of them didn’t even feel any difference, probably just thinking it's just a flu or something – just feeling a little bit unwell,” Edilyong told VOA Monday.

In late 2013, another large outbreak erupted in French Polynesia, with the first links to the virus causing Guillain-Barré syndrome, a neurological illness with paralysis as its main feature.

But the relatively obscure disease did not end up on the front pages globally until the latest outbreak emerged in Brazil – where several thousand cases have been reported since last year – of a suspected link to infected pregnant women giving birth to babies with microcephaly, a fetal deformity that causes abnormally small heads.

There were no such defects linked to Zika on Yap after the 2007 outbreak, but officials there, in view of what has emerged out of Brazil, are now examining birth records more closely, Edilyong told VOA.

There has also been no link so far between Zika and microcephaly in Southeast Asia, according to the WHO's regional office here.

Malaysian and Singaporean public health officials have warned of a high risk of contagion if the virus is introduced there.

The Philippines health department is calling Zika a “real and present” risk amplified by weather conditions caused by the El Niño phenomenon that will likely lead to more ideal conditions for mosquitoes to breed.

Governments in the Americas and the Caribbean, including Colombia, Ecuador, El Salvador, Jamaica and Puerto Rico, have warned women to delay conceiving until the Zika outbreak is brought under control.

No treatment or vaccine is available, although a Canadian researcher has been quoted as saying one might be ready within this year. Medical experts, however, say it could take several years of testing a vaccine before it is deemed safe.