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Good microcirculation indicates increased lifespan

A study on centenarians links sphingotec's biomarker bio-Adrenomedullin to longevity

Human longevity has been previously linked by researchers to genetic factors, calorie restriction, and certain life-style factors such as physical activity or the Mediterranean diet. Now, Italian researchers from La Sapienza University in Rome have identified an additional factor, which significantly contributes to a longer life. In a pilot study on some of the oldest people of the world, they discovered that the perfusion of organs and muscles of the centenarians was as efficient as that in people who were 30 years younger. Results of the CIAO (Cilento Intitiative on Aging Outcome) pilot study, presented today in the Italian town of Pollica, suggest that low blood levels of the peptide hormone Adrenomedullin (bio-ADM) are an indicator for such a good microcirculation. Making longevity measurable has long been a scientific goal as it could open up the avenue to a systematic identification of factors contributing to an extended life span.

Prof. Salvatore Di Somma and his team carried out comprehensive health and life style assessments of two study groups that live in the Cilento region, located in the province of Salerno in southern Italy: In the first were 29 so-called 'SuperAgers' (median age 92 years), while the second was made up of 52 younger relatives (median age 60 years, living in the same household) who are expected to live just as long because they have the same genetic background and have been exposed to the same environmental and lifestyle factors. Blood biomarker analyses were carried out by the diagnostic company sphingotec (Hennigsdorf, Germany). It measured levels of the heart-function biomarker MR-proANP, as well as a marker for kidney function (penKid) and bio-ADM. The last is a regulator of vasodilation and blood vessel integrity, which both affect blood pressure. The results were compared to those of a cohort of 194 healthy persons (median age 63.9 years), who were monitored over eight years in the earlier Malmö Preventive Project (MPP, Principal Investigator Professor Olle Melander, Lund University, Sweden).

As expected, low values of MR-proANP and penKid among the subjects in the two younger control groups indicated no signs of heart or kidney dysfunction. In contrast, both biomarkers were elevated in the SuperAgers, possibly due to the process of organ aging. However, even though the older group had levels of the two biomarkers that were as high as those found in patients experiencing heart failure (HF) or acute kidney injury (AKI), they were in clinically good condition. Surprisingly, in the group of SuperAgers, the bio-ADM values - which are often pathologically elevated in HF or AKI patients - were as low as those in both reference groups.

"Very low concentrations of this biomarker indicate a well-functioning endothelial and microcirculatory system allowing good blood perfusion of organs and muscles," concludes Di Somma. A good microcirculation is what makes marathon runners perform better at the same heart rate than the average man or woman on the street.

"We are excited about the connection between bio-ADM levels and a good microcirculation as an indicator for good quality of life", says sphingotec founder Andreas Bergmann, who was instrumental in developing the bio-ADM assay. "If bio-ADM proves to be a reliable biomarker for longevity this will open up the avenue to a systematic analysis of the factors contributing to longevity", he adds. "We are excited to contribute to the identification of lifestyle factors ensuring a good microcirculation."

The researchers are currently planning to extend the pilot study to 2,000 people from the Cilento region. One major goal of the follow-up study is to investigate whether certain components of the local Mediterranean diet could affect the bio-ADM level. The cuisine typical to the region traditionally uses number of plants native to the area. Another idea is to bring people with high bio-ADM levels to Cilento and measure whether the local environment has an effect on levels of the microcirculation biomarker.

The CIAO (Cilento Intitiative on Aging Outcome) study was designed to identify life style, genetic and epigenetic factors contributing to longevity in the Cilento region. With an average life expectancy of 92 years for women (Italian average: 84) and 85 years for men (Italian average: 79), the Cilento has one of the world's highest concentrations of centenarians - even higher than in Okinawa (Japan), the most intensively investigated centenarian hotspot. The contributors to the current pilot study were identified through local physicians who acquired the informed consent of their patients. A mobile bus equipped with all instrumentation for a comprehensive health assessment was used to visit the study participants. Additionally, blood samples for biomarker analysis were taken and participants were interviewed about their life style habits.

Microcirculation describes blood flow through the smallest vessels (capillaries) in the circulatory system. In these regions, oxygen and nutrients are directly delivered to cells, while metabolic debris, toxins and CO2 are winnowed out. Blood pressure and body temperature is also controlled by the microcirculation through dilation or constriction of the capillary network that penetrates muscles, organs and skin. If put end-to-end, the body's capillaries would stretch 90,000-110,000 kilometers - more than twice the circumference of Earth. If placed side-by-side, they would cover an area the size of two football fields (500-700 sqm). On average, people have around 200-300 capillaries/mm^2, but endurance athletes like runners can have up to 40% more (300-500 capillaries/mm^2). This contributes to better muscle perfusion, oxygen supply and performance.

Salvatore Di Somma (63), Professor of Internal Medicine at the University La Sapienza in Rome, is the organizer of the CIAO pilot study. Strong personal links have given him unique access to the population of centenarians living in the Cilento. In previous studies, he identified rosemary as an ethnobotanically conserved part of the local Mediterranean cuisine that might could be contributing to longevity in the region. Conserved gene variants associated with longevity were also identified in Cilento's population in the Southern Italy Centenarian Study (SICS). The variants affect insulin sensitivity (FOXOA3, CAMMIV), RNA editing (ADARB1^{+2}) and the aromatase pathway (Cyp19, ESR1). Additionally, a unique profile of lipids in the membrane of red blood cells (erythrocytes) was identified in 2008 within the the framework of the SICS study

Centenarian hotspots: Several regions have been identified by National Geographic writer Dan Buettner as longevity hotspots. They include Okinawa (Japan), Sardinia (Italy), Nicoya (Costa Rica), Icaria (Greece) and a group of Seventh-day Adventists living in Loma Linda (US, California). The Cilento, a mountainous region 150 kilometres south from Naples, is another hotspot of centenarians. Although it didn't earn a mention in Buettner's book on the so-called "Blue zones" of centenarians, people who live there are getting older than in Okinawa, Japan, the world's very best-studied longevity hot-spot. Life expectation of women living in the Cilento (92 years) is 8 years above the Italian average; and that of men (85 years) 6 years above, anyway.

Adrenomedullin is a soluble peptide hormone. Mainly released by the inner layer of blood vessels (endothelial cells), its biological function is to control vasodilation, an important regulator of blood pressure and organ perfusion. In several studies involving more than 16.000 patients, the plasma level of the bioactive Adrenomedullin (bio-ADM) has been proven to predict and provide an early diagnosis for circulation dysfunction. For instance, bio-ADM blood levels rise 2-3 days before septic shock occurs. Elevated levels of bio-ADM are a specific indicator of vasodilation and leakage from microcirculatory capillaries, which in sepsis patients subsequently lead to severe hypotension, malperfusion of organs (for which the body can't compensate by increasing the heart rate), shock and multiple organ failure. Low bio-ADM blood levels, in contrast, are a specific indicator for an intact microcirculation, ensuring good muscle and organ blood supply without any cardiovascular stress.

sphingotec GmbH (Hennigsdorf, Germany) develops innovative biomarkers for the early diagnosis, prediction and monitoring of severe medical conditions, such as cardiovascular

diseases, sepsis, kidney dysfunction and cancer, supporting treatment and prevention strategies. Located on the outskirts of Berlin, the company was established in 2002. Its founder Dr. Andreas Bergmann was one of the founders of B.R.A.H.M.S. AG, which has become part of ThermoFisher Scientific. As the company's former Chief Research Officer, he was responsible for the development of the "gold standard" sepsis biomarker Procalcitonin (B.R.A.H.M.S. PCT™).
More information at http://www.sphingotec.com/info-center/ciao-study-press-material/.

http://apne.ws/2ccX2pE

Study: Typhoons that slam Asia getting much stronger

Typhoons that slam into land in the northwestern Pacific - especially the biggest tropical cyclones of the bunch - have gotten considerably stronger since the 1970s, a new study concludes.

By SETH BORENSTEIN

WASHINGTON (AP) -- Overall, landfalling Asian typhoon intensity has increased by about 12 percent in nearly four decades. But the change is most noticeable for storms with winds of 209 kilometers per hour or more (130 mph), those in categories 4 and 5. Since 1977, they've gone from a once-a-year occurrence to four times a year, according to a study Monday in the journal Nature Geoscience.

These are storms like Lionrock that in August killed at least 17 people, about half of them elderly residents of a Japanese nursing home, and Haiyan - one of the strongest storms on record, killing more than 6,000 people in the Philippines in 2013.

Study lead author Wei Mei, a climate scientist at the University of North Carolina, connects the strengthening of these storms to warmer seawater near the coasts. That provides more fuel for the typhoons. Along much of the Asian coast, water has warmed by nearly 0.8 degrees (1.4 degrees Fahrenheit) since the late 1970s. Mei didn't study why the water is warming, but says it is probably due to a combination of natural local weather phenomena and warming from the burning of fossil fuels.

Mei and two other outside scientists say it is too early to say precisely that the increased intensity is from man-made climate change.

But as the world warms more in the future, stronger storms are likely to get even more intense, especially north of 20 degrees North latitude, where eastern China, Taiwan, Korea and Japan are located, Mei says.

Colorado State University hurricane researcher Phil Klotzbach says the study makes sense and raises interesting questions, but adds that some of the storms before 1987 might have had their wind speeds under-estimated.

Mei said he thinks that time period actually had better measurements because planes were then flying into storms to gauge their strength.

Mei didn't study tropical cyclone intensification in other parts of the world.

Nature Geoscience: http://www.nature.com/ngeo/index.html

http://bit.ly/2c7GmfW

Study: Earth's carbon points to planetary smashup

Element ratios suggest Earth collided with Mercury-like planet

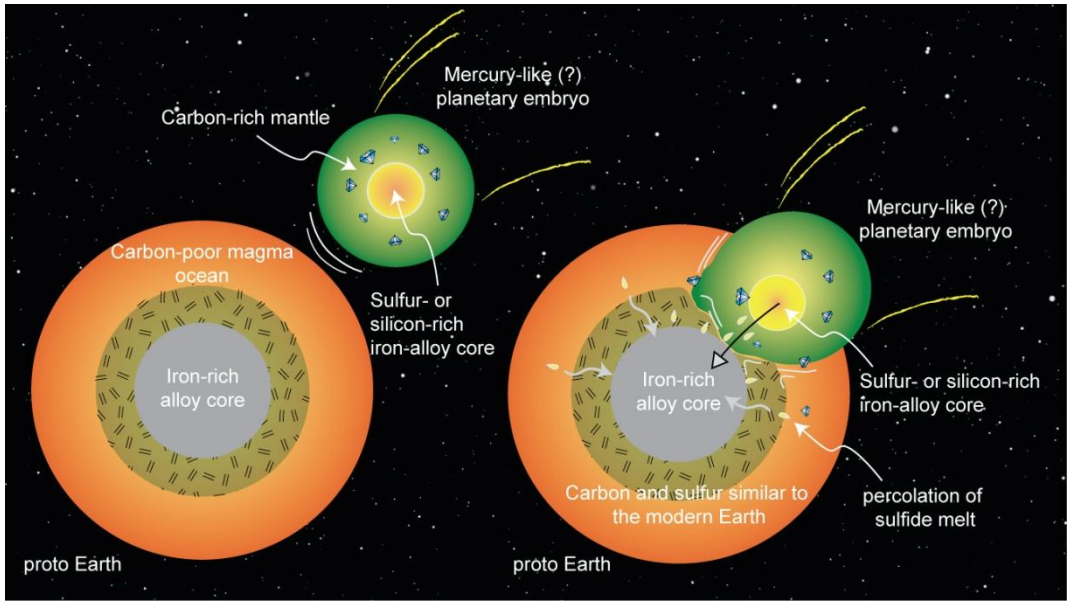
HOUSTON - Research by Rice University Earth scientists suggests that virtually all of Earth's life-giving carbon could have come from a collision about 4.4 billion years ago between Earth and an embryonic planet similar to Mercury.

In a new study this week in Nature Geoscience, Rice petrologist Rajdeep Dasgupta and colleagues offer a new answer to a long-debated geological question: How did carbon-based life develop on Earth, given that most of the planet's carbon should have either boiled away in the planet's earliest days or become locked in Earth's core?

"The challenge is to explain the origin of the volatile elements like carbon that remain outside the core in the mantle portion of our planet," said Dasgupta, who co-authored the study with lead author and Rice postdoctoral researcher Yuan Li, Rice research scientist Kyusei Tsuno and Woods Hole Oceanographic Institute colleagues Brian Monteleone and Nobumichi Shimizu.

Dasgupta's lab specializes in recreating the high-pressure and high-temperature conditions that exist deep inside Earth and other rocky planets. His team squeezes rocks in hydraulic presses that can

simulate conditions about 250 miles below Earth's surface or at the core-mantle boundary of smaller planets like Mercury.



A schematic depiction of early Earth's merger with an embryonic planet similar to Mercury, a scenario supported by new high-pressure, high-temperature experiments at Rice University. Magma ocean processes could lead planetary embryos to develop silicon- or sulfur-rich metallic cores and carbon-rich outer layers. If Earth merged with such a planet early in its history, it could explain how Earth acquired its carbon and sulfur. **(Figure courtesy of Rajdeep Dasgupta)**

"Even before this paper, we had published several studies that showed that even if carbon did not vaporize into space when the planet was largely molten, it would end up in the metallic core of our planet, because the iron-rich alloys there have a strong affinity for carbon," Dasgupta said.

Earth's core, which is mostly iron, makes up about one-third of the planet's mass. Earth's silicate mantle accounts for the other two-thirds and extends more than 1,500 miles below Earth's surface. Earth's crust and atmosphere are so thin that they account for less than 1 percent of the planet's mass. The mantle, atmosphere and crust constantly exchange elements, including the volatile elements needed for life.

If Earth's initial allotment of carbon boiled away into space or got stuck in the core, where did the carbon in the mantle and biosphere come from?

"One popular idea has been that volatile elements like carbon, sulfur, nitrogen and hydrogen were added after Earth's core finished forming," said Li, who is now a staff scientist at Guangzhou Institute of Geochemistry, Chinese Academy of Sciences. "Any of those elements that fell to Earth in meteorites and comets more than about 100 million years after the solar system formed could have avoided the intense heat of the magma ocean that covered Earth up to that point.

"The problem with that idea is that while it can account for the abundance of many of these elements, there are no known meteorites that would produce the ratio of volatile elements in the silicate portion of our planet," Li said.

In late 2013, Dasgupta's team began thinking about unconventional ways to address the issue of volatiles and core composition, and they decided to conduct experiments to gauge how sulfur or silicon might alter the affinity of iron for carbon. The idea didn't come from Earth studies, but from some of Earth's planetary neighbors.

"We thought we definitely needed to break away from the conventional core composition of just iron and nickel and carbon," Dasgupta recalled. "So we began exploring very sulfur-rich and silicon-rich alloys, in part because the core of Mars is thought to be sulfur-rich and the core of Mercury is thought to be relatively silicon-rich. "It was a compositional spectrum that seemed relevant, if not for our own planet, then definitely in the scheme of all the terrestrial planetary bodies that we have in our solar system," he said.

The experiments revealed that carbon could be excluded from the core -- and relegated to the silicate mantle -- if the iron alloys in the core were rich in either silicon or sulfur.

"The key data revealed how the partitioning of carbon between the metallic and silicate portions of terrestrial planets varies as a function

of the variables like temperature, pressure and sulfur or silicon content," Li said.

The team mapped out the relative concentrations of carbon that would arise under various levels of sulfur and silicon enrichment, and the researchers compared those concentrations to the known volatiles in Earth's silicate mantle.

"One scenario that explains the carbon-to-sulfur ratio and carbon abundance is that an embryonic planet like Mercury, which had already formed a silicon-rich core, collided with and was absorbed by Earth," Dasgupta said. "Because it's a massive body, the dynamics could work in a way that the core of that planet would go directly to the core of our planet, and the carbon-rich mantle would mix with Earth's mantle.

"In this paper, we focused on carbon and sulfur," he said. "Much more work will need to be done to reconcile all of the volatile elements, but at least in terms of the carbon-sulfur abundances and the carbon-sulfur ratio, we find this scenario could explain Earth's present carbon and sulfur budgets."

A copy of the paper is available at: http://dx.doi.org/10.1038/ngeo2801

http://bit.ly/2ck1wLB

Obesity linked to improved survival in kidney

Despite being a risk factor for kidney cancer, obesity was linked to improved survival

BOSTON -- Obesity almost always increases cancer risk and worsens outcomes, but researchers led by scientists at Dana-Farber Cancer Institute report that overweight patients with advanced kidney cancer had significantly longer survival than those who were normal or underweight. Having a high body mass index (BMI) is a well-established risk factor for clear cell renal cell carcinoma, the most common type of kidney cancer. (BMI is the ratio of weight in kilograms divided by the squared height in meters.)

Yet, paradoxically, the study published in the Journal of Clinical Oncology involving thousands of patients in four databases demonstrated that when overweight individuals developed kidney cancer - especially in its advanced, metastatic form - their disease progressed more slowly and they lived longer than their normal-weight counterparts.

In one cohort of nearly 2,000 patients, the median overall survival of patients with high BMI (overweight or obese) was 25.6 months compared to 17.1 months for patients with low BMI. The mortality rate for the overweight cancer patients was 16 percent less over the course of the study, which began in 2003.

The report's authors, led by senior and corresponding author Toni K. Choueiri, MD, director of the Lank Center for Genitourinary Oncology at Dana-Farber, noted previous research showed that kidney cancer diagnosed in obese patients had less-dangerous pathological characteristics, and when treated with targeted therapies, these patients, even when their disease had spread, had better overall survival.

In the new study, Choueiri and his colleagues, including first author Laurence Albiges, PhD, formerly a visiting scientist at Dana-Farber, now GU Medical Oncology Lead at Institut Gustave Roussy in France, confirmed these findings in four separate databases, which Choueiri said "makes this a very strong study."

The International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) provided records on 1,975 patients who had received targeted therapies. Their height and weight were recorded at the initiation of therapy. In a validation set, the scientists also analyzed pooled data on 4.657 patients treated for kidney cancer in clinical trials between 2003 and 2013.

Another dataset, from The Cancer Genome Atlas project, included clinical and genomic information on 324 kidney cancer patients. The fourth database included cancer tissue samples from 146 kidney cancer patients treated at Dana-Farber and other Harvard-affiliated hospitals. . Using these two databases, the investigators searched for molecular differences between the high- and low-BMI patients that

might explain why kidney tumors in obese patients were less aggressive and responded better to treatment.

The TGCA analysis didn't reveal any differences in the tumors' DNA, such as gene mutations, that might account for the disparity. But when the scientists looked at gene expression - the rate at which genetic information was being used by the cell to make proteins - they spotted a difference. Expression of a gene called fatty acid synthase (FASN) was found to be decreased in patients with high BMI compared to normal weight patients.

FASN is key enzyme in lipogenesis - cells' production of fatty acids - and overexpression of FASN has previously been found in many types of cancer - so much so that FASN has been called a metabolic oncogene. FASN has been associated with poor prognosis in several types of cancer, including kidney cancer.

Since FASN expression was decreased, or "downregulated," in overweight and obese kidney cancer patients, that could explain why these individuals fared better than those who were of normal weight and had increased FASN gene expression.

Why FASN is downregulated in obese patients isn't yet known, but the authors of the study say the results provide a rationale for experiments aimed at inhibiting FASN expression in kidney cancer patients - regardless of their BMI - in an effort to improve outcomes. FASN inhibitors, including some derived from natural products, have been in development for several years and are considered a promising approach to cancer treatment. "We plan to test FASN inhibitors in an animal model as a possible therapy for kidney cancer," said Choueiri.

The research was supported by the Dana-Farber/Harvard Cancer Center Kidney Cancer SPORE Grant No. P50 CA101942-01 and the Kidney Cancer Foundation.

http://bbc.in/2c74VKs

Vitamin D 'significantly reduces severe asthma attacks'

Taking Vitamin D supplements in addition to asthma medication appears to cut the risk of severe asthma attacks, a review of evidence suggests.

An independent review by the Cochrane research body of nine clinical trials found it also cut the rate of asthma attacks needing steroid treatment.

But researchers say it is unclear whether it only helps patients who are vitamin D deficient. They say more studies are needed before they can give patients official advice. They recommend talking to a GP or pharmacist to get advice before taking a vitamin D supplement.

The Cochrane review's lead author, Professor Adrian Martineau, said they found vitamin D "significantly reduced the risk of severe asthma attacks, without causing side effects". They found taking vitamin D reduced the risk of severe asthma attacks requiring a hospital admission or a visit to A&E from 6% to 3%. They also found the rate of asthma attacks needing steroid treatment dropped from 0.44 to 0.28 attacks per person per year. But they found that vitamin D did not improve lung function or day-to-day asthma symptoms.

Vitamin D

Known as the "sunshine" vitamin, it is found in food and is made in the body when the skin is exposed to sunshine

One in five adults and one in six children in England are thought to have low levels of vitamin D

Limited amounts of the vitamin are found in foods such as oily fish, eggs and fortified cereals

For most people the bulk of their vitamin D comes from sunlight

Low vitamin D levels can lead to brittle bones and rickets in children

Vitamin D can boost immunity and dampen down inflammation

It is possible to overdose from vitamin D - but that would be five times the amount of vitamin D that was given in these trials

The researchers looked at nine recent clinical trials - seven involving 435 children and two studies involving 658 adults, lasting up to a year.

Prof Martineau called the review "an exciting result" but acknowledged "some caution is warranted" and further study is needed.

The trials were mainly carried out on adults with mild or moderate asthma so further testing is needed to see the affect on children and those with severe asthma "to find out whether these patient groups

will also benefit", he said. He said further analyses were on-going and results should be available in the next few months.

In July Public Health England recommended that everyone should consider taking vitamin D supplements in autumn and winter.

An extensive review of evidence suggested everyone over the age of one needs to consume 10 micrograms of vitamin D each day in order to protect bone and muscle health. And public health officials said, in winter months, people should consider getting this from 10 microgram supplements, if their diet is unlikely to provide it.

The level of vitamin D taken in these clinical trials was much higher than this recommendation at 25 to 50 micrograms per day.

In the UK, 5.4 million people are being treated for asthma - that is one in 11 of the population. Every day there are 185 hospital admissions and three deaths because of the condition.

Dr Erika Kennington, Asthma UK's head of research, said: "While this research shows promise, more evidence is needed to conclusively show whether Vitamin D can reduce asthma attacks and symptoms.

"With so many different types of asthma it could be that Vitamin D may benefit some people with the condition but not others. Asthma UK's research centres are working hard to discover how and why Vitamin D affects asthma symptoms and if it could be a potential treatment in the future."

'Visit your GP'

Prof Martineau pointed out that in the study, vitamin D was added on to asthma medication the patients were already taking. He explained: "We don't want people giving up taking their asthma treatment."

He also warned against taking vitamin D without advice.

"Going to see your GP is a key part of the message we want to give - I don't think it would be appropriate to just start taking vitamin D without knowing whether you have vitamin D deficiency or not and we don't yet know what the threshold of vitamin D is below which you will have a benefit."

Dr Rebecca Normansell, a GP from the Cochrane body, said asthma patients are not routinely tested for their vitamin D levels, but following further study "it may be that that will be something that we should be considering as a reason to test vitamin D".

"Talking with your pharmacist or GP is a great place to start as there may be other things that could be done for you as well to improve your asthma beyond thinking about your vitamin D," she said.

Dr Imran Rafi, from the Royal College of General Practitioners (RCGP), called the research "encouraging".

"However, more work still needs to be done in gathering the evidence, particularly around effectiveness for young people and children - especially as it currently affects as many as one in 11 children."

He said he looked forward to seeing the results of further clinical trials to get a better understanding of this potential method of treatment.

"It is important to remember that not every drug is suitable for every patient and if a patient has asthma, they shouldn't make any changes to their medication without first discussing it with their family doctor."

http://bbc.in/2cae5YH

Doctors urged to offer 'exercise outdoors' prescriptions

Doctors in England and Wales should offer overweight patients "green space" prescriptions to get them exercising outdoors, says the Local Government Association.

The prescriptions could provide free visits to national parks or gardening sessions at National Trust properties, for example. A small number of GPs already do this. The LGA says it needs to become universal policy to tackle the nation's obesity crisis. It's calling on NHS Clinical Commissioning Groups to drive the initiative forward.

In Dorset, doctors already prescribe walks, conservation work, gardening and sailing. East Riding of Yorkshire Council has developed an IT system which links up GPs with leisure centres so they can book patients directly on to exercise plans.

The LGA, which took on responsibility for public health under the recent NHS shake-up, says exercise prescriptions would encourage people to be more active, lose weight and keep fit.

Spokeswoman Izzi Seccombe said: "There are some instances where rather than prescribing a pill, advising on some type of moderate physical activity outdoors could be far more beneficial to the patient.

"There are already some good examples where this is being piloted in the UK and it is something we should consider on a nationwide basis."

The Royal College of General Practitioners said any decision to invest in social prescribing schemes, and roll them out more widely, must not be an alternative to investing in general practice services.

Spokesman Dr Steve Mowle said: "Social prescribing schemes can certainly be beneficial to a patient's overall health and wellbeing - as some pilots have shown - but to be effective, there needs to be better integration between health and community services, so that GPs and our teams can signpost our patients most appropriately."

One in four women and one in five men in England do less than 30 minutes of moderate physical activity per week - way below the recommended amount of 150 minutes per week.

Physical activity can help to prevent and manage over 20 chronic conditions and diseases, including some cancers, heart disease, type 2 diabetes and depression.

People who do regular physical activity have:

up to a 35% lower risk of coronary heart disease and stroke
up to a 50% lower risk of type 2 diabetes
up to a 50% lower risk of colon cancer
up to a 20% lower risk of breast cancer
a 30% lower risk of early death
up to an 83% lower risk of osteoarthritis
up to a 68% lower risk of hip fracture
a 30% lower risk of falls (among older adults)
up to a 30% lower risk of depression
up to a 30% lower risk of dementia

Source: NHS Choices

http://bit.ly/2caegDn

Is sex in later years good for your health?

Findings challenge widely held assumption that sex brings uniform health benefits to everyone

EAST LANSING, Mich. --- Having sex frequently - and enjoying it - puts older men at higher risk for heart attacks and other cardiovascular problems. For older women, however, good sex may actually lower the risk of hypertension.

That's according to the first large-scale study of how sex affects heart health in later life. The federally funded research, led by a Michigan State University scholar, is slated to be published online Sept. 6 in the Journal of Health and Social Behavior.

"These findings challenge the widely held assumption that sex brings uniform health benefits to everyone," said Hui Liu, MSU associate professor of sociology.

Liu and colleagues analyzed survey data from 2,204 people in the National Social Life, Health and Aging Project. Participants were aged 57-85 when the first wave of data was collected in 2005-06; another round of data was collected five years later. Cardiovascular risk was measured as hypertension, rapid heart rate, elevated C-reactive protein and general cardiovascular events: heart attack, heart failure and stroke.

Older men who had sex once a week or more were much more likely to experience cardiovascular events five years later than men who were sexually inactive, the study found. This risk was not found among older women.

"Strikingly, we find that having sex once a week or more puts older men at a risk for experiencing cardiovascular events that is almost two times greater than older men who are sexually inactive," said Liu. "Moreover, older men who found sex with their partner extremely pleasurable or satisfying had higher risk of cardiovascular events than men who did not feel so."

She said the findings suggest the strain and demands from a sexual relationship may be more relevant for men as they get older, become increasingly frail and suffer more sexual problems.

"Because older men have more difficulties reaching orgasm for medical or emotional reasons than do their younger counterparts, they may exert themselves to a greater degree of exhaustion and create more stress on their cardiovascular system in order to achieve climax."

Testosterone levels and the use of medication to improve sexual function may also play a role. "Although scientific evidence is still rare," Liu said, "it is likely that such sexual medication or supplements have negative effects on older men's cardiovascular health."

Ultimately, while moderate amounts of sex may promote health among older men, having sex too frequently or too enjoyably may be a risk factor for cardiovascular problems, Liu said. "Physicians should talk to older male patients about potential risks of high levels of sexual activity and perhaps screen those who frequently have sex for cardiovascular issues."

For women, it was a different story. Female participants who found sex to be extremely pleasurable or satisfying had lower risk of hypertension five years later than female participants who did not feel so. "For women, we have good news: Good sexual quality may protect older women from cardiovascular risk in later life," Liu said.

Previous studies suggest that strong, deep and close relationship is an important source of social and emotional support, which may reduce stress and promote psychological well-being and, in turn, cardiovascular health.

"This may be more relevant to women than to men," Liu said, "because men in all relationships, regardless of quality, are more likely to receive support from their partner than are women. However, only women in good quality relationships may acquire such benefits from their partner."

Moreover, the female sexual hormone released during orgasm may also promote women's health, she said.

Liu's co-authors are Linda Waite, professor at the University of Chicago, Shannon Shen, an MSU graduate and Donna Wang, professor of medicine at MSU.

The research was partially funded by the National Institute on Aging, the National Institute of Child Health and Human Development, the Office of Behavioral and Social Sciences Research, and the National Heart, Lung and Blood Institute, which are all part of the National Institutes of Health.

http://bit.ly/2cafZIO

Pediatricians Issue New Flu Shot Recommendations for Kids

Pediatricians Issue New Flu Shot Recommendations for Kids

By Agata Blaszczak-Boxe

Children ages 6 months and older should receive the flu vaccine by an injection this flu season, and should not get the nasal flu spray because it doesn't provide enough protection against the virus, according to new recommendations from the American Academy of Pediatrics.

Research conducted by the Centers for Disease Control and Prevention found that the nasal spray version of the flu vaccine did not protect children against certain strains of the flu virus that were among the most prominent strains during the past three flu seasons, the researchers said. For example, studies showed that, among children ages 2 to 17 who had received the nasal spray version of the flu vaccine, the vaccine was only 3 percent effective during the 2015-2016 flu season, whereas the injected vaccine was 63 percent effective.

"New research shows that the flu shot provided significantly better protection in recent flu seasons compared with the nasal spray vaccine," Dr. Henry H. Bernstein, a pediatrician at Northwell Health in New Hyde Park, New York, who co-authored a policy statement on the new recommendations, said in a press release. "We want to provide children with the best protection possible against flu, and these recent studies show the flu shot is likely to provide a higher level of protection."

The flu shot remains the best available means of preventing flu, the researchers said in the policy statement, published today (Sept. 6) in the journal Pediatrics.

Special efforts should be made to vaccinate children with certain medical conditions, such as asthma or diabetes, because these conditions increase the risk of developing complications if children get the flu, the researchers said.

Women who are pregnant or breast-feeding are also encouraged to get the flu shot, the researchers said. Pregnant women have a high risk of complications from the flu, and they can safely receive the flu shot at any point during pregnancy, the researchers said. Getting the shot during pregnancy also provides protection for infants during the first 6 months of life, the researchers said.

"Pregnant women can help protect themselves and their unborn children by getting the vaccine," Dr. Wendy Sue Swanson, a pediatrician at Seattle Children's Hospital who co-authored the policy statement, said in a press release. "Because the flu virus is common and unpredictable, it can cause serious complications even in healthy children."

Doctors should start offering the flu vaccine to their patients no later than October because receiving the shot early in the flu season is expected to provide protection against the virus for the entire season, the researchers said. And because flu outbreaks can also occur later in the season, doctors should continue offering the vaccine to patients until June 30 of next year, the researchers said.

"The influenza vaccine is an essential, every-year vaccine for infants beginning at [age] 6 months, children and teens," Swanson said. "Protecting children from influenza with the vaccine, early in the respiratory season, is the best protection pediatricians and parents can provide."

Bernstein said he hopes that this season, when the intranasal vaccine will not be available, both children and adults will receive flu shots. The flu causes hundreds of thousands of hospitalizations and thousands of deaths every year, he noted. "We need to do whatever we can to protect as many people as we can to reduce morbidity and mortality," he told Live Science.

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Research shows it may be time to abandon dreaded digital rectal exam

The dreaded finger exam to check for prostate cancer used to be a mainstay of check-ups for older men.

WINSTON-SALEM, N.C. - With its value now in question, some doctors share the risks and benefits with their patients and let them decide. So, should they or shouldn't they?

"The evidence suggests that in most cases, it is time to abandon the digital rectal exam (DRE)," said Ryan Terlecki, M.D., a Wake Forest Baptist urologist who recently published an article on the topic in Current Medical Research and Opinion. "Our findings will likely be welcomed by patients and doctors alike."

Terlecki said the DRE, referred to by some urologists as a "clinical relic," subjects a large number of men to invasive, potentially uncomfortable examinations for relatively minimal gain. In addition, it may deter some men from undergoing any test for prostate cancer.

The issue Terlecki's team explored was whether the DRE is needed when another more accurate test that measures prostate-specific antigen (PSA) in the blood is available. PSA is a protein that is often elevated in men with prostate cancer.

"Many practitioners continue to perform DRE in attempts to identify men with aggressive prostate cancer who could die from the disease," said Terlecki. "In the era of PSA testing, we wanted to explore whether it's time to abandon the digital exam."

To reach their conclusion, Terlecki's research team reviewed both medical literature and the results of a nationwide screening trial in which 38,340 men received annual DRE exams and PSA tests for three years. They were then followed for up to 13 years.

Of interest to Terlecki's team were the 5,064 men who had a normal PSA test but an "abnormal" DRE. Only 2 percent of these men had what is known as clinically relevant prostate cancer, which means it may need to be monitored or treated.

"The DRE does capture an additional small population of men with significant prostate cancer, but it also unnecessarily subjects a large number of men to the test," he said.

Until 2012, men over 50 (age 40 for African-Americans) were urged to have both DRE and PSA tests annually. That was before the United States Preventive Services Task Forces recommended against routine PSA testing because it could lead to over-treatment of slow-growing, non-harmful tumors. The panel did not address DRE, which was the primary method of detecting prostate cancer prior to the blood test.

As a result of the task force's recommendation, there has been confusion and controversy about whether men should be screened for prostate cancer. Some organizations recommend against any screening and others recommend PSA screening, but only if men are counseled about the potential benefits and risks.

In previous studies, PSA had been shown to outperform DRE in detecting significant disease. The current analysis confirmed that PSA is superior to DRE as an independent screen for prostate cancer. PSA testing detected 680 cases of significant cancer, compared to 317 cases for DRE.

"When PSA testing is used, the DRE rarely assists in diagnosing significant disease," said Terlecki. "In cases where PSA testing is used, the DRE should be abandoned in common clinical practice."

There is still a place for DRE testing for certain patients, Terlecki said. For example, a patient with abnormal PSA who is "on the fence" about having a biopsy, may feel more comfortable proceeding with the procedure if a DRE is also abnormal, he said.

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Twins should be delivered at 37 weeks to minimize deaths, say experts

Study provides crucial information to help mothers plan for delivery

Twins should be delivered at 37 weeks' gestation to minimise stillbirths and newborn deaths, and there is no clear evidence to support routine delivery before 36 week's gestation, finds a large international study in The BMJ today. It is well known that the risk of stillbirth is higher in twin pregnancies than in singleton pregnancies. Uncomplicated twin pregnancies are often delivered early in an attempt to prevent stillbirth, but the optimal gestational age for delivery that minimises risks to newborns is not known.

Current recommendations vary on the timing of delivery, starting from 34 up to 37 weeks' gestation in monochorionic twin pregnancies (twins that share the same placenta) and from 37 up to 39 weeks in dichorionic twin pregnancies (twins that have two individual placentas). So an international team of researchers decided to examine the evidence behind these recommendations.

They analysed the results of 32 studies, published within the past 10 years, of women with uncomplicated twin pregnancies that reported rates of stillbirth and neonatal mortality (defined as death up to 28 days after delivery) at various gestational ages after 34 weeks.

Overall the studies included 35,171 twin pregnancies (29,685 dichorionic and 5,486 monochorionic). Study design and quality were taken into account to minimise bias.

The researchers looked specifically at the balance between the risk of stillbirths from expectant management ('watchful waiting') and the risk of neonatal death from delivery beyond 34 weeks.

They found that, in dichorionic pregnancies, the risk of stillbirths and neonatal death were balanced until 37 weeks' gestation. However, delay in delivery by a week (to 38 weeks) led to an additional 8.8 deaths per 1,000 due to an increase in stillbirth.

In monochorionic pregnancies, the risk of stillbirth appears to be higher than neonatal death beyond 36 weeks' gestation. But more data are needed to make a clear recommendation on best time to deliver monochorionic pregnancies.

Rates of neonatal morbidity (including respiratory distress syndrome, septicaemia, or neonatal seizures) and admission to the neonatal intensive care unit showed a consistent reduction with increasing gestational age in both monochorionic and dichorionic pregnancies.

Based on these estimates, the researchers suggest that, for women with dichorionic twin pregnancies, delivery should be considered at 37 weeks' gestation "to prevent the significant increase in stillbirths associated with expectant management compared with the risk of neonatal deaths associated with early delivery."

In monochorionic twin pregnancies, "there is no clear evidence to support routine delivery before 36 weeks' gestation," they say.

The authors point out that the actual risk of stillbirth near term "might be higher than reported estimates because of the policy of planned delivery in twin pregnancies." But say, "our study provides comprehensive estimates comparing risks of stillbirth and neonatal mortality at various gestational ages, which is required for the planning of delivery in uncomplicated twin pregnancies."

This information "will complement the ongoing national and international efforts to reduce the rates of stillbirths and unexpected neonatal complications in babies born near term," they conclude.

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Electric fans may exacerbate heat issues for seniors, study finds

Using electric fans to relieve high heat and humidity may have the opposite effect for seniors

DALLAS - Using electric fans to relieve high levels of heat and humidity may, surprisingly, have the opposite effect for seniors, a study by UT Southwestern Medical Center heart specialists suggests.

The heart rate and internal temperature of seniors exposed to 107 degree Fahrenheit temperatures and increasing humidity levels climbed even higher when they tried to cool off with fans - instead of falling as expected, according to study findings reported in JAMA.

"Although differences were small, the cumulative effect could become clinically important during prolonged heat exposure, such as during extreme heat waves," said Dr. Craig Crandall, Professor of Internal Medicine at UT Southwestern and with the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas, a joint operation of Texas Health Presbyterian Hospital Dallas and UT Southwestern.

"We know that fans keep young adults cooler by increasing the evaporation of sweat," Dr. Crandall said. "We surmise that age-related impairments in sweating capacity make fans an ineffective means of cooling for the elderly during exceptionally hot days, and may, in fact, increase thermal and cardiac strain."

Researchers studied the physiological responses of a small group of elderly patients in a high-heat, high-humidity environment. Participants between the ages of 60 and 80 were observed for approximately two hours in a room with the temperature set at a sweltering 107 degrees Fahrenheit and a humidity level that was gradually increased from 30 percent to 70 percent. Not surprisingly, both heart rate and internal body temperature rose as the humidity level in the room rose.

The eight individuals in the study were tested under those conditions without a fan and, on a separate occasion, with an electric fan. Unexpectedly, the participants' heart rates were 10 beats per minute higher and their internal temperatures 0.5 degrees Fahrenheit higher when a fan was part of the experimental environment. Typical heart rates are 60 to 100 beats per minute.

Although these findings suggest that fan use may be counterproductive for seniors during heat waves, the investigators propose that fan use may still be beneficial under less extreme environmental conditions, though this needs to be confirmed.

During severe heat waves seniors who do not live in an air-conditioned home should maintain hydration while seeking an air-conditioned environment such as a family member or friend's home, a community center, or a shopping mall, Dr. Crandall said.

The findings appear online in a research letter in JAMA. Funding for the study was provided by the National Institutes of Health, the Department of Defense, and the Natural Sciences and Engineering Research Council of Canada. Other researchers from UT Southwestern and the Institute for Exercise and Environmental Medicine included Dr. Daniel Gagnon, Dr. Steven Romero, and Dr. Matthew Cramer.

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Blood samples from 9-year-olds can predict bipolar symptoms

High anxiety? Manic behaviour may start with inflammation in childhood

By Helen Thomson

High levels of inflammation as a child may predict a higher risk of manic behaviour in later life, a finding that could lead to new ways of treating conditions like bipolar disorder.

Hypomania involves spells of hyperactivity and is often a symptom of mood disorders, including bipolar disorder, seasonal affective disorder and some kinds of psychosis. People experiencing hypomania may take more risks, feel more confident and become impatient with others. After spells like this, they may "crash", needing to sleep for long periods and sometimes remembering little about the previous few days.

Earlier studies suggested a link between inflammation and mood disorders, prompting Joseph Hayes at University College London and his team to see if inflammation as a child might lead to mental health problems later.

Analysing data from more than 1700 people, his team identified a significant link between high levels of a chemical involved in inflammation at age 9, and experiencing aspects of hypomania at age 22.

Brain changes

The chemical, called IL-6, is normally secreted by white blood cells to stimulate an inflammatory immune response to infection or trauma. Hayes's team says it is unclear how inflammation in childhood could induce symptoms of hypomania but IL-6 is known to affect the brain. A study that used injections to increase IL-6 in the blood of healthy volunteers found that this caused symptoms of anxiety, and reduced performance in memory tests.

There is also evidence that IL-6 can affect brain activity in a region called the subgenual cingulate. This region is thought to govern a vast network of brain areas, including those that affect mood and anxiety, sleep, memory and self-esteem.

The team suggests that targeting inflammatory pathways may help treat conditions such as bipolar disorder. "The study provides important new evidence in support of a role for inflammation in pathological increases in mood," says Neil Harrison at Brighton & Sussex Medical School in the UK. "Taken together with results from earlier studies, this suggests that high levels of inflammation during childhood increase the risk of disorders of mood later in life."

Journal reference: Psychological Medicine, DOI: 10.1017/S0033291716001574

http://bit.ly/2clXxy1

Japan measles outbreak hits 41 cases, foreign strain accounting for majority

Latest total has already surpassed the 35 cases of measles logged over past year

By Roland Shichijo

TOKYO (TR) – There were nine more cases of measles since last week, bringing the total number of people with the virus to 41, the National Institute of Infectious Diseases (NIID) announced on Tuesday.

Officials are investigating reports of several cases breaking out at a Justin Bieber concert held in Chiba Prefecture last month as well as among workers at Kansai International Airport, TV Asahi reports.

The figure for the outbreak at the airport is expected to rise since numerous cases have yet to be reported to the health center, CBnews reported. The latest total has already surpassed the 35 cases of measles logged in the last one-year period, local media reported.

By administrative district, Chiba Prefeture currently holds the highest number of cases at 12, followed by Tokyo and Hyogo Prefecture with 6 each, Saitama and Osaka Prefecture with 3 each, and Mie Prefecture with 2, according to CBnews.

Foreign strain D8

The World Health Organization announced that Japan eradicated measles in March 2015 after a measles outbreak seven years earlier

infected more than 10,000 people. Japan had met a WHO requirement which mandated that domestic cases be brought under control for over three years aside. Cases contracted overseas are excluded from the requirement.

But a foreign strain of measles known as D8 has seen Japan face a constant stream of imported measles cases since the start of this year, with the strain accounting for 60 percent of domestic cases as of Sunday, according to the NIID.

The Japanese Society for Infection Prevention and Control said that there could be more "measles outbreaks in various locations in the future," urging medical institutions to report cases to the NIID to receive advice on treatment and follow-up care.

If a doctor suspects an individual with rash or high fever has measles, the society is urging them to examine their vaccination and travel records and aim for an early diagnosis, as well as quarantine any infected patients and implement airborne infection control.

Measles is a highly contagious airborne disease. Symptoms usually develop 10 days after exposure. The Ministry of Health, Labor and Welfare is urging citizens to quickly seek medical attention if symptoms like high fever and a rash start to appear.

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Bacteria lurking in blood could be culprit in countless diseases

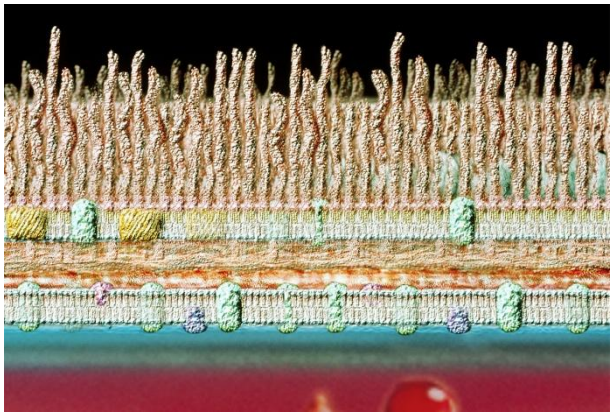
Could microbes be to blame for a host of diseases we thought they had nothing to do with?

By Debora MacKenzie

Researchers have found that bacteria in the blood of healthy people may help trigger strokes and heart attacks, and perhaps also contribute to conditions like Alzheimer's disease, diabetes and arthritis.

All of these disorders involve inflammation – a general activation of the immune system that normally serves to fight infection, but that can get out of control and cause damage. These conditions are also all linked to overactive blood clotting, excessive levels of iron in the blood, and sheets of abnormally folded proteins.

No one knows why these traits are linked to so many diseases, but finding out could help us stop them.



Lipopolysaccharides coating a bacterial cell wall (top) may have an insidious role to play in disease **Russell Kightly/Science Photo Library**

To see if bacteria could be playing a role in all this, Douglas Kell at the University of Manchester, UK, and Resia Pretorius, at the University of Pretoria in South Africa, have been looking at their ability to disrupt clotting.

Blood has always been considered free from microbes, because bacteria don't grow when it is put in a culture dish.

But recent DNA sequencing methods reveal that each millilitre of blood in fact contains around 1000 bacterial cells.

These bacteria are usually dormant. But they can be revived when iron becomes available in the blood, and begin secreting lipopolysaccharides (LPS) – molecules on their cell walls that are recognised by the immune system and stimulate inflammation.

Clotting catalyst

Kell and Pretorius wondered if LPS might also directly affect clotting. Most dormant bacteria in our blood comes from our gut. They mixed LPS from the common gut bacteria *Escherichia coli* with fibrinogen, a small protein in the blood that normally forms the fibrin scaffolds of clots.

The LPS changed the fibrinogen, encouraging it to form abnormal clots that look a lot like those involved in heart attacks, strokes and deep vein thrombosis.

"In all inflammatory conditions we have noted a matted, denser fibrin structure, without the typical 'spaghetti structure' found in healthy individuals," says Pretorius. Just one molecule of LPS in a mixture of a hundred million fibrinogen molecules was enough to encourage the formation of these misformed clots.

This means LPS must act as a catalyst, says Kell. They think LPS bends fibrinogen out of shape, and this shape-change spreads from protein to protein in a similar way to the deformation associated with prion proteins that cause BSE.

And since LPS triggers inflammation, it increases levels of fibrinogen in the blood, further raising the risk of the aberrant disease-linked clots. Because of their weird structure, these clots are also resistant to being broken down by blood enzymes. Together, these effects could be raising the risk of aberrant clotting, leading to heart attacks and strokes.

Fighting inflammation

Overactive clotting is also a feature of inflammatory conditions like rheumatoid arthritis and Alzheimer's. These conditions involve excess levels of iron. The body normally keeps levels of free iron in the blood low to keep bacteria dormant and block their growth.

"We think bugs are involved in all these diseases," says Kell. Their observation that LPS causes fibrin to form mats, and the fact that LPS also binds to many other proteins, could implicate it in forming the amyloid mats seen in other inflammatory diseases, such as those in in the brains of people with Alzheimer's and Parkinson's disease.

Earlier this year, other researchers found that injecting bacteria into the brains of mice prompted them to form amyloid plaques overnight.

What does this all mean for these diseases? Further research could open up several new approaches for tackling them, from removing dormant microbes from our blood, to blocking the inflammatory proteins that they shed.

Journal reference: *Journal of the Royal Society Interface*, DOI: 10.1098/rsif.2016.0539

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New tumor analysis method identifies high-risk prostate cancer

Cancer cells' genetic pathways show which patients are likely to develop aggressive types of the disease

LOS ANGELES - Scientists at Cedars-Sinai have developed a new way to identify which prostate cancer patients are likely to develop aggressive types of the disease even if their tumors at first appear to be lower risk. The new findings could help physicians prescribe the most effective treatments for each patient based on how genes are activated in the individual tumor.

"These findings raise the possibility that by determining the gene expression profile of a patient's tumor, physicians may be able to identify aggressive disease at the outset of diagnosis and start treatment earlier," said Sungyong You, PhD, an instructor in the Cedars-Sinai Department of Surgery and the first author of the study.

Although other studies have used genetic data to identify subtypes of prostate cancer, this is the first large-scale study to link clinical outcomes to subtypes based on the processes by which genes are turned on and off in the cancer cells. The study was published in the journal Cancer Research by the American Association for Cancer Research.

Prostate cancer affects about 1 in 7 men during their lifetimes and is the second-leading cause of cancer deaths among U.S. men, according to the American Cancer Society. Most tumors grow slowly and are not life threatening, but certain types of prostate cancer can spread to other organs and be fatal.

The new findings divide prostate tumors into three subtypes based on each tumor's gene activation pathways. When the researchers matched this data with clinical outcomes for more than 4,600 patient specimens in medical databases, they found these subtypes were associated with different levels of disease progression.

The study's conclusions address a major challenge in current standards of care for prostate cancer: Without knowing a tumor's underlying biology, physicians cannot reliably predict which of their patients will develop dangerous forms of the disease.

"About 60 percent of prostate cancer patients we treat won't progress to aggressive cancer. The problem was that we didn't have a way of knowing which patients fall into that 60 percent," said Michael Freeman, PhD, director of Cancer Biology and Therapeutics Research in the Cedars-Sinai Department of Biomedical Sciences and the study's principal investigator. "We hope our findings help physicians provide more patients with optimal treatments, resulting in healthier outcomes."

The new research could lead to a change in the way treatment decisions are made for prostate cancer patients. Currently, physicians rely heavily on a scale called the Gleason grade. The Gleason grade ranks the cancer cells, found by surgical biopsies of the tumor, from 2 to 10 based on how closely the cancerous cells resemble normal prostate cells. The lower the grade, the lower the risk the cancer is judged to pose.

But the Cedars-Sinai research suggests that some prostate cancer patients may not receive needed treatments in a timely way. Others may receive unnecessary treatments, with significant side effects. Among the commonly prescribed therapies are radiation, hormone therapy and surgical removal of the prostate.

Currently, patients with low-grade tumors often receive no treatment and instead are closely monitored, under a strategy known as active surveillance. The new study indicates active surveillance may not be enough for some of these patients.

The study showed that one of the three subtypes of prostate cancer the researchers identified, which they called PCS1, was generally aggressive. In the patients they studied, this subtype showed a high likelihood of spreading and progressing to poor clinical outcomes, including fatalities. Patients experienced poor outcomes even when the tumors had been assigned low Gleason grades. The two other subtypes, PCS2 and PCS3, progressed more slowly.

An additional advantage to the new subtyping is that it can be performed on tumor cells circulating in the blood. This finding has the potential to improve real-time monitoring of tumor evolution during treatment, You said.

This study was supported by grants from the National Institutes of Health under award numbers R01DK087806, R01CA143777 and 2P01 CA098912); the Department of Defense Prostate Cancer Research Program under award number W81XWH-14-1-0152; the Urology Care Foundation Research Scholars Program; the Spielberg Family Discovery Fund; and the Prostate Cancer Foundation.

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Medication against schizophrenia inhibits pancreatic cancer

Blocking dopamine receptor exposes cancer cells to biochemical stress, inhibiting cancer growth

Cancer of the pancreas is an extremely aggressive disease with a dismal prognosis. The number of cases that is newly diagnosed with this type of cancer each year is almost the same as the one of people who succumb to it. While advances in prevention, early detection and treatment have led to a drop in mortality rates in most other cancer types, a growing number of people in Germany and world-wide develop pancreatic cancer and die from it.

"The tumors do not cause any signs or symptoms for a long time and are therefore diagnosed late," says Jörg Hoheisel from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg. "In addition, the tumor biology is very aggressive, i.e., the cancer starts spreading metastases early on. And to make things worse, pancreatic cancer rapidly develops resistance against available chemotherapy drugs."

Therefore, scientists are making great efforts to identify novel molecular targets that can be attacked to fight pancreatic cancer. Hoheisel and his colleagues from Heidelberg, Tübingen, Liverpool, Verona, Toronto and Montreal undertook a large-scale analysis of

gene activities in 195 pancreatic cancer cases. "We leveraged quantitative and computational biology approaches that we have established in order to identify genes that may play a central role in several pancreatic cancer-relevant signaling pathways among almost 3,000 genes that exhibited abnormally high or low activities" said Riazalhosseini of McGill University who co-led the study with Hoheisel., In this way, they identified the dopamine receptor DRD2. The DRD2 gene was significantly more active in cancer cells than in healthy pancreatic cells, and the levels of DRD2 receptor protein found in the cancer cells were four times the normal.

Blocking the dopamine receptor inhibits cancer growth

The dopamine receptor mediates the effect of the dopamine neurotransmitter in the brain. Dopamine is an important brain chemical that increases motivation and drive. How can a receptor protein that is known to clinicians primarily for its role in schizophrenia and psychotic disorders influence the malignant characteristics of cancer cells? The researchers pursued this question in pancreatic cancer cell lines in which they had turned off the DRD2 gene. They observed that these cells in fact grew more slowly and formed smaller tumors when transferred to mice.

DRD2 is a key molecule in many psychotic diseases and is therefore targeted by numerous psychopharmaceutical agents. Drugs that block the function of DRD2 ("dopamine antagonists") have been available since the 1950s. Among them is the antipsychotic pimozide. Using this substance, the investigators collaborating with Hoheisel succeeded in substantially slowing down the growth and impeding the mobility of pancreatic cancer cell lines.

The researchers transferred human pancreatic cancer cells to mice and allowed them to grow into tumors. After treating the animals with another dopamine antagonist - haloperidol, a medication that is often prescribed to treat schizophrenia - they developed smaller tumors and, more importantly, fewer metastases than untreated animals.

"We do not know yet whether haloperidol or related medications have the same effect in pancreatic cancer patients as they have in tumor cells and mice," Hoheisel said. He added as an interesting observation that schizophrenia patients, who are treated mostly with dopamine antagonists, have a lower rate of solid tumors on the whole than the general population. It is therefore possible that the cancer-inhibiting effect might not be restricted to the pancreas.

The DKFZ researchers now plan to examine in a study with pancreatic cancer patients whether drugs from the group of dopamine antagonists have a favorable effect on the course of the disease. For this, they will continue collaborating closely with Markus W. Büchler from Heidelberg University Hospital and the colleagues at McGill University in Montreal with the goal of treating pancreatic cancer patients. "We are very lucky to have come across established medications. This should make the required and laborious safety examinations easier," said Hoheisel.

Dopamine receptor protects cancer cells from biochemical stress

The DKFZ researchers additionally wanted to gain an understanding of the molecular mechanisms by which the dopamine receptor drives cancer growth. Normally, DRD2 prevents cells from experiencing biochemical stress via a crucial intracellular signaling molecule called cAMP. After blocking DRD2, the rapidly dividing cancer cells are particularly exposed to this kind of stress. This leads to a breakdown of the cell division cycle and then to cell self-destruction (apoptosis).

The investigators found higher-than-normal activity of the DRD2 gene already in chronic pancreatitis, which is considered to be a precancerous stage of pancreatic cancer. Other authors have also described increased activity levels of the DRD2 gene in cancer stem cells. Hoheisel and colleagues therefore think that this alteration occurs at a very early stage of cancer development.

Pouria Jandaghi, Hamed S. Najafabadi, Andrea S. Bauer, Andreas I. Papadakis, Matteo Fassan, Anita Hall, Anie Monast, Magnus von Knebel Doeberitz, John P. Neoptolemos, Eithne Costello, William Greenhalf, Aldo Scarpa, Bence Sipos, Daniel Auld, Mark Lathrop, Morag Park, Markus W. Büchler, Oliver Strobel, Thilo Hackert, Nathalia A. Giese, George

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http://bit.ly/2cafGeq

Sugar transforms a traditional Chinese medicine into a cruise missile

Anticancer compound becomes more soluble and selective after glucose is attached

More than 20 years ago, a billboard in China piqued the interest of a chemical biologist. It endorsed an extract from the plant known as the "thunder god vine"***(雷公藤)*** as an immunosuppressant. A brief review of published research revealed that the extract's key ingredient -- the small molecule triptolide -- had been identified 20 years before that billboard ad, and it could stop cells from multiplying.

Now, that chemical biologist and his colleagues at the Johns Hopkins University School of Medicine report that tests of triptolide in human cells and mice are vastly improved by the chemical attachment of glucose to the triptolide molecule. The chemical add-on makes the molecule more soluble and essentially turns it into a "cruise missile" that preferentially seeks out cancer cells, the research says. The change might also decrease side effects in patients and make the drug easier to administer. A summary of the research is published in the journal Angewandte Chemie and was published online on Aug. 30.

"We have a long way to go before we can test this derivative of triptolide in humans, and we think that additional adjustments could improve it even more," says Jun O. Liu, Ph.D., professor of pharmacology and molecular sciences at the Johns Hopkins University School of Medicine and a member of the Johns Hopkins Kimmel Cancer Center, "but it already has the key characteristics we've been looking for: It is quite water soluble, and it prefers cancer cells over healthy cells."

Liu, a native of a small town north of Shanghai in China, explains that the thunder god vine has been used in traditional Chinese medicine for more than 400 years, mostly to calm an overactive immune system, which can cause diseases like rheumatoid arthritis and multiple sclerosis.

His laboratory specializes in figuring out how natural compounds with known healing properties exert their effects on human cells. Five years ago, he and his colleagues discovered that triptolide halts cell growth by interfering with the protein XPB, part of the large protein machine transcription factor IIH, which, in turn, is needed by enzyme complex RNA polymerase II to make mRNA.

Because triptolide halts cell growth, it works well to fight the multiplication of cancer cells, Liu says, both in lab-grown cells and in laboratory animals with cancer. Unfortunately, it -- and many of its derivatives -- has failed to work well in patients because it doesn't dissolve well in water or blood, and has too many side effects due to its indiscriminate killing of healthy cells as well as tumor cells.

Liu's latest research sought to "train" triptolide to target cancer cells by exploiting the knowledge that most cancer cells make extra copies of proteins, called glucose transporters. Those transporters form tunnels through a cell's membrane to import enough glucose to fuel rapid growth. By attaching glucose to triptolide, the researchers hoped to trick the cancer cells into importing the cell-killing poison, as had been done successfully with other anticancer drugs.

"We were looking for something that could be administered intravenously, remain stable in the blood and then become active as soon as it was imported into cancer cells," says Liu.

To begin, the chemists designed and synthesized five derivatives of triptolide, dubbed glutriptolides. Each derivative had glucose attached to the same spot on the triptolide molecule but had different "linkers" connecting them.

An initial experiment showed that none of the glutriptolides were good at blocking the activity of purified transcription factor IIH. Liu explains that what might seem like bad news was actually a positive

result, since it suggested that the drugs would only be active once they entered cells and had their glucose attachments removed.

When the five glutriptolides were tested on human embryonic kidney cells, glutriptolide 2 slowed down cell growth better than the rest and is the only derivative they continued to study.

In later test tube and cell experiments, the researchers confirmed that glutriptolide 2 works just like triptolide -- by interfering with XPB -- though it does so only in higher concentrations. They also showed that a cancer cell line (DLD1-Mut) known to produce lots of glucose transporter 1 was more sensitive to glutriptolide 2's effects than a similar cell line (DLD1-WT) without extra copies of the transporter.

When the researchers assessed triptolide's effects on a variety of healthy cells and cancer cells in parallel with glutriptolide 2, they found that triptolide tended to equally slow the growth of healthy cells and cancer cells, while glutriptolide 2 was eight times more effective against cancer cells, on average. Liu says this result suggests that the new compound -- if tested in humans -- may be more selective against cancer cells and could therefore have fewer side effects.

Finally, due to the differences in the compounds' general toxicity, tests showed that mice could tolerate a dose of 0.2 milligram/kilogram of triptolide and 1 milligram/kilogram of glutriptolide 2. At those doses, glutriptolide 2 eradicated tumors more quickly in mice with prostate cancer and prevented tumor cells from reappearing for a full three weeks after treatment had stopped.

"We were totally surprised to see that sustained antitumor activity," says Liu. "It's something we want to study further." The group plans to test additional modifications to the biochemical links that connect glucose to triptolide to see if it can further decrease the compound's toxicity to healthy cells and increase its effectiveness against cancerous ones.

The work was accomplished through a close international collaboration among three research groups led by Liu, Martin Pomper of the Johns Hopkins University School of Medicine and Biao Yu of the Chinese Academy of Sciences. Other authors of the report include Qing-Li He, Il Minn, Sarah Head and Emmanuel Datan of the Johns Hopkins University School of Medicine, and Qiaoling Wang and Peng Xu of the Shanghai Institute of Organic Chemistry at the Chinese Academy of Sciences.

This work was supported by a Synergy Award from the Johns Hopkins University School of Medicine and the Johns Hopkins Institute for Clinical and Translational Research, which is funded in part by the National Center for Advancing Translational Sciences (UL1 TR 001079).

A nondisclosure agreement for the invention/technology described in this publication has been executed between The Johns Hopkins University and Rapafusyn Pharmaceuticals Inc. Dr. Liu is a co-founder of and a Scientific Advisory Board Member for Rapafusyn Pharmaceuticals Inc. This arrangement has been reviewed and approved by The Johns Hopkins University in accordance with its conflict of interest policies.

http://bit.ly/2ca8WyR

Fruit flies yield clues on cancerous tumor hotspots

Epithelial tissues lining surfaces of organs have hot spots for cancerous tumors

TALLAHASSEE, Fla. -- A Florida State University research team, in coordination with a team from Japan, has found that the epithelial tissues that line the surfaces of organs throughout the body intrinsically have hot spots for cancerous tumors. They discovered this by examining a common household pest -- the fruit fly.

"Flies and humans have a lot in common in terms of genes and pathways for developing cancer," said Wu-Min Deng, professor of biological science at Florida State and the senior author on the paper.

Deng and his now former postdoctoral researcher Yoichiro Tamori found that in the fruit fly, tumors always originated from specific regions of the epithelial tissue.

Their findings are laid out in a study published in PLOS Biology.

Deng and Tamori were interested in examining basic pathways and tissue structures where tumors might form. Many scientists study the development in fruit flies as a model to determine the basic fundamentals of several diseases, including cancer.

"At its heart, this is basic research investigating how cancer gets started," Deng said. "What are the tissue microenvironments that facilitate tumor formation?"

In examining fruit flies, researchers looked at the developing epithelial tissues in fruit fly larvae, called imaginal discs. The discs eventually form an outer layer structure of an adult fly. These discs are formed by sheets of cells called epithelia which have distinct upper and lower sides.

In mammals, similarly, epithelia cover all surfaces and line all cavities of the body. More than 80 percent of human cancers are originated from epithelial tissues.

Deng and his team used genetic engineering to turn off tumor suppressor genes in the larvae that are also found in humans and other animals. After they inactivated the tumor suppressor gene, the researchers discovered that tumors always originate from a specific area of the disc.

These tumor hotspots all involved an oncogenic signaling pathway that has been shown to be involved in many types of human cancers. Signaling pathways are essentially the communication networks within a cell telling it to perform a specific function.

Researchers found that on the basal - or underside - of the epithelial sheets, the tumor hotspot had a unique and rigid structure. Because of this robust structure at the basal side, pro-tumor cells pop out of the apical side - or top of the sheet - of the epithelia and start tumor formation.

But in other areas of the epithelial tissue -- what researchers called a tumor cold spot -- the basal side of the tissue was more loosely constructed and pro-tumor cells were extruded from the basal side and die.

Deng said he and Tamori hope to continue their work looking at cancer and delve deeper into the signaling pathways and tissues in mammal systems

"If we know what intrinsic factors cause tumor formation we may be able to harness it and learn more," Deng said. "The more we know, the better we can get at treating and preventing cancer."

The other co-author on the paper is Emiko Suzuki, a colleague of Tamori's at the National Institute of Genetics in Japan.

http://bit.ly/2c2FVGo

Ginger and chili peppers could work together to lower cancer risk

Compound in ginger could counteract capsaicin's potentially harmful effects

For many people, there's nothing more satisfying than a hot, spicy meal. But some research has suggested that capsaicin, the compound that gives chili peppers their kick, might cause cancer. Now researchers show in mouse studies that the pungent compound in ginger, 6-ginergol, could counteract capsaicin's potentially harmful effects. In combination with the capsaicin, 6-gingerol could lower the risk of cancer, they say. The study appears in ACS' Journal of Agricultural and Food Chemistry.

Both chili peppers and ginger are widely used spices in certain cuisines, particularly in Asia, and have been studied for potential health effects. Although some studies have shown that peppers can have benefits, others suggest that diets rich in capsaicin might be associated with stomach cancer. Ginger, however, has shown promise as a health-promoting ingredient. Oddly enough, capsaicin and 6-gingerol both bind to the same cellular receptor -- one that is related to tumor growth. Jiahuan Li, Gangjun Du and colleagues wanted to further investigate this apparent contradiction.

Over several weeks, the researchers fed mice prone to lung cancer either capsaicin or 6-gingerol alone, or a combination of both. During the study period, all of the mice that received only capsaicin

developed lung carcinomas while only half of the mice fed 6-gingerol did. Surprisingly, an even lower percentage -- only 20 percent -- of the mice given both compounds developed cancer. The researchers also dug into the potential molecular underpinnings of how the compounds interact to lead to this effect.

The authors acknowledge funding from the National Natural Science Foundation of China.
The abstract that accompanies this study is available here.

http://bit.ly/2cnxlnV

Hospitals Jack Up Costs 'Strategically,' Study Finds

Imagine getting the bill for an ordinary dinner and noticing, in tiny print, that the restaurant charged you $40 for coffee. Surely you'd be upset.

By Christopher Wanjek | September 7, 2016 06:03pm ET

It turns out that hospitals inflate specific prices all the time in ways that aren't transparent to the patient, according to a new study that appeared today (Sept. 7) in the journal Health Affairs.

Researchers at Johns Hopkins University in Baltimore found that many hospitals charged more than 20 times the cost of some services, particularly for certain services like CT scans and anesthesiology. The researchers said that the pattern of charging suggests that hospitals strategically look for surreptitious ways to boost revenue.

"Hospitals apparently mark up higher in the departments with more complex services, because it is more difficult for patients to compare prices in these departments," Ge Bai, who led the study and is an assistant professor at the Johns Hopkins Carey Business School, said in a statement. [7 Medical Myths Even Doctors Believe]

Other high-tech services with exorbitant markups include MRI, electrocardiology (tests of the heart's electrical patterns) and electroencephalography (tests of the brain's impulse patterns), according to the findings. The services that had fees that were more in line with their actual costs to hospitals included "old-school" physical therapy and nursing, the researchers found.

The markups occurred in all types of hospitals, both private and nonprofit, the researchers said. Yet hospitals with the highest markups, on average, tended to be for-profit hospitals with strong power within their markets, because of either their system affiliations or their dominance of regional markets. In other words, those hospitals that can mark up prices, do mark up prices, according to the researchers.

The pricing can have serious consequences for the payer, the researchers said. For example, hospitals whose costs for a CT scan run at about $100 may charge a patient $2,850 for a CT scan, the study found.

"[The markups] affect uninsured and out-of-network patients, auto insurers and casualty and workers' compensation insurers," said Gerard Anderson, a professor at the Johns Hopkins Bloomberg School of Public Health and a co-author on the study. "The high charges have led to personal bankruptcy, avoidance of needed medical services and much higher insurance premiums."

In their study, based on 2013 Medicare and other data from nearly 2,500 U.S. hospitals, the researchers compared a hospital's overall charge-to-cost ratio, which is the ratio of what the hospital charged compared to the hospital's actual medical expense. The charge is recorded on a document called a chargemaster, which is an exhaustive list of the prices for all hospital procedures and supplies.

In 2013, the average hospital with more than 50 beds had an overall charge-to-cost ratio of 4.32 — that is, the hospital charged $4.32 for every $1 of its own costs. However, at most hospitals that they examined, the researchers found that the charge-to-cost ratio was far higher in departments that were technologically advanced. The highest was in the CT department, with an average ratio of 28.5. [5 Amazing Technologies That Are Revolutionizing Biotech]

While understanding that hospitals need to generate revenue, the researchers recommend a cap on markups and consistency from department to department. They also suggest more transparency, by requiring hospitals to provide patients with examples in clear language of rates from area hospitals or what Medicare would pay.

"There is no regulation that prohibits hospitals from increasing revenues," Bai told Live Science. "The problem is when they raise rates on people that have no ability to say no because they have an emergency and cannot compare prices." This includes uninsured and out-of-network patients, "because they don't have bargaining power against hospitals," Bai added.

"We realize that any policy proposal to limit hospital markups would face a very strong challenge from the hospital lobby," Anderson said. "But we believe the markup should be held to a point that's fair to all concerned — hospitals, insurers and patients alike."

The researchers noted that Johns Hopkins Hospital has a charge-to-cost ratio of 1.3, among the lowest 1 percent of the sample studied. Maryland, the state in which the hospital is located, in general has the lowest ratios of any other state, they said.

http://bbc.in/2cbEmnd

Malaria stopped with single dose of new compound

Scientists say they have found a new compound that stops malaria in animal studies with a single, low dose.

By Michelle Roberts Health editor, BBC News online

Tests in mice showed the one-off treatment prevented infection for the full 30 days of the study. The chemical compound fought early infection in the liver, as well as malaria parasites that were circulating in the blood. The researchers hope their early work, published in the journal, Nature, could lead to new drugs for people.

Malaria is spread to humans by the bites of infected female mosquitoes and it is estimated that about half of the world's population is at risk of catching the disease.

In 2015, there were 214 million new cases of malaria and 438,000 malaria deaths, according to the World Health Organization.

Aside from avoiding bites by using insecticides and bed nets, people can protect themselves against malaria by taking antimalarial drugs. But existing treatments are less than perfect - people have to take repeated doses and the parasites that cause malaria are developing resistance to these drugs.

Need for new drugs

Along the Cambodia-Thailand border, one type of malaria parasite - P. falciparum - has become resistant to almost all available antimalarial medicines.

Dr Nobutaka Kato and colleagues, from Massachusetts Institute of Technology and Harvard, searched a library of more than 100,000 compounds for a new treatment. They were hunting for something that would work in an entirely new way to existing drugs.

The compound they found targets an enzyme called phenylalanyl-tRNA synthetase and appears to wipe out parasites before they can multiple in the liver and be released in bigger numbers into the bloodstream.

Lead researcher Prof Stuart Schreiber hopes the findings will lead to the discovery of better antimalarials in coming years.

He said: "We invite the scientific community to use this database as a jumping off point for their work developing antimalarial therapies."

The work was funded by the Bill & Melinda Gates Foundation.

Prof David Baker of the London School of Hygiene & Tropical Medicine said the findings were exciting. "The advantage of a single dose antimalarial is that it potentially reduces costs and removes the issue of patients not completing the course of treatment.

"One of the safety tests they ran on the new compounds gave results suggesting that there may be a degree of toxicity in human cells, but hopefully the chemists will be able to modify the compounds to remove this issue."

http://bit.ly/2cH9T1o

Deadly Scrub Typhus Bacteria Found on Island Off Chile

Scrub typhus has now taken hold in a part of South America and may have become endemic there

LONDON — Scrub typhus, a deadly disease common in Southeast Asia and spread by microscopic biting mites known as chiggers, has now

taken hold in a part of South America and may have become endemic there, scientists said Wednesday.

The tropical disease, which kills at least 140,000 people a year in the Asia-Pacific region, has been confirmed in a cluster of cases on a large island off Chile, 12,000 kilometers from its usual haunts on the other side of the Pacific. Scrub typhus has been known of for years, and the bacteria that cause it were first identified in Japan in 1930.

Chiggers transmit the bacteria, Orientia tsutsugamushi, and they spread through the lymphatic fluid. Those infected find the illness can begin quite suddenly, with shaking chills, fever, severe headache, infection of the mucus membrane in the eyes, and lymph node swelling. Until 2006, scrub typhus was thought to be limited to an area called the "tsutsugamushi triangle," from Pakistan in the west to far eastern Russia in the east to northern Australia in the south.

Wider distribution?

But writing in The New England Journal of Medicine, researchers from Britain's Oxford University and the Pontificia Universidad Católica and Universidad del Desarrollo in Chile said the cases found off Chile's mainland "suggest there may be a much wider global distribution than previously understood."

In 2006, two cases of scrub typhus were found outside the triangle. One, in the Middle East, was caused by a previously unrecorded bacteria related to tsutsugamushi and named Orientia Chuto. The second was found on Chiloe island, just off mainland Chile.

In January 2015 and again in early 2016, three more cases were discovered in Ancud, on the northern coast of Chiloe.

"Scrub typhus is a common disease but a neglected one," said Paul Newton, director of the Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit, which collaborated in the study.

"Given that it is known to cause approximately a million clinical cases, and kills at least 140,000 people each year, this evidence of an even bigger burden of disease in another part of the world highlights the need for more research and attention to it."

http://bit.ly/2ccdCmK

Hip fractures: Most elderly unlikely to fully recover

New study supports the need for frank discussions about the likelihood of ever making a full recovery

One in every two older persons who have suffered a hip fracture will never be as physically active and independent as they were before. The odds are even lower for the very old and those with dementia or other ailments, says Victoria Tang of the University of California in the US. She led an observational study[1] in the Journal of General Internal Medicine, published by Springer.

Around 300, 000 older Americans are hospitalized and receive surgery because of hip fractures annually. Although efforts are made to provide rehabilitation to patients so that they can enjoy the same level of physical activity as they were used to before the injury, many become increasingly frail and dependent on others.

To make an informed assessment of how well older adults recover from a hip fracture, Tang and her colleagues compared the physical condition and ability of 733 adults older than 65 years before and after the fracture. Their particulars were retrieved from the Health and Retirement Study (HRS), a nationally representative longitudinal study that measures changes in the health and economic circumstances of Americans as they age. Participants' functional recovery was measured based on how they were still independently able to care for themselves post-injury in terms of bathing, dressing, eating and going to the bathroom on their own. Factors such as their ability to walk around a street block or climb stairs without resting were noted, as well as their age and health status prior to the hip fracture.

"The likelihood of recovery to pre-fracture level of function was less than 50 percent regardless of one's previous level of function," Tang says. "The likelihood of returning to a high level of function was particularly low in those who were older than age 85, had multiple comorbid conditions, or had dementia."

Of all subjects, 31 percent returned to their prior daily functioning; 34 percent and 41 percent were respectively able to move and climb stairs as before. Things were only marginally better for those who were physically very active before their injury. Of them, 36 percent could go on living independently without assistance, 32 percent had no difficulty walking one block, and 29 percent had no problems climbing stairs.

Tang believes it is essential to be aware of expected outcomes after a hip fracture, so that patients, families and supportive caregivers can set realistic expectations to meet additional needs once the patients return home.

"Ascertainment of the patient's values and goals of care is critical at this juncture in order to optimize quality of life and assist in future medical decision making," says Tang, who called for more frank discussions about the matter.

[1.] *Tang, V.L. et al. (2016). Rates of Recovery to Pre-Fracture Function in Older Persons with Hip Fracture: an Observational Study, Journal of General Internal Medicine. DOI 10.1007/s11606-016-3848-*

http://bit.ly/2cqmxUT

New electrical stimulation therapy may improve hand function after stroke

American Heart Association Rapid Access Journal Report

DALLAS - A new electrical stimulation therapy helped stroke survivors with hand weakness improve hand dexterity more than an existing stimulation technique, according to new research in the American Heart Association's journal Stroke.

About 800,000 people in the United States have strokes each year, according to the American Heart Association. Stroke usually results in some degree of paralysis or partial paralysis on one side of the body, which can result in survivors having difficulty opening a hand. A common therapy in stroke rehabilitation uses low levels of electric current to stimulate the paralyzed muscles to open the hand, improve muscle strength and possibly restore hand function. Stimulation intensity, cycle timing, and repetitions are set by a therapist.

In the new experimental therapy developed by researchers at the MetroHealth System, Case Western Reserve University and the Cleveland Functional Electrical Stimulation Center, patients control the stimulation to their weak hand by wearing a glove with sensors on the opposite, unaffected hand. When the patient opens their unaffected hand, they receive a corresponding amount of stimulation that opens their weak stroke-affected hand. This puts the patient back in control of their hand and enables them to participate in therapy with the assistance of electrical stimulation.

"Based on positive findings from our previous studies, we sought to determine if the new glove-controlled hand stimulation therapy could be more effective than the common therapy in improving hand dexterity in patients who are more than six months past their stroke," said Jayme S. Knutson, Ph.D., senior author of the study and an assistant professor of Physical Medicine and Rehabilitation at Case Western Reserve University School of Medicine in Cleveland, Ohio.

Researchers enrolled 80 stroke survivors. For 12 weeks, half the survivors received therapy using the new glove, and the remainder received the common therapy. Both groups used an electrical stimulator on their own at home for 10 hours a week, plus 3 hours per week practicing hand tasks with an occupational therapist in the lab. Hand function was measured before and after therapy with a standard dexterity test that measured the number of blocks participants can pick up, lift over a barrier and release in another area on a table within a 60 second period. They found:

Patients who received the new therapy had greater improvement on the dexterity test (4.6 blocks) than the common group (1.8 blocks).

Patients who had the greatest improvements in hand dexterity following the new therapy were less than two years post-stroke and had at least some finger movement when they started the study. These patients saw an improvement of 9.6 blocks on the dexterity test, compared to 4.1 blocks in the common group.

Patients with no finger movement also saw improvements in arm movement after the new therapy.

At treatment end, 97 percent of the participants who received the new therapy agreed that they could use their hand better than at the start of the study.

Because the therapy is new and this was a single-site study, researchers don't know if similar results will also be seen in other rehab centers. They plan to perform a multi-site study to confirm their results, as well as measure quality of life improvements for patients. And while the researchers speculate that the new therapy may be changing neural connections in the brain that control hand dexterity, additional studies are needed to determine what effects it may have on the central nervous system.

The study also demonstrates that stroke patients can effectively use technology for self-administered therapy at home. "Home-based therapy is becoming increasingly important to offset increasing healthcare costs and to meet the need for high doses of therapy that are critical for attaining the best outcomes," Knutson said. "The more therapy a patient can get the better potential outcome they will get."

Co-authors are Douglas D. Gunzler, Ph.D.; Richard D. Wilson, M.D. and John Chae, M.D. Author disclosures are on the manuscript.

The study was funded by the National Center for Medical Rehabilitation Research of the National Institute of Child Health and Human Development.

http://bit.ly/2cz6sJP

New 'Trojan horse' antibody strategy shows promise against all Ebola viruses

Advance could work against other viruses

BRONX, NY - In research published online today in Science, a team of scientists describe a new therapeutic strategy to target a hidden Achilles' heel shared by all known types of Ebola virus. Two antibodies developed with this strategy blocked the invasion of human cells by all five ebolaviruses, and one of them protected mice exposed to lethal doses of Ebola Zaire and Sudan, the two most dangerous. The team included scientists from Albert Einstein College of Medicine, U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Integrated Biotherapeutics, Vanderbilt University Medical Center, and The Scripps Research Institute.

Ebolaviruses cause a highly fatal disease for which no approved vaccines or treatments are available. About two dozen Ebola outbreaks have been documented since 1976, when infections first occurred in villages along the Ebola River in Africa. The largest outbreak in history--the 2014-2015 Western Africa epidemic--caused more than 11,000 deaths and infected approximately 29,000 people.

Monoclonal antibodies, which bind to and neutralize specific pathogens and toxins, have emerged as the most promising treatments for Ebola patients. A critical problem, however, is that most antibody therapies target only one specific ebolavirus. For example, the most promising experimental therapy--ZMappTM, a cocktail of three monoclonal antibodies--is specific for Ebola virus Zaire, and doesn't work against the other two viruses (Sudan and Bundibugyo), which have both caused major outbreaks. The broad-spectrum antibodies developed by the research team represent an important advance against one of the world's most dangerous pathogens.

Exploiting Ebola's Achilles' Heel

In 2011, a team that included co-senior authors Kartik Chandran, Ph.D. professor of microbiology & immunology at Einstein, and John M. Dye, Ph.D., chief of viral immunology at USAMRIID, discovered that all filoviruses (the family to which ebolaviruses and the more distantly related Marburg virus belong) have an Achilles' heel: To infect and multiply in human cells, they must all bind to a host-cell protein called Niemann-Pick C1 (NPC1).

But capitalizing on that knowledge required a completely new approach to targeting viruses: exploiting the fact that Ebola and many other viruses must enter host cell compartments called lysosomes. Once safely inside the lysosomes, the viruses transform and expose key portions of their exterior that the research team successfully targeted using monoclonal antibodies.

To gain entry to cells, filoviruses bind to the host cell's outer membrane via glycoproteins (proteins to which carbohydrate chains are attached) that bristle from the virus's surface. (See illustration.) A portion of the cell membrane then surrounds the virus and pinches off, eventually developing into a lysosome--a membrane-bound,

intracellular compartment filled with enzymes to digest foreign and cellular components.

Filoviruses then use the host cells' resources to break out of their lysosomal "prisons" so they can enter the host cell's cytoplasm to multiply. Enzymes in the lysosome slice a "cap" from the virus's glycoproteins, unveiling a site that binds to the NPC1 embedded in the lysosome membrane.

NPC1, which normally helps transport cholesterol within the cell, offers Ebola virus its only means of escaping the lysosome and multiplying. By fitting its protein "key" into the NPC1 "lock," the virus fuses itself to the lysosome membrane. (See illustration close-up.) Now the virus can propel its RNA from the lysosome and into the cell's cytoplasm, where it can finally replicate itself.

Penetrating an Invisibility Cloak

The research team realized that monoclonal antibodies could potentially thwart all filovirus infections by neutralizing the viral protein that binds to NPC1, or by neutralizing NPC1 itself. There was just one problem: Reflecting Ebola's ingenuity, both targets reside only in lysosomes deep within cells--making them invisible to the immune system and shielded from attack by conventional antibodies.

Dr. Chandran, Dr. Dye and co-senior author Jonathan R. Lai, Ph.D., associate professor of biochemistry at Einstein and an expert in engineering antibodies, devised a clever "Trojan Horse" strategy for overcoming the virus's invisibility cloak: Just as the citizens of Troy unwittingly pulled a wooden horse filled with Greek soldiers into their walled city, they tricked the viruses into carrying the means of their own destruction along with them into host cells.

To do so, the research team synthesized two types of "bispecific" antibodies, each consisting of two monoclonal antibodies combined into one molecule. One bispecific antibody was devised to neutralize the viral protein that binds to NPC1, the other to target NPC1. Both had one monoclonal antibody in common: antibody FVM09, which binds to the surface glycoproteins of all ebolaviruses while the virus is outside cells, allowing the bispecific antibodies to hitch a ride with the virus into the lysosome. FVM09 was developed by co-senior author M. Javad Aman, Ph.D. at Integrated Biotherapeutics.

Once in the lysosome, the bispecific antibodies are released from the viral surface when enzymes in the lysosome slice off the glycoprotein caps--allowing the business ends of the bispecific antibodies to swing into action.

One bispecific antibody combined FVM09 with antibody MR72, which was isolated from a human survivor of Marburg virus infection by co-senior author James E. Crowe Jr., M.D., director of the Vanderbilt Vaccine Center. MR72 targets the NPC1-binding viral protein that is unveiled by all filoviruses in lysosomes. The second bispecific antibody links FVM09 to antibody mAb-548, developed at Einstein, which zeroes in on NPC1. With one bispecific antibody targeting the "lock" (NPC1) and the other targeting the "key" (the virus's NPC1-binding protein), both had the potential for preventing Ebola virus from interacting with NPC1 and escaping from the lysosome into the cytoplasm.

Putting Antibodies to the Test

The researchers then tested their bispecific antibodies against ebolaviruses in the lab. They initially used a harmless virus (vesicular stomatitis virus) that had been genetically engineered to display glycoproteins from all five ebolaviruses on its surface. The researchers incubated the bispecific antibodies with the Ebola-like viruses and then added the mixtures to human cells in tissue culture. Both bispecific antibodies successfully neutralized all five viruses. Work in the high-containment facilities at USAMRIID confirmed that these antibodies also blocked infection by the actual Zaire, Sudan, and Bundibugyo ebolaviruses.

Next came studies at USAMRIID to test whether the two bispecific antibodies could protect mice infected with the two most dangerous ebolaviruses, Zaire and Sudan. Researchers, led by Dr. Dye,

administered the bispecific antibodies two days after mice were exposed to a lethal dose of virus.

The bispecific antibody that targeted the viral binding protein provided good protection to mice exposed to both viruses. As expected, the bispecific antibody that targeted NPC1 did not protect mice. It was designed to bind specifically to human NPC1, which differs slightly in structure from the NPC1 protein found in mice.

As a next step, both bispecific antibodies will need to be tested in nonhuman primates, the current gold standard for anti-Ebola therapeutics.

The paper is titled "A 'Trojan Horse' Bispecific Antibody Strategy for Broad Protection Against Ebolaviruses." In addition to Drs. Chandran, Lai, Dye, Aman and Crowe, contributors include co-first author Anna Wec, M.S., co-first author Elisabeth Nyakatura, Ph.D., Eva Mittler, Ph.D., John Christin, Rohit Jangra, Ph.D., M.V.Sc., and Sushma Bharrhan, Ph.D., all at Einstein; co-first author Andrew Herbert, Ph.D., Ana Kuehne, and Russell Bakken at USAMRIID; Katie Howell, Ph.D., Frederick Holtsberg, Ph.D., and Sergey Shulenin, Ph.D., at Integrated Biotherapeutics, Inc; Andrew Flyak, Ph.D., at Vanderbilt University Medical Center; and Zachary Bornholdt, Ph.D., and Erica Ollmann Saphire, Ph.D., at The Scripps Research Institute.

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Jonathan R. Lai, Ph.D., co-senior author: "It's impossible to predict where the next ebolavirus outbreak will occur or which virus will cause it. So the best therapy would be a monoclonal antibody that is active against the glycoproteins of all five ebolaviruses--and until our study, no such antibody had demonstrated the ability to do that. We hope that further testing in nonhuman primates will establish our antibodies as safe and effective for treating those exposed to any ebolavirus."

Kartik Chandran, Ph.D., co-senior author: "We would love to extend this approach to Ebola's distant cousin, Marburg virus, to create a true pan-filovirus therapeutic antibody. Furthermore, we hope that our Trojan Horse antibody strategy of targeting viruses in lysosomes might work against other disease-causing viruses like flu, dengue, or Lassa, which, like Ebola, also enter host-cell lysosomes as part of their life cycles."

John M. Dye, Ph.D., co-senior author: "Our team of scientists took the 'Trojan Horse' concept from the chalkboard to a product that has the capacity to provide a viable treatment for all filoviruses, both known and emerging. This work highlights the power of governmental, academic and industrial researchers collaborating together to solve a complex and important public health problem."

M. Javad Aman, Ph.D., co-senior author: "The success in co-opting the virus itself to dispatch a lethal weapon against ebolaviruses in the lysosomes marks a turning point in development of smart therapeutics against infectious diseases. Similar strategies could be devised against several other viral and bacterial pathogens or toxins that are unleashed inside the lysosomal compartments."

James Crowe Jr., M.D., co-senior author: "We were intrigued to find this remarkable naturally occurring antibody that has the capacity to bind to both Marburg and Ebola viruses. The team's feat of delivering the antibody into cells using creative engineering tricks so that it can kill Ebola inside cells is very exciting."

http://bit.ly/2cI2Dme

Study finds earthquakes can trigger near-instantaneous aftershocks on different faults

Scripps scientists are studying earthquake aftershocks to better understand their triggers

According to a new study by scientists at Scripps Institution of Oceanography at the University of California San Diego, a large earthquake on one fault can trigger large aftershocks on separate faults within just a few minutes. These findings have important implications for earthquake hazard prone regions like California where ruptures on complex fault systems may cascade and lead to mega-earthquakes.

In the study, published in the Sept. 9 issue of the journal Science, Scripps geophysicist Peter Shearer and Scripps graduate student Wenyuan Fan discovered 48 previously unidentified large aftershocks from 2004 to 2015 that occurred within seconds to minutes after magnitude 7 to 8 earthquakes on faults adjacent to the mainshock ruptures.

In one instance along the Sundra arc subduction zone, where the magnitude 9 Sumatra-Andaman mega-earthquake occurred off the coast of Indonesia in 2004, a magnitude 7 quake triggered two large aftershocks over 200 kilometers (124 miles) away. These aftershocks miles away reveal that stress can be transferred almost instantaneously

by the passing seismic waves from one fault to another within the earthquake fault system.

"The results are particularly important because of their seismic hazard implications for complex fault systems, like California," said Fan, the lead author of the study. "By studying this type of triggering, we might be able to forecast hosting faults for large earthquakes."

Large earthquakes often cause aftershock sequences that can last for months. Scientists generally believe that most aftershocks are triggered by stress changes caused by the permanent movement of the fault during the main seismic event, and mainly occur near the mainshock rupture where these stress changes are largest. The new findings show that large early aftershocks can also be triggered by seismic wave transients, where the locations of the main quake and the aftershock may not be directly connected.

"Multiple fault system interactions are not fully considered in seismic hazard analyses, and this study might motivate future modeling efforts to account for these effects," said Shearer, the senior author of the study. *The National Science Foundation funded the study.*

http://bit.ly/2cKTQUJ

Reactive oxygen species switch immune cells from migratory to murderous

How do neutrophils transition from superheroes to killing machines?

Neutrophils are the superheroes of the body's immune system. Normally mild-mannered, they travel through the bloodstream until they reach an emergency situation, such as a cut or infection, where they switch into battle-mode to engulf and destroy foreign invaders.

How do these microscopic avengers transition from silent, patrolling responders to merciless killing machines?

Researchers from the University of Illinois at Chicago, the National Institutes of Health and Fudan University in Shanghai have found that the key is a receptor molecule in the cell that senses reactive oxygen species. The finding is published in the journal Developmental Cell.

Reactive oxygen species, or ROS, are produced by the body as a byproduct of metabolism. They are harmful to cells at high levels, because they can bond to and damage molecules that the cell relies on, like DNA.

A receptor called TRPM2 acts as an ROS sensor or gauge inside the neutrophil. When ROS levels are low, the neutrophil is on the move, looking for infections to fight. As the neutrophil nears a wound site and begins to encounter foreign particles or bacteria, it engulfs them and generates a killing burst of ROS to destroy the captured enemy. TRPM2 senses these consistent, high levels of ROS inside the cell and puts the neutrophil in park, so the cell stays in place to continue killing invading microbes.

"The neutrophil senses a dramatic increase in reactive oxygen species as it gets closer to the wound site, and this triggers the shutdown of the migration of the cell," said Jingsong Xu, assistant professor of pharmacology in the UIC College of Medicine and corresponding author on the paper.

"Once the neutrophil ceases moving, it just kills one bacteria or pathogen after another -- and can concentrate on doing its job of cleaning up the site," Xu said.

To shut down migration, TRPM2 must be chemically oxidized, which is what happens when it is exposed to reactive oxygen species. In its oxidized state, TRPM2 binds to another receptor called FPR1, which inactivates the signaling process that causes neutrophils to wander.

Drugs that target the TRMP2 receptor could be useful in preventing the migration of too many neutrophils to a wound site, Xu said.

"Too many neutrophils in a small area can actually damage tissue," he said.

Co-authors on the study are Asrar Malik, Gang Wang, Luyang Cao, Xiaowen Liu, Nathan Sieracki, Anke Di, Shalina Taylor, Xiaojia Huang, Chinnaswarmy Tiruppathi, You-yang Zhao and Xiaopei Gao of the UIC College of Medicine; Xi Wen and Tian Jin of the National Institute of Allergy and Infectious Diseases; Yong Chen of the National Heart, Lung, and Blood Institute; and Yuanlin Song and Chunxue Bai of Fudan University.

http://bbc.in/2ciVz0U

This invention by a British student could save millions of lives across the world

A 22-year-old British student has invented a mobile fridge that could save millions of lives across the world.

By Michael Baggs

Will Broadway's "Isobar" has been designed to keep vaccines at the ideal temperature while in transit in developing countries.

And Will doesn't plan to make money from his creation.

His focus is to get it to people who need it, which is why he won't be trying to get a patent. "I make things every day for people who have everything," Will, an industrial design and technology graduate from Loughborough University, tells Newsbeat.

"I wanted to make something for people who have next to nothing. It should be a basic human right, in my opinion, to have a vaccination.

"I don't think that it should be patented to restrict use."

Will's Isobar has won him the annual James Dyson Award, open to students across the world with a simple brief - design something that solves a problem. Current methods of transporting vaccines can result in the vaccines freezing before reaching their destination in countries where poverty and conflict are major obstacles.

The device maintains a steady two to eight degrees for 30 days. It works by heating ammonia and water to create ammonia vapours, which are then released into its main chamber when cooling is needed.

Here's how the chemical reaction works inside the Isobar

Will was inspired to start work on a portable refrigeration unit in 2012 when he visited Cambodia and parts of south east Asia.

"These trips sparked an interest," he says.

"It pushed me. Something needs to be solved for this major issue."

Having previously worked at a medical device consultancy, Will has first-hand experience of how large companies monetise life-saving products.

"Medical products have such a big mark up that it's unreasonable for people around the world to purchase these items," he says.

"If it is the best thing available, then it should be out there saving lives."

It has been estimated that Will's invention could save the lives of 1.5 million people across the world, a number he says is "astonishing".

Having now finished his degree, his focus is taking the Isobar into production - something he plans to oversee.

"I would be hands on, all the way through it, knowing that it works," he says. "It's amazing to just give it a go, even in my back yard, and see the potential of the technology."

The product has been designed to transport vaccines, but already Broadway sees potential for other medical uses in the developing world and beyond.

"Blood donations, organ transplants - if they get stuck in traffic, you still use cold-packs that really aren't adequate for long periods of time," he says.

There is also a potential, non-medical use for Isobar which could be monetised in the Western world.

"It's risky but but there is potential for commercial cooling. It would be a great thing to take on a five day trip where you have no power," he says.

But he insists vaccine delivery is the primary function of his invention.

"It has been applied to what is hopefully the right avenue for the technology."

http://bbc.in/2cCc9Xn

Statins benefits underestimated, review says

The benefits of the cholesterol-reducing drug statins are underestimated and the harms exaggerated, a major review suggests.

By Caroline Parkinson Health editor, BBC News website

Published in the Lancet and backed by a number of major health organisations, it says statins lower heart attack and stroke risk. The review also suggests side effects such as muscle pain do occur, although in relatively few people. But critics say healthy people are unnecessarily taking medication.

Dummy drug effect

Statins reduce the build-up of fatty plaques that lead to blockages in blood vessels. According to the report authors:

About six million people are currently taking statins in the UK

Of those, two million are on them because they have already had a heart attack, stroke or other cardiovascular event

The remaining four million take statins because of risk factors such as age, blood pressure or diabetes

Up to two million more should possibly take statins

The Lancet review, led by Prof Rory Collins from the Clinical Trial Service Unit at the University of Oxford, looked at the available evidence for the effects of taking an average 40mg daily dose of statins in 10,000 patients over five years.

It suggested cholesterol levels would be lowered enough to prevent 1,000 "major cardiovascular events" such as heart attacks, strokes and coronary artery bypasses in people who had existing vascular disease - and 500 in people who were at risk due to age or other illnesses such as high blood pressure or diabetes.

'It's better than the risk of a heart attack'

Stephen Sangster, who lives in Orpington with his wife and two children explains why he takes the drugs. "I've been taking statins for three months now. I'm 34. My high cholesterol was picked up by a work health assessment. Dietary changes made no impact.

"With my dad dying of heart attack young last year, statins give me comfort that they will probably give me a longer life. So I can live with the small chance of side effects.

"So far I've only experienced a bit of dizziness, and I don't know even if that's related to statins. Also it's better than the risk of a heart attack.

"My cholesterol was 9.3 and within a month of taking statins it's back down to below four. "Cholesterol is a hidden danger. It's such a simple test. More people should be encouraged to take it. "I wonder how many other younger people would benefit from a statin, but don't realise they have an issue. "

The review also said randomised controlled trials - where neither patient nor doctor know who is on the real drug and who is on a dummy version - suggested the average dose led to a relatively low level of side effects. In the same 10,000 population, there would be some side effects, including between 50 and 100 cases of adverse events such as muscle pain, it said. Observational studies - where people know they are taking the drug and will have been told of known side effects including muscle pain - had higher rates.

Question marks

Prof Collins said: "Our review shows that the numbers of people who avoid heart attacks and strokes by taking statin therapy are very much larger than the numbers who have side effects with it.

"In addition, whereas most of the side effects can be reversed with no residual effects by stopping the statin, the effects of a heart attack or stroke not being prevented are irreversible and can be devastating.

"Consequently, there is a serious cost to public health from making misleading claims about high side effect rates that inappropriately dissuade people from taking statin therapy despite the proven benefits."

The Royal College of GPs (RCGP) and the British Heart Foundation are among a number of major organisations backing the report.

Dr Maureen Baker, who chairs the RCGP, said: "We hope this research reassures patients that in the majority of cases statins are safe

and effective drugs - but in most cases where adverse side effects are seen, these are reversible by stopping taking statins."

Dr June Raine, of medicines watchdog the Medicines and healthcare products Regulatory Agency said: "The benefits of statins are well established and are considered to outweigh the risk of side-effects in the majority of patients.

"Any new significant information on the efficacy or safety of statins will be carefully reviewed and action will be taken if required."

However, critics said the review was not the final word on statins.

Fiona Godlee, editor of the British Medical Journal, said: "This still does not address the calls for a thorough, independent review of the evidence of statins. "This is especially important in view of the guidance which recommends that large numbers of healthy people should take a tablet every day."

And London cardiologist Dr Assem Malhotra said: "There are serious question marks about the reliability of industry-sponsored studies on the side effects of statins, and essentially that's what this review is.

"And a lot of the scientists involved in the original studies were involved in this review. It is not an independent review."

http://bit.ly/2cNqQ5i

Japan measles outbreak: 7 more cases confirmed in Hyogo

Officials in Amagasaki City, Hyogo Prefecture have confirmed 7 more cases of measles

By Roland Shichijo

HYOGO (TR) – Seven more cases of measles were confirmed here on Thursday as Japan grapples with a mostly foreign strain of the virus it once eradicated years ago.

Six people in Amagasaki City were infected by an outbreak of measles originating from a nursery, while a 14-year-old female middle school student was confirmed to be infected on Tuesday, the Asahi Shimbun reports (September 8).

Amagasaki officials are screening several other children who are exhibiting symptoms, adding that none of the infected individuals recently traveled or visited Kansai International Airport.

But a female worker at the airport in her 20s who has measles returned home to Amagasaki on August 24 and broke out with a fever and rash, officials said. Officials have yet to determine if the infected worker came into contact with any of the seven individuals.

A 5-year-old boy at the nursery was exhibiting symptoms like runny nose since August 22 and later broke out with a fever reaching 40 degrees Centigrade, officials said. A doctor referred the boy to city officials, who found that measles had spread to the boy's mother, three other children and a nursery worker in her 30s.

The infected middle school student broke out with a fever and rashes on Saturday, city officials said, adding that she and the boy were on their way to recovery.

http://bit.ly/2cO5I74

Drones get first anti-laser lasers to stop being shot down

Lasers have entered the arms race.

As more countries equip their militaries with high-energy laser weapons, new defences are needed. Enter Helios, an anti-laser laser that aims to protect drones and other vehicles. Laser weapons have been around for a few decades, but they are becoming much more widely used.

Drones now need protection **Erik Simonsen/Getty By David Hambling**

The US military has large numbers of hand-held and vehicle-mounted lasers that it can use to dazzle the enemy, for example. And its warship USS Ponce now carries lasers powerful enough to shoot drones out of the sky.

It is not just the US military that has lasers. In August, the Ukrainian border guard service said that three of its guards experienced retinal burns while observing separatist activity through binoculars. They believe that a laser was used against them. This followed an earlier incident in which the service said that one of its reconnaissance aircraft was targeted by a Russian soldier with a hand-held laser in Crimea. "If this trend continues, it is an escalation of the conflict," says California-based defence analyst and author Robert Bunker.

The USS Ponce's laser can shoot down aircraft **U.S. Navy photo by John F. Williams/Released**

To defend against military lasers, Adsys Controls of Irvine, California, has created Helios, which can be carried on drones. To do much damage, an offensive laser needs to remain focused on its target for several seconds. Helios stops a laser from doing this by disrupting the systems controlling the beam – the Achilles' heel for all such weapons. "Beam control is a critical function of high-energy lasers," says Adsys CEO Brian Goldberg.

Helios can detect an incoming laser beam and identify its key characteristics, such as power, wavelength, pulse frequency and its source. Helios then interferes with the beam control – possibly by firing back a low-power laser of its own – so the attacking laser cannot fix on the target. "It provides permanent protection," says Goldberg. "It's not just buying time."

He will not say exactly how the interference is done, but it may involve fooling the control system into thinking it is hitting its target despite the laser actually pointing a few metres to the side. A direct hit would have produced a big burst of reflected light, so a pulse sent back by an anti-laser laser could make it look like the original laser was on target.

But Helios could be susceptible to the same trick, says Roland Smith, a plasma physicist at Imperial College London. "If it puts out enough power to disrupt targeting, that makes it visible and a target itself," he says. "If the laser weapon knows it is being jammed, it could engage the jammer."

http://bit.ly/2cq0FZ4

Double negative leads to big positive against bladder cancer metastasis

Detailing a new link in the chain that leads to bladder cancer metastasis.

The popular kids' card game "Exploding Kittens" teaches a concept critical to cancer science: When a player plays a "Nope" card, the subsequent player may lay another "Nope", thus creating a double-negative that becomes a positive, allowing the initial action to proceed. A paper, stemming from a longstanding collaboration between investigators at the University of Colorado Cancer Center and Yale, published in the journal Cancer Cell, demonstrates a similar strategy that bladder cancer uses to proliferate. By "Noping" the cancer-suppressing gene RhoDGI2, the disease evades a mechanism designed to stop its ability to metastasize. Now new understanding of this mechanism may allow doctors and researchers to Nope this Nope - stopping bladder cancer's ability to stop the tumor-suppressing gene RhoDGI2, thus allowing its initial action to proceed.

Here is how it works:

Circulating cancer cells recruit elements of the body's immune system to prime the tissue environment for the development of new tumors. The current study demonstrates a promising strategy to block the immune system's mistaken collaboration with cancer cells, resulting in the inability of circulating cells to seed new sites of metastasis.

"Working with bladder cancer cells, we were able to show not only how immune system macrophages recognize and aid circulating

cancer cells, but also how we might intercede to block this mechanism," says Dan Theodorescu, MD, PhD, director of the University of Colorado Cancer Center and the paper's co-senior author. The finding takes place in the context of the well-known tumor-suppressor gene RhoDGI2. Activity of this gene and the protein it encodes restricts the ability of bladder cancer cells, and potentially other circulating cancer cells, to grow at new sites of attachment. In fact, it is these sites of metastasis, specifically in the lung that can make bladder cancer fatal. Previous work in the Theodorescu lab published in the Journal of Clinical Investigation in 2011 and 2012 has shown one side of how loss of RhoDGI2 affects cancer growth: loss of RhoGDI2 allows a cancer cell to increase production of proteins called Endothelin and Versican, which signal immune system macrophages to the site of the cancer cells. These macrophages promote the development of new tumors by producing various cancer growth-promoting substances.

The current paper shows that one of these substances is the protein osteopontin. Basically, loss of RhoDGI2 leads to increased Endothelin and Versican, which brings macrophages, which secrete osteopontin, which signals tumor cells to reinitiate stem-cell-like programs that promote growth and survival. Osteopontin does this by binding to CD44 receptors on the surface of newly-attached bladder cancer cells, jumpstarting their ability to act as seeds of a new tumor site. CD44 is a cell surface glycoprotein that is overexpressed to some extent by almost all tumors of epithelial origin and plays an important role in tumor initiation and metastasis. CD44 is a compelling marker for cancer stem cells of many solid malignancies.

When the investigators blocked this osteopontin signaling pathway in animal models, bladder cancer cells were not able form metastases in the lungs and lymph nodes. Likewise, expression of osteopontin was associated with poor outcomes in human bladder cancer patients.

"Interestingly, blocking CD44 did nothing against the local tumor growth. The effect was very robust, but was limited to stopping the initial formation of metastasis," says Martin Schwartz, the Robert W. Berliner Professor of Medicine at Yale and the paper's co-senior author. Again, it is the ability of bladder cancer to invade the lung (and the brain) that makes the disease potentially fatal, and not the activity of the primary tumor itself. Thus treatment strategies targeting metastasis, potentially by blocking osteopontin binding to CD44, offer a compelling way to decrease mortality from the disease.

"What this paper shows is that targeting macrophages and/or CD44 are potential clinical therapeutic options," Theodorescu says. "Also, this demonstrates that when you lose RhoDGI2, it causes the cancer to attract macrophages that in turn secrete osteopontin, which stimulates cancer aggressiveness," he says.

Several years ago, Theodorescu discovered RhoDGI2 as a suppressor of tumor growth at metastatic sites and has worked on it since then. Now there is another step in this understanding. And each step presents another opportunity for doctors and researchers to insert a misstep. RhoDGI2, CD44, versican and osteopontin represent nodes in a signaling web that allows cancer metastasis. "Noping" cancer's "nope" in this web at any point may save lives.

http://bit.ly/2cPEdqG

Measuring new hormone may reduce teenagers wrongly diagnosed with PCOS

PCOS misdiagnosis rates in teenagers may be reduced by measuring blood levels of irisin

Measuring blood levels of the recently discovered hormone irisin may improve diagnosis rates of teenagers with polycystic ovary syndrome, according to research presented today at the 55th Annual European Society for Paediatric Endocrinology Meeting

Measuring blood levels of the recently discovered hormone irisin may improve diagnosis rates of teenagers with polycystic ovary syndrome, according to research presented today at the 55th Annual European Society for Paediatric Endocrinology Meeting. The findings may

reduce the number of unnecessary treatments prescribed to otherwise healthy girls.

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting up to 12% of women. Women with PCOS are more likely to suffer from irregular periods, have excessive levels of male hormones and may have difficulty in conceiving due to irregularities in the ovaries. Doctors are cautious when diagnosing PCOS in teenagers because the symptoms can be confused with normal pubertal changes. Having tools that make diagnoses more accurate can reduce unnecessary treatment for otherwise healthy teenagers at a critical stage in their lives.

The cause of PCOS is unknown and there is currently no cure for the condition. Previous studies have associated high levels of irisin, a newly discovered hormone which is released from muscles and regulates energy metabolism, with PCOS in adults.

In this study, Greek researchers from Aghia Sophia Children's Hospital in Athens compared the hormones of 23 teenagers with PCOS with 17 healthy teenagers of the same age and BMI. They found that teenagers with PCOS had significantly higher irisin levels compared to the control group, and that this was associated with higher levels of the male sex hormone testosterone, a key marker of PCOS.

The findings suggest that irisin could be a marker for PCOS allowing the condition to be diagnosed more easily. "Teenagers who get an early diagnosis of PCOS can sooner start to deal with the physical and psychological symptoms caused by this lifelong condition," said lead researcher Dr Flora Bacopoulou. "Whether it's through counselling or medication, girls can manage their symptoms and decrease the risk of further complications such as fertility problems, hirsutism (excessive hair growth) and type-2 diabetes".

The group will next focus on confirming their results and investigate the biological role of irisin in PCOS. "If high irisin levels in teenagers with PCOS is established, this could lead to the development of treatments for PCOS. Lifestyle changes and different exercise-related signals that regulate the secretion of irisin could provide a potential option for the management of PCOS. The potential of irisin as a meaningful drug target in PCOS is very promising," said Dr Bacopoulou.