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Middle East HEALTH

Serving the region for 40 years

May - June 2017

'Black Snowball'

This is what Syrian refugees call depression

- 300 million worldwide affected
- WHO puts spotlight on illness as few seek treatment

Sickle cell anaemia breakthrough

Gene therapy trial results in complete remission of disease in 13-year-old

Deadly environment

1.7 million children die from pollution each year

In the News:

- Yemeni doctor wins top international award
- Researchers honoured with King Faisal prize
- WHO lists priority bacteria for R&D of new antibiotics
- New 'gene-silencer' drug reduces cholesterol by over 50%

Bahrain BD3, **Egypt** E£40, **Iran** IRR75, **Iraq** IQD3,400, **Jordan** JD5, **Kuwait** KD3, **Lebanon** LBP12,000, **Oman** RO3, **Qatar** QR30, **Saudi Arabia** SR30, **Syria** £S400, **UAE** Dh30, **Yemen** YR1,600

HELIOS Prevention Center in Germany

For a healthy living: Identifying risks & defining measures

Many women hardly find time to focus on their health – the personally tailored check-ups at HPC help to prevent diseases, such as obesity, heart attacks or specific types of cancer.

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**Rebranding will be completed by March 2018.*

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Children's Hospital of Pittsburgh of UPMC is a leading international center for liver transplantation as a treatment for metabolic disease.

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We've performed more liver transplants for patients with metabolic disease than any other transplant center.

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Our experience, expertise, and commitment to innovation and compassionate care are reasons why patients and families from around the world travel to Children's Hospital of Pittsburgh of UPMC. For a free phone consultation with one of our experts on liver transplantation as a therapeutic option for metabolic disease, please visit **www.chp.edu/metabolic** or send an email to **international@chp.edu**

Sources: Internal data, Hillman Center for Pediatric Transplantation; Scientific Registry of Transplant Recipients (www.srtr.org), December 2015 release.

Children's Hospital of Pittsburgh | of UPMC

Prognosis

Depression

The WHO estimates that depression affects some 300 million people worldwide and is considered such a common illness that they made it the core theme of the World Health Day focus on April 7. The organisation notes that few people seek treatment and at its worst, depression can lead to suicide. There are more than 800,000 suicides a year worldwide.

Closer to home, it is a major issue with Syrian refugees who have fled the war. They call it the 'black snowball' as it is an accumulation of anxiety and stress from losing all their worldly belongings and the horrific experience of war that can lead to severe depression. In this issue, read the account of a psychotherapist helping Syrian refugees in Turkey.

In a major scientific breakthrough, researchers have used 'gene therapy' to cure sickle-cell anaemia. In a trial with a 13-year-old boy they have successfully used gene therapy to achieve complete remission of the genetic disease in the boy. Although this is still in the early phase, the implications of this trial are important for this region where the prevalence of sickle cell anaemia is particularly high.

In the Women's Health focus we look at several new developments. One of these is the issuing of new global guidelines for HPV vaccination.

In our focus on surgery, we report on a doctor from Mayo Clinic who has made it his mission to improve neurosurgical techniques and has become a specialist in 'awake craniotomy' for the resection of difficult brain tumours. The awake craniotomy minimises the use of anaesthesia and along with a camera placed in front of the patient's face – which he introduced – he can monitor facial changes during the surgery in response to questions, to ensure the preservation of critical parts of the brain.

In this issue, you'll find a wealth of interesting news and research developments from the region and the world.

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Middle East HEALTH
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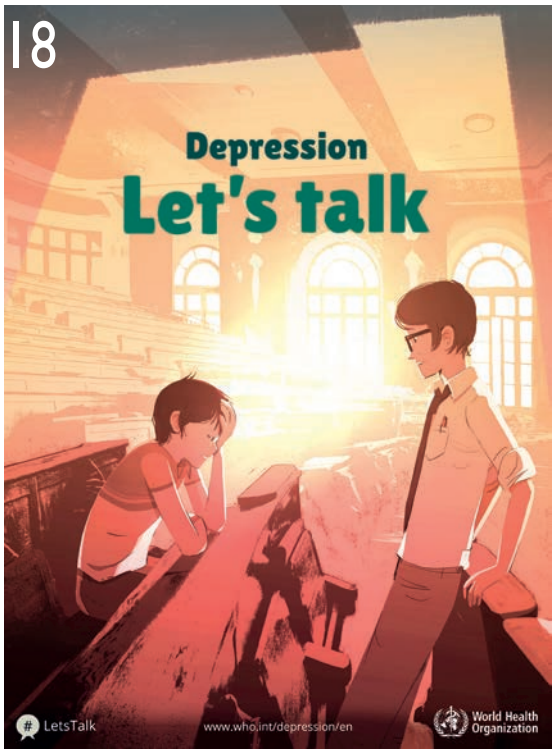

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COVER IMAGE
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We're boldly *moving forward* in heart care

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middle east monitor

Update from around the region

Dr Dhekra Annuzaili (right)

Yemeni doctor wins top international award

Dr Dhekra Annuzaili, from Sanaa, Yemen is the winner of the first ever *Women in Focus Exceptional Service Award* – a prestigious international accolade celebrating the crucial role women play in the ongoing fight against Neglected Tropical Diseases (NTDs).

The 49-year-old's tireless work in Yemen made her a unanimous winner with the judging panel and she was invited to accept her trophy at a prominent awards ceremony in Geneva, Switzerland on 19 April.

Since graduating from medical school in 1991, in Yemen, Dr Dhekra has shown incredible commitment to her work on maternal and child health development, improving overall health and nutritional programmes across the country. Dr Dhekra moved to the field of NTDs, in 2009, specialising in Schistosomiasis Control. As a woman working in a country with one of the lowest rankings of gender equality in the world, Dr Dhekra has overcome extreme personal obstacles and yet her commitment to NTD control and in serving Yemen never wavered. With her support, Yemen's National Schistosomiasis Control Program has made great strides towards controlling schistosomiasis and intestinal worms.

Dr Dhekra also works as an advisor on health and development issues for several agencies of the United Nations, USAID, World Bank and local NGOs in Yemen.

Dr Dhekra was delighted with her award as it will help to highlight the issue of NTDs in Yemen. "I am thrilled to be the first recipient of this award and I am collecting it on behalf of all of the women working hard to fight NTDs in Yemen. My main aim is to reach children and contribute to the improvement of their overall health. It might sound strange, but I believe I'm lucky to be working in such a difficult field, under difficult conditions. It's completely worth it to see positive improvements in the health of children, students and the community as a whole."

As 2017 marks the 5th anniversary of the World Health Organization's roadmap on NTDs and the London Declaration, the Women in Focus awards celebrate this milestone by recognising the inspirational women working behind the scenes helping to control, eliminate and eradicate 10 neglected tropical diseases.

King Salman honours scientists

King Salman bin Abdulaziz Al-Saud of Saudi Arabia honoured the winners of the King Faisal International Prize 2017 at a ceremony in Riyadh on 4 April.

The King Faisal International Prize honours exceptional achievements in a number of key areas, including Arabic Language & Literature, Medicine, and Science. Among the winners in the 39th session of the award this year were four scientists and researchers.

Giving away the award, King Salman commended the efforts of the scientists and researchers in creating a better world.

King Salman handed over the King Faisal International Prize for Medicine to Professor Tadamitsu Kishimoto of Japan for developing a novel biologic therapy for autoimmune diseases. Kishimoto is the Professor of Immunology Frontier Research Center at Osaka University.

King Salman also presented the King Faisal International Prize for Science; shared this year by Professor Daniel Loss and Professor Laurens Molenkamp, physicists from Switzerland and Germany. Loss is the Professor of the Department of Physics, University of Basel, while Molenkamp is Professor and Head, MBE Unit, University of Wurzburg.

Prof. Loss won the award in recognition of his work on the theory of spin dynamics and spin coherence in quantum dots, which has practical applications in spin quantum computers. Professor Molenkamp was honoured for his work in the experimental field of spintronics.

On the occasion, Prof. Kishimoto said: "The King Faisal International Prize deserves to be commended for encouraging efforts in the knowledge and research arena around the world. I am proud to be a recipient of this renowned prize, which has this year helped draw attention to the importance of immunology. This award will help further enrich research based initiatives to understand more about the human immune system."

A world-renowned immunologist, Prof. Kishimoto, through his work of more than 30 years, is responsible for discovering interleukin-6 (IL-6), its receptor and signalling pathways. He established the physiological function of the IL-6 pathway and its role in inflammatory and autoimmune diseases. Subsequently, he developed an IL-6 receptor-blocking antibody into a biological therapy, leading the clinical development of this therapy towards the first approval for the treatment of rheumatoid arthritis.

Qayyara Hospital in Mosul reopened

Five months after Al-Qayyara Hospital in Mosul was forced to close down due to extensive damages, the facility has been re-opened to provide trauma care and obstetric services to populations affected by the ongoing conflict. The hospital, which re-opened on 7 March, will respond to increasing health needs of people fleeing their homes in West Mosul, as military operations to retake the city continue.

"WHO and partners have stepped up

health care delivery to cope with the new exodus of displaced population fleeing West Mosul," said Altaf Musani, WHO Representative in Iraq. "The urgency of the situation means that only the ground floor of the hospital is functioning at this stage, but this will ensure referral health services are now available near the front lines, and that more lives can be saved through timely medical care," he added.

Al-Qayyara Hospital is a secondary referral facility serving the entire catchment area in Al Qayyara, south of Mosul. Trauma cases from west Mosul who are stabilized at WHO-supported trauma stabilization points will now be transferred to the hospital for advanced surgical treatment. With support from WHO, the hospital is equipped with 2 operation theatres, a blood bank, laboratory, and X-ray, ultrasound, and sterilization units. There are currently 45 medical staff working in the hospital, including 6 surgeons and 4 anesthetists. In the first week since its opening from 7 to 13 March, the hospital conducted 540 surgical consultations and 1014 obstetric consultations, including 532 normal deliveries and 32 cesarean deliveries.

Renovation work in the hospital was carried out by WHO implementing partner WAHA. Together with national health authorities, WHO is supporting the provision of trauma care services through the delivery of medicines, medical supplies and equipment, and incentives for health workers. Obstetric services are provided with support from UNFPA. The hospital is one of many health facilities in Iraq supported by WHO through generous donations from the European Commission's Humanitarian Aid Office (ECHO), Office of Foreign Disaster Assistance (OFDA), the Government of Kuwait, and the Central Emergency Response Fund (CERF).

Leaders in nursing discuss health improvement strategies for ME

The Honor Society of Nursing, Sigma Theta Tau International (STTI) convened a regional meeting of the Global Advisory Panel on the Future of Nursing and Midwifery (GAPFON) in March in Abu Dhabi in collaboration with the Emirates Nursing Association (ENA). More than 30 key nursing and midwifery leaders from 13 countries in the Middle East region participated.

"The Global Advisory Panel on the Future of Nursing and Midwifery is an important conference to identify and develop recommendations to address the most important issues facing health at the global level," said Her Royal Highness Princess Muna Al-Hussein of Jordan, Patron of the GAPFON Middle East Regional Meeting. "Nurses and midwives will play an integral role in leading change to improve the quality of life of people globally by capitalizing on their best assets and collective potentials."

Dr Huda Abu-Saad, Professor of Nursing Science and Director of the Hariri School of Nursing at the American University of Beirut added: "GAPFON is a visionary and commendable initiative with promising global impact that brings regional leaders together to discuss the future of nursing and midwifery and their impact at the global level."

Participants confirmed that priority issues and action strategies to achieve global health must focus on leadership, policy/regulation, education, and workforce. Participants felt strongly that these priorities are inter-related and each is integral to the achievement of regional goals. Additionally, they noted that recommendations for action in any of these areas must be evidence-based and linked to achievement of outcomes.

These stakeholders verbalized the importance of developing nursing and midwifery leaders and positioning them in roles where they can be most effective. They noted the importance of leveraging the return on investment that nurses and midwives contribute to the attainment of health. The stakeholders reiterated that promoting quality nursing/midwifery practice and education, including the development and promotion of community initiatives, social justice, and human rights, are areas where nurses and midwives have a pivotal leadership role. They agreed that health promotion focused on disease prevention is vital, along with the importance of adequate preparedness and response to natural and man-made disasters. They also agreed that education, awareness, and timely treat-

ment of mental health issues is a priority in this region.

During their discussions, stakeholders identified specific strategies to enhance health, including utilizing data and evidence to inform health policy and to increase national commitment and funding. They also stressed the importance of employing an accountability framework, including state-of-the-art technology, to monitor and evaluate performance against targets. In addition, the participants recognized the need for coalition-building and interprofessional collaboration at all levels to improve health, along with the development of an adequate, competent nursing/midwifery workforce. These strategies are especially important to address the consequences of frequently overlooked or minimized mental health concerns, including those stemming from violence, poverty, and natural disasters. The strategies identified by the Middle East stakeholders are congruent with the United Nations' Sustainable Development Goals (SDGs).

The GAPFON Middle East Regional Meeting represents one of seven global regions where STTI is holding meetings. In the coming months, STTI will convene the remaining two meetings, to be held in Europe and Africa. Data from these meetings will provide the basis for an overall action plan with regional policy implications. GAPFON will analyse and prioritize key recommendations that address each of the region's challenges in both global and regional summary reports and will post these reports at *www.gapfon.org*.

UK's Priory Group opens wellbeing centre for mental health care in DHCC

The UK's Priory, which is most commonly associated with treating celebrities, has just opened its first overseas facility in Dubai's Healthcare City (DHCC).

The Priory Wellbeing Centre, which is now accepting patients, provides treatment for a wide range of conditions including depression, stress, addiction, and anxiety-related conditions including obsessive compulsive disorder (OCD) and panic attacks.

Will Goodwin, managing director of Priory Group in the Middle East, said: "The UK mental healthcare system is considered among the best in the world. I am extremely excited to expand our care internationally, particularly within the UAE.

"Every year many people reach the point of needing mental health support. Our specialists can provide confidential bespoke support and treatment tailored to particular needs and goals."

The Priory Group has invested Dh2 million in the centre which will be staffed by psychiatrists and counsellors, led by Priory's Middle East Medical Director, Dr Saaed Islam.

Dr Islam said: "The opening of this new wellbeing centre, under the internationally acclaimed Priory brand, will be a huge asset to the effective delivery of mental health services in Dubai and will allow our team to reach out to patients - both Emirati as well as expats. We know from the ongoing success of these clinics in London and other key cities across the UK that there is a demand for accessible mental health support and treatment and I believe that nobody – whatever their age, gender, profession or culture - should ever be scared or ashamed to seek help."

He added: "There are many reasons why a region or country sees a higher prevalence of a specific condition but we hope that by offering a friendly and discreet service, we can play an active part in identifying and addressing these issues and supporting our patients towards long-term recovery."

Al Jalila Foundation receives grant for UAE-based vitamin D deficiency study

The Al Jalila Foundation has received a two-year Health Access Grant for US$100,000 from Medtronic Foundation.

The grant will fund a research programme focusing on Vitamin D deficiency in adults and children across the United Arab Emirates. The study will focus on early detection, evaluation, and treatment of vitamin D deficiency. The grant will allow Al Jalila Foundation – a philanthropic organisation dedicated to transforming lives through medical education and research – to screen thousands across the UAE to promote early detection and prevention of the debilitating disease.

Medtronic's Majid Kaddoumi presents the grant to Dr Abdulkareem Sultan Al Olama, Chief Executive Officer, Al Jalila Foundation

According to the International Osteoporosis Foundation (IOF), up to 90% of those living in the emirates suffer from a Vitamin D deficiency. IOF stated that the number of UAE residents suffering from the deficiency, which causes osteoporosis, a bone degeneration disease, is one of the highest in the world with the highest incidences among women. Osteoporosis causes the deterioration of bone tissue and creates low bone mass, leading to bone fragility and a higher risk of broken bones.

Dr Abdulkareem Sultan Al Olama, Chief Executive Officer, Al Jalila Foundation said: "Vitamin D deficiency has become a global health concern. Studies have shown that insufficient levels of Vitamin D can lead to a number of chronic illnesses and life-threatening diseases. We are grateful to the Medtronic Foundation for their support and look forward to working together on this important study. It is our hope that through increased awareness and early detection patients will be better equipped to manage the disease to lead a healthy, happy and productive life."

Medtronic Foundation Health Access Grants are awarded in 72 different com-

munities around the world in recognition of community-based programs and organizations that demonstrate a commitment to expanding access to chronic disease care for the underserved.

Immunisation campaign protects 5 million children against polio in war-torn Yemen

In an effort to keep Yemen polio-free, nearly 5 million children under the age of 5 have been vaccinated in a nationwide campaign covering all governorates in the country. The campaign was supported by a partnership between the World Bank, UNICEF and WHO launched in February 2017.

Despite intensifying violence in Sa'ada governorate, more than 369,000 children between the ages of 6 months and 15 years were immunized against measles – a highly contagious and potentially fatal disease – and over 155,000 children under the age of 5 were vaccinated against polio.

Thousands of dedicated health workers, health educators, religious leaders and local council officials played a key role in mobilizing their communities to maximize the immunization campaign's reach. Thanks to their support, high-risk groups, such as internally displaced persons and refugees, have also been vaccinated.

"WHO, UNICEF and the World Bank, are working closely with health authorities to keep Yemen polio-free and curb the spread of measles," said Dr Nevio Zagaria, WHO Representative in Yemen. "This partnership provides continuous support to national health authorities to increase vaccination coverage for vulnerable children across Yemen."

Before 2006, measles was one of the leading causes of death in children under 5 years old in Yemen. But several measles campaigns supported by WHO, UNICEF and the World Bank have succeeded in drastically reducing child deaths from the disease.

The 2 year-long conflict in Yemen has all but destroyed the country's health system, including the national immunization programme to protect all children from preventable diseases. WHO and UNICEF have provided sustained support for the programme, along with other essential health services for children, including:

- Delivering fuel, generators and solar-powered refrigerators to keep vaccines at a constant cool temperature,
- Support for transferring vaccines from national and governorate cold rooms to local health facilities and vaccination teams.

"Every minute, the situation of Yemen's children gets worse. It is unacceptable that children in Yemen are dying of preventable diseases. This is why, together with partners, we are sparing no effort to save more lives," said Meritxell Relaño, UNICEF Representative in Yemen.

"The World Bank is committed to investing in children's health, which is a vital investment in the country's future, through working with our UN partners in Yemen and strengthening the local health institutions," said Sandra Bloemenkamp, World Bank Country Manager for Yemen.

Immunization campaigns are critical to keep Yemen polio-free – a major priority for WHO, UNICEF and the World Bank – and to help minimize the risk of poliovirus being imported into the country. Vaccination is one of the safest and most cost-effective health interventions to protect children from potentially fatal and debilitating diseases.

UAEU device brings extra hand to OR

Medical technology developed at United Arab Emirates University (UAEU) is set to help surgeons navigate complex and delicate procedures by acting as a robotic aid to accuracy.

Created within UAEU's College of Engineering, the Manipulator for Surgical Tools – for which patent approval has now been secured – employs a novel compactor robotic manipulator which is specially configured with a remote "centre-of-motion" function that effectively gives the surgeon an extra hand.

The device can easily and accurately manipulate and reorient special-purpose surgical tools for minimally-invasive procedures – including those used to treat some forms of cancer – with a freedom range of two degrees, and lock them in place. Capable of operating either manually, autonomously, or via remote control, it has also been designed in a way that ensures it stays out of the surgeon's field of view as they work in a confined area where even the slightest twitch or error is unthinkable.

"The tools which this device can manipulate are used in surgeries such as biopsies, where it helps the surgeon reorient the needle before inserting it," explained Dr Basem Yousef, Associate Professor of Mechanical Engineering, College of Engineering, UAEU.

"It can also be used for a type of radiotherapy called brachytherapy – a procedure used to treat lung, prostate and breast cancer – where radioactive seeds are planted to break up cancer cells. The device helps to implant these seeds. That is the overall aim – to help the surgeon by making the process more efficient and more accurate."

The device comprises a sophisticated joint-link structure and configuration that allow the surgeon to comfortably manoeuvre the tool at a "pivot point" – typically where it enters the patient's body – while avoiding the keyhole being widened. MEH

worldwide monitor

Update from around the globe

Encyclopedia of DNA Elements to be expanded for researchers

The US National Institutes of Health plans to expand its Encyclopedia of DNA Elements (ENCODE) Project, a genomics resource used by many scientists to study human health and disease. Funded by the National Human Genome Research Institute (NHGRI), part of NIH, the ENCODE Project is generating a catalogue of all the genes and regulatory elements -- the parts of the genome that control whether genes are active or not – in humans and select model organisms. With four years of additional support, NHGRI builds on a long-standing commitment to developing freely available genomics resources for use by the scientific community.

"ENCODE has created high-quality and easily accessible sets of data, tools and analyses that are being used extensively in studies to interpret genome sequences and to understand the consequence of genomic variation," said Elise Feingold, Ph.D., a program director in the Division of Genome Sciences at NHGRI. "These awards provide the opportunity to strengthen this foundation by expanding the breadth and depth of the resource."

Since launching in 2003, ENCODE has funded a network of researchers to develop and apply methods for mapping candidate functional elements in the genome, and to analyse the enormous database of generated genomic information. The data and tools generated by ENCODE are organized by two groups: a data coordinating centre, which houses the data and provides access to the resource through an open-access portal, and a data analysis centre, which synthesizes the data into an encyclopaedia for use by the research community.

Pending the availability of funds, NHGRI plans to commit up to US$31.5 million in fiscal year 2017 for these awards. With this funding, ENCODE will expand the scope of these efforts to include characterization centres, which will study the biological role that candidate functional elements may play and develop methods to determine how they contribute to gene regulation in a variety of cell types and model systems. Additionally, the project will enhance the ENCODE catalogue by developing a way to incorporate data provided by the research community, and will use biological samples from research participants who have explicitly consented for unrestricted sharing of their genomic data.

At its core, ENCODE is about enabling the scientific community to make discoveries by using basic science approaches to understand genomes at the most fundamental level. Its catalogue of genomic information can be used for a variety of research projects – for example, generating hypotheses about what goes wrong in specific diseases or understanding the processes that determine how the same genome sequence is used in different parts of the body to make cells with specialized functions. More than 1,600 scientific publications by the research community have used ENCODE data or tools.

"We found that many of the people that are using the ENCODE resource are doing so for disease studies, and this attests to its translational value," said Mike Pazin, Ph.D., a program director in NHGRI's Division of Genome Sciences.

on the WEB ENCODE Project
www.genome.gov/10005107/encode-project

Dengue vaccine phase 3 trial gets underway

Takeda Pharmaceutical Company has completed enrollment of 20,100 children and adolescents ages 4 through 16 in its global, pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial, a double-blind, randomized and placebo-controlled study designed to evaluate the efficacy, safety and immunogenicity of its live-attenuated tetravalent dengue vaccine candidate (TAK-003).

The study is taking place in eight dengue-endemic countries in Latin America and Asia: Brazil, Colombia, Panama, Dominican Republic, Nicaragua, Philippines, Thailand and Sri Lanka. While dengue can affect people of all ages, it is a leading cause of serious illness among children in some countries in Latin America and Asia. The enrollment of children and adolescents between the ages of 4 and 16 years underscores the significant burden of dengue disease across the entire pediatric age range. Initial results of the TIDES trial are expected in 2018.

TIDES will build on previous studies which have assessed the tolerability, safety and immunogenicity of the vaccine against all four dengue serotypes in multiple age groups to determine whether the vaccine helps prevent symptomatic dengue.

"This enrollment milestone demonstrates our commitment to a thorough evaluation of the safety and efficacy of our vaccine candidates and, subject to licensure, ensuring that they are available to all populations at risk. It follows Takeda's recent decision to invest more than 100 million euros to build a new plant for the manufacturing of TAK-003," said Rajeev Venkayya, MD, President of the Global Vaccine Business Unit at Takeda.

TIDES Phase 3 trial is investigating the

efficacy, safety and immunogenicity of two doses of TAK-003 administered three months apart.

The primary outcome measure is vaccine protection against virologically-confirmed dengue of any severity, caused by any of the four dengue virus serotypes, regardless of whether a subject has been previously exposed to dengue. Secondary endpoints include vaccine efficacy in preventing dengue induced by each dengue serotype, vaccine efficacy in preventing hospitalization due to dengue induced by any serotype, vaccine efficacy in preventing severe dengue induced by any serotype, frequency and severity of Adverse Events (AEs) or Serious Adverse Events (SAEs), and seropositivity rate and geometric mean titers (GMTs) of neutralizing antibodies in the immunogenicity subset.

WHO lists bacteria for which new antibiotics are urgently needed

WHO has published its first ever list of antibiotic-resistant "priority pathogens" – a catalogue of 12 families of bacteria that pose the greatest threat to human health.

The list was drawn up in a bid to guide and promote research and development (R&D) of new antibiotics, as part of WHO's efforts to address growing global resistance to antimicrobial medicines.

The list highlights in particular the threat of gram-negative bacteria that are resistant to multiple antibiotics. These bacteria have built-in abilities to find new ways to resist treatment and can pass along genetic material that allows other bacteria to become drug-resistant as well.

"This list is a new tool to ensure R&D responds to urgent public health needs," says Dr Marie-Paule Kieny, WHO's Assistant Director-General for Health Systems and Innovation. "Antibiotic resistance is growing, and we are fast running out of treatment options. If we leave it to market forces alone, the new antibiotics we most urgently need are not going to be developed in time."

The WHO list is divided into three categories according to the urgency of need for new antibiotics: critical, high and medium priority.

The most critical group of all includes multidrug resistant bacteria that pose a particular threat in hospitals, nursing homes, and among patients whose care requires devices such as ventilators and blood catheters. They include *Acinetobacter, Pseudomonas* and various Enterobacteriaceae (including *Klebsiella, E. coli, Serratia*, and *Proteus*). They can cause severe and often deadly infections such as bloodstream infections and pneumonia.

These bacteria have become resistant to a large number of antibiotics, including carbapenems and third generation cephalosporins – the best available antibiotics for treating multi-drug resistant bacteria.

The second and third tiers in the list – the high and medium priority categories – contain other increasingly drug-resistant bacteria that cause more common diseases such as gonorrhoea and food poisoning caused by *salmonella*.

The list is intended to spur governments to put in place policies that incentivize basic science and advanced R&D by both publicly funded agencies and the private sector investing in new antibiotic discovery. It will provide guidance to new R&D initiatives such as the WHO/Drugs for Neglected Diseases initiative (DNDi) Global Antibiotic R&D Partnership that is engaging in not-for-profit development of new antibiotics.

Tuberculosis – whose resistance to traditional treatment has been growing in recent years – was not included in the list because it is targeted by other, dedicated programmes. Other bacteria that were not included, such as *streptococcus* A and B and chlamydia, have low levels of resistance to existing treatments and do not currently pose a significant public health threat.

While more R&D is vital, alone, it cannot solve the problem. To address resistance, there must also be better prevention of infections and appropriate use of existing antibiotics in humans and animals, as well as rational use of any new antibiotics that are developed in future.

WHO priority pathogens list for R&D of new antibiotics

Priority 1: CRITICAL

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

Priority 2: HIGH

- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter spp.*, fluoroquinolone-resistant
- *Salmonellae*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella spp.*, fluoroquinolone-resistant

WHO issues ethics guidance to protect rights of TB patients

New tuberculosis (TB) ethics guidance, launched by WHO, aims to help ensure that countries implementing the End TB Strategy adhere to sound ethical standards to protect the rights of all those affected.

TB, the world's top infectious disease killer, claims 5000 lives each day. The heaviest burden is carried by communities which already face socio-economic challenges: migrants, refugees, prisoners, ethnic minorities, miners and others working and living in risk-prone settings,

and marginalized women, children and older people.

"TB strikes some of the world's poorest people hardest," said Dr Margaret Chan, former WHO Director-General. "WHO is determined to overcome the stigma, discrimination, and other barriers that prevent so many of these people from obtaining the services they so badly need."

Poverty, malnutrition, poor housing and sanitation, compounded by other risk factors such as HIV, tobacco, alcohol use and diabetes, can put people at heightened risk of TB and make it harder for them to access care. More than a third (4.3 million) of people with TB go undiagnosed or unreported, some receive no care at all and others access care of questionable quality.

The new WHO ethics guidance addresses contentious issues such as, the isolation of contagious patients, the rights of TB patients in prison, discriminatory policies against migrants affected by TB, among others. It emphasizes five key ethical obligations for governments, health workers, care providers, nongovernmental organizations, researchers and other stakeholders to:

- provide patients with the social support they need to fulfil their responsibilities
- refrain from isolating TB patients before exhausting all options to enable treatment adherence and only under very specific conditions
- enable "key populations" to access same standard of care offered to other citizens
- ensure all health workers operate in a safe environment
- rapidly share evidence from research to inform national and global TB policy updates.

Protecting human rights, ethics and equity are principles which underpin WHO's End TB Strategy. But it is not easy to apply these principles on the ground. Patients, communities, health workers, policy makers and other stakeholders frequently face conflicts and ethical dilemmas. The current multidrug-resistant TB (MDR-TB) crisis and the health security threat it poses accentuate the situation even further.

"Only when evidence-based, effective interventions are informed by a sound ethical framework, and respect for human rights, will we be successful in reaching our ambitious goals of ending the TB epidemic and achieving universal health coverage. The SDG aspiration of leaving no one behind is centred on this," said Dr Mario Raviglione, Director, WHO Global TB Programme.

"The guidance we have released aims to identify the ethical predicaments faced in TB care delivery, and highlights key actions that can be taken to address them," he added.

on the WEB Ethics guidance for the implementation of the End TB Strategy
www.who.int/tb/publications/2017/ethics-guidance

Global Patient Safety Challenge on Medication Safety launched

WHO has launched a global initiative to reduce severe, avoidable medication-associated harm in all countries by 50% over the next 5 years.

The Global Patient Safety Challenge on Medication Safety aims to address the weaknesses in health systems that lead to medication errors and the severe harm that results. It lays out ways to improve the way medicines are prescribed, distributed and consumed, and increase awareness among patients about the risks associated with the improper use of medication.

Medication errors cause at least one death every day and injure approximately 1.3 million people annually in the United States alone. While low- and middle-income countries are estimated to have similar rates of medication-related adverse events to high-income countries, the impact is about twice as much in terms of the number of years of healthy life lost. Many countries lack good data, which will be gathered as part of the initiative.

Globally, the cost associated with medication errors has been estimated at US$42 billion annually or almost 1% of total global health expenditure.

Both health workers and patients can make mistakes that result in severe harm, such as ordering, prescribing, dispensing,

preparing, administering or consuming the wrong medication or the wrong dose at the wrong time. But all medication errors are potentially avoidable. Preventing errors and the harm that results requires putting systems and procedures in place to ensure the right patient receives the right medication at the right dose via the right route at the right time.

Medication errors can be caused by health worker fatigue, overcrowding, staff shortages, poor training and the wrong information being given to patients, among other reasons. Any one of these, or a combination, can affect the prescribing, dispensing, consumption, and monitoring of medications, which can result in severe harm, disability and even death.

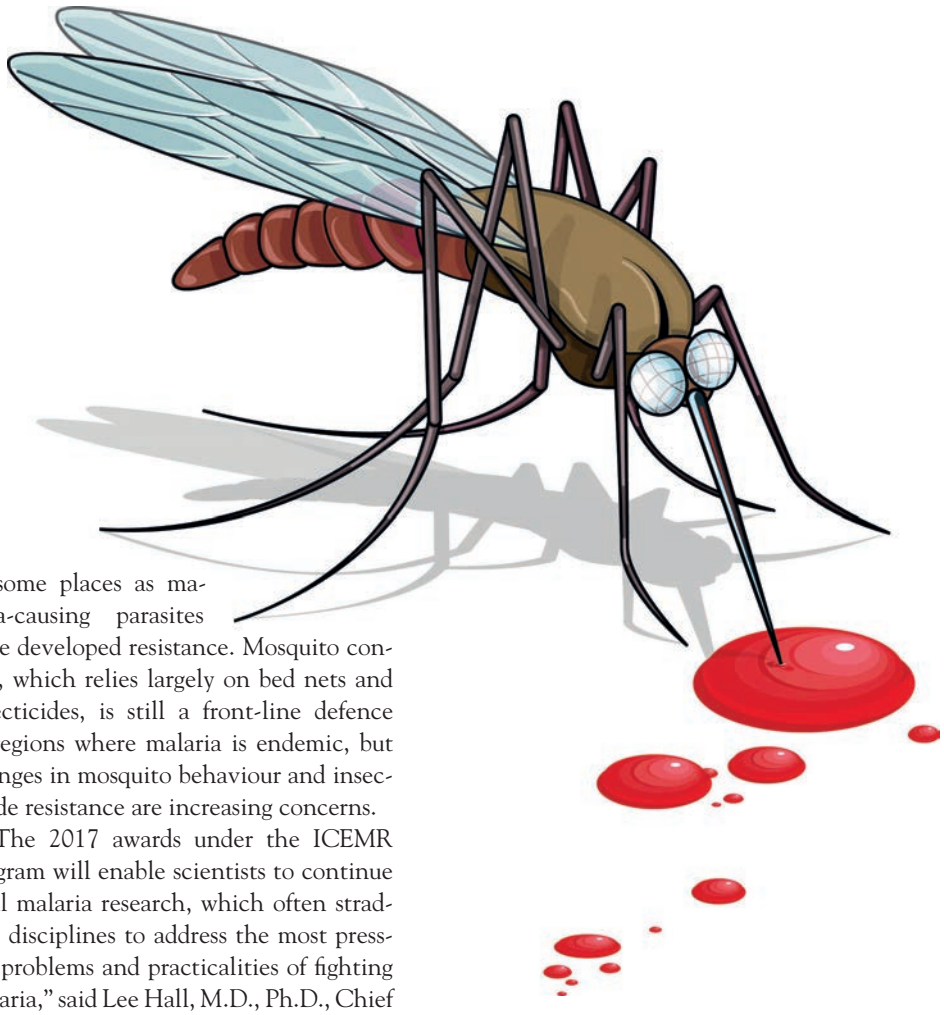
Most harm arises from systems failures in the way care is organized and coordinated, especially when multiple health providers are involved in a patient's care. An organizational culture that routinely implements best practices and that avoids blame when mistakes are made is the best environment for safe care.

The Challenge calls on countries to take early priority action to address these key factors: including medicines with a high risk of harm if used improperly; patients who take multiple medications for different diseases and conditions; and patients going through transitions of care, in order to reduce medication errors and harm to patients.

The actions planned in the Challenge will be focused on four areas: patients and the public; health care professionals; medicines as products; and systems and practices of medication. The Challenge aims to make

improvements in each stage of the medication use process including prescribing, dispensing, administering, monitoring and use. WHO aims to provide guidance and develop strategies, plans and tools to ensure that the medication process has the safety of patients at its core, in all health care facilities.

This challenge is WHO's third global patient safety challenge, following the Clean Care is Safe Care challenge on hand hygiene in 2005 and the Safe Surgery Saves Lives challenge in 2008.



US NIAID funds international malaria research centres

The US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, announced approximately US$9 million in first-year funding, subject to availability, for seven malaria research centres around the world. The 7-year awards continue NIAID's 2010 program that created the International Centers of Excellence for Malaria Research (ICEMRs) in regions where malaria is endemic. The awards fund three new and four existing centres that work in 14 countries in Africa, Asia and Latin America.

"NIAID-supported ICEMRs have made significant contributions to malaria research since their creation in July 2010," said NIAID Director Anthony S. Fauci, M.D. "We look forward to their continued multidisciplinary efforts to further our understanding of the complex interactions between human hosts, mosquito vectors and the Plasmodium parasites that cause malaria, so that we may work toward controlling, eliminating and eventually eradicating this global scourge."

Despite significant progress in reducing malaria incidence and mortality, the World Health Organization estimates that 212 million new cases of malaria and 429,000 malaria deaths occurred in 2015, mostly in Africa. Although numerous vaccine candidates to prevent malaria are in development, none have been approved for widespread use. Effective malaria drugs are available, but some have severe side effects, may be difficult to procure in remote regions, and are losing their effectiveness in some places as malaria-causing parasites have developed resistance. Mosquito control, which relies largely on bed nets and insecticides, is still a front-line defence in regions where malaria is endemic, but changes in mosquito behaviour and insecticide resistance are increasing concerns.

"The 2017 awards under the ICEMR program will enable scientists to continue vital malaria research, which often straddles disciplines to address the most pressing problems and practicalities of fighting malaria," said Lee Hall, M.D., Ph.D., Chief of NIAID's Parasitology and International Programs Branch.

Under the previous awards, ICEMR researchers found evidence that some current rapid diagnostic tests are failing to detect malaria in some regions because malaria parasites do not always express the antigen the test is designed to detect. ICEMR research also has confirmed a significant shift in the behaviour of some malaria-carrying mosquitoes, perhaps in response to malaria control measures. Malaria is typically transmitted by Anopheles mosquitoes biting indoors late at night, but more mosquitoes now appear to be biting outdoors and earlier in the evening, when people are not sleeping under protective bed nets.

The recipients of the ICEMR awards announced today are as follows:

- Amazonian Center of Excellence in Malaria Research. Lead Institution: University of California, San Diego.
- Multidisciplinary Research for Malaria Control and Prevention in West Africa*. Lead Institution: University of Sciences, Techniques & Technologies of Bamako, Bamako, Mali.
- Malaria Transmission and the Impact of Control Efforts in Southern and Central Africa. Lead Institution: Johns Hopkins Bloomberg School of Public Health, Baltimore.
- Program for Resistance, Immunology, Surveillance & Modeling of Malaria in Uganda (PRISM). Lead Institution: University of California, San Francisco.
- Environmental Modifications in sub-Saharan Africa: Changing Epidemiology, Transmission and Pathogenesis of Plasmodium falciparum and P. vivax Malaria*. Lead Institution: University of California, Irvine.
- Southeast Asia Malaria Research Center. Lead Institution: Pennsylvania State University, University Park.
- Myanmar Regional Center of Excellence for Malaria Research*. Lead Institution: University of Maryland School of Medicine, Baltimore.

*This is a new ICEMR institution. MEH

the laboratory

Medical research news from around the world

Photo by James McEntee

Kendall Nettles, TSRI Associate Professor

Researchers discover key to drug resistance in common breast cancer treatment

Three-quarters of all breast cancer tumours are driven by the hormone oestrogen. These tumours are frequently treated with drugs to suppress oestrogen receptor activity, but unfortunately, at least half of patients do not respond to these treatments, leaving them with drug-resistant tumours and few options.

Now, scientists from the Florida campus of The Scripps Research Institute (TSRI), the University of California (UC), San Diego and the University of Illinois have found that two immune system molecules may be key to the development of drug resistance in oestrogen-driven breast cancers. The researchers believe this finding may open the door to novel therapeutic approaches and influence treatment decisions for the tens of thousands of patients who suffer from oestrogen-driven breast cancers.

These molecules, which are cytokines called interleukin 1 beta (IL1) and tumour necrosis factor alpha (TNF), had previously been linked to the spread of drug-resistant cancer, but scientists were unsure of the exact mechanisms that led these molecules to drive drug resistance.

The study published in the journal *Molecular Cell*, reveals that IL1 and TNF turn on pathways that modify the actual shape of the oestrogen receptor. This phenomenon appears to drive resistance to the common anti-cancer drug tamoxifen.

"Cytokines change the shape of the oestrogen receptor, and that change overrides the inhibitory effects of tamoxifen and leads to drug resistance," said TSRI Associate Professor Kendall Nettles, who led the new study alongside senior author Christopher K. Glass and study first author Joshua D. Stender of UC San Diego. "These findings dramatically alter our understanding of the biological actions of pro-inflammatory cytokines in breast cancer cells."

Using a combination of genomic, cellular, biochemical and structural approaches, the researchers found that the way these cytokines alter the oestrogen receptor are sufficient to induce growth of breast cancer cells in the absence of oestrogen, precisely what happens when breast cancer is initially treated with an endocrine therapy like tamoxifen. Scientists found that in addition to reversing tamoxifen suppression of growth, cytokine activation of the oestrogen receptor also enhanced the invasive properties of a specific line of human breast cancer cells known as MCF-7, the most studied human breast cancer cell in in the world.

Using x-ray crystallography, Prof. Nettles and his colleagues developed an atomic snapshot of the oestrogen receptor to show how these shape changes occur and how the process might be blocked.

Nettles pointed out that both inflammation and immune cells are known causes of resistance, but if that inflammation can be blocked, resistance can be reduced or eliminated.

"These tumours can reprogram the immune cells to their advantage so that the cells become tumour supportive," Prof. Nettles said. "We think we can produce hormone therapies that can, in essence, re-reprogram the immune system or prevent it from altering the receptor in the first place, which is an obvious strategy for blocking these adverse effects. Importantly, our atomic snapshot of the receptor showed that the same mechanism can explain how Her2Neu or other growth promoting factors, as well as certain invasion and motility signals also cause resistance to anti-hormone therapies."

• **doi:** 10.1016/j.molcel.2017.02.008

New understanding of blood-brain barrier

US National Institutes of Health researchers studying zebrafish have determined that a population of cells that protect the brain against diseases and harmful substances are not immune cells, as had previously been thought, but instead likely arise from the lining of the circulatory system.

This basic science finding may have implications for understanding age-related decline in brain functioning and how HIV infects brain cells.

The study, appears online in *eLife*, was conducted by researchers at NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and National Human Genome Research Institute and the Japanese National Institute of Genetics.

The blood-brain barrier is the layer of cells that line the blood vessels of the brain. The inner cell layer that lines vessels, known as the endothelium, is present in all the blood vessels of the body. Within the blood vessels of the brain, endothelial cells and other adjacent cells form a tight barrier that helps to prevent toxins and microbes from entering the brain. Although their function is not completely understood, a special population of cells covering the blood vessels on the brain's surface is thought to contribute to the organ's protection. The cells act as sentries, engulfing toxins, cellular wastes and microbes and then encasing them in sphere-like structures called vesicles. These sentry cells are called fluorescent granular perithelial cells (FGPs) because the vesicles they contain give off a yellow glow in the presence of light.

In the current study, the researchers showed that FGPs are present on the surface of the zebrafish brain and that these blood vessel-associated FGPs do not arise

from the immune system, as had been previously thought, but from endothelial cells themselves.

FGPs are thought to be important in a variety of human brain disorders and conditions. These cells appear to be a major entry point for HIV infection of the brain. Age-related decline in cognitive function is associated with a decline in the scavenging function of FGPs. "Learning more about how FGPs function may lead to a greater understanding of dementia and other conditions," said the study's senior author, Brant Weinstein, Ph.D., of NICHD's Section on Vertebrate Organogenesis.

The Weinstein lab studies zebrafish to understand how the blood and lymphatic systems develop. Because the young fish are transparent, it is possible to see the developing circulatory system while observing the fish under a light microscope. As part of this effort, Dr Weinstein and his colleagues inserted a gene for a protein that turns green into the cells that line the endothelium of selected embryonic veins and in the lymphatic system -- the network of vessels through which immune cells travel in the body. In addition to seeing green lymphatic cells in the zebrafish embryos, the researchers noticed that green cells also covered the surface of the tiny fish's brains.

Upon closer inspection, the researchers tentatively identified these cells as FGPs. Because they turned green, it was apparent that they arose from endothelial cells. Until the current study, FGPs were thought to be macrophages, a type of immune cell. The researchers conducted additional experiments to confirm the origins of the FGPs, including analysing what proteins were being made by their DNA. These proteins most closely resembled those made by endothelial cells in the lymphatic system, not the proteins made by macrophages or other immune cells. In another series of experiments, they inserted a green fluorescent protein into the tissues that give rise to blood and lymph vessels in embryonic zebrafish. Using time lapse photography, the researchers captured images of FGPs arising from the vessels' endothelium. When zebrafish with the green fluorescing endothelial gene matured, the researchers observed green FGPs on the surface of the fish's brains -- confirming that these cells arose from endothelial tissue.

The researchers hope to conduct further studies of how FGPs interact with blood vessels and the blood-brain barrier.

Diabetes damages small blood vessels around heart, ups risk of heart attack

Diabetics have a significantly higher risk of suffering a heart attack. A research team at the Technical University of Munich (TUM) has now identified one of the causes: Diabetes is associated with the loss of small blood vessels around the heart. This in turn affects the entire cardiac muscle. A genetic therapy that promotes the growth of blood vessels may offer a remedy.

The coronary vessels can be compared to a road network. Veins and arteries form the main transportation routes, with countless small and minuscule connecting roads and access pathways branching off from them. If one of these little pathways is blocked, it has very little impact on the overall traffic flow. But if enough of the off-ramps are closed, the traffic on the main highway becomes very dense. In a worst-case scenario, the entire system comes to a standstill: a heart attack.

A team headed by TUM has found out that diabetes can lead to these very conditions. The scientists working with Dr Rabea Hinkel and Prof. Christian Kupatt, cardiologists at TUM's Klinikum rechts der Isar, have reported their results in the *Journal of the American College of Cardiology*.

In their research they compared blood vessels of patients with and without diabetes undergoing heart transplants. The conclusion: The samples from diabetics showed significantly reduced numbers of small blood vessels around the heart.

In the laboratory the team was able to show that elevated blood sugar levels are associated with a loss of cells known as pericytes. "These cells normally form a layer wrapped around the small blood vessels," explains Hinkel. "We believe that this layer has a stabilizing function. When it is damaged, the entire blood vessel becomes unstable and ultimately breaks up."

Animal experiments confirmed the assumption of a steady decrease in capillary density around the heart when diabetes is left untreated. "Diabetes often remains undetected in patients for years or even decades. Over that long period, massive damage can occur," says Hinkel.

The loss of capillaries is not irreversible, however. In their study, Hinkel and Kupatt applied a genetic therapy to stimulate heart cells to increase production of the molecule thymosin beta 4, a protein whose effects include stimulating the growth of pericytes. In this way, the team at TUM was able to induce the growth of lasting and functional capillary networks.

"It will be a while before this kind of therapy can be used in humans," says Christian Kupatt. "But we were able to show for the first time in a transgenic large animal model, which closely models human type I diabetes mellitus, how diabetes damages the heart. That opens up new perspectives for treating patients. It also further reinforces our awareness of how important it is to diagnose diabetes early."

• **doi:** 10.1016/j.jacc.2016.10.058.

Link between herpes virus and brain cancer disputed with new study

In a rigorous study of tumour tissue collected from 125 patients with aggressive brain cancers, researchers at Johns Hopkins say they have found no evidence of cytomegalovirus (CMV) infection and conclude that a link between the two diseases, as claimed by earlier reports, likely does not exist.

As early as 2002, the Johns Hopkins team says, several studies reported that tumour cells isolated within glioblastomas and other gliomas were infected with CMV, a herpes virus that infects more than half of all adults by age 40 and is related to viruses that cause chickenpox and mononucleosis.

The Johns Hopkins team cautioned that studies to confirm their finding are needed to absolutely rule out any role for the common

CMV in glioblastoma and other cancers that arise in neurological support cells called glial cells. But they say their study substantially weakens the likelihood of that role.

"We have found no evidence of CMV in these tissues, and if there is no virus, targeting that virus to affect cancer using antiviral drugs or tailored vaccines doesn't make biological sense," says Angelo M. De Marzo, M.D., Ph.D., professor of pathology, oncology and urology at the Johns Hopkins Kimmel Cancer Center.

A report on the research was published December 29, 2016 in *Clinical Cancer Research*.

Because other viruses are associated with some cancers, notably HPV, which causes most cervical and some head and neck cancers; and Epstein-Barr virus, which causes some lymphomas, those earlier findings generated excitement about the potential for antiviral therapies to improve the usually poor outlook for people with gliomas.

However, explains Matthias Holdhoff, M.D., Ph.D., associate professor of oncology and neurosurgery at the Johns Hopkins Kimmel Cancer Center, other laboratories found no evidence of the virus in these types of tumours. "Significant resources have already gone into this field of study," he says, "making it very important to definitively answer the question of whether there's an association between CMV and gliomas or not."

- **doi:** 10.1158/1078-0432.CCR-16-1490

Insomnia associated with increased risk of heart attack and stroke

Insomnia is associated with increased risk of heart attack and stroke, according to research published March 31, 2017 in the *European Journal of Preventive Cardiology*.

"Sleep is important for biological recovery and takes around a third of our lifetime, but in modern society more and more people complain of insomnia," said first author Qiao He, a Master's degree student at China Medical University, Shenyang, China. "For example, it is reported that approximately one-third of the general population in Germany has suffered from insomnia symptoms."

"Researchers have found associations between insomnia and poor health outcomes," continued He. "But the links between insomnia and heart disease or stroke have been inconsistent."

The current meta-analysis assessed the association between insomnia symptoms and incidence or death from cardiovascular disease (acute myocardial infarction, coronary heart disease, heart failure), stroke, or a combination of events. Insomnia symptoms included difficulty initiating sleep, difficulty maintaining sleep, early-morning awakening, and non-restorative sleep.

The authors analysed 15 prospective cohort studies with a total of 160,867 participants. During a median follow-up of three to 29.6 years, there were 11,702 adverse events.

There were significant associations between difficulty initiating sleep, difficulty maintaining sleep, and non-restorative sleep and the risk of heart disease and stroke, with increased relative risks of 1.27, 1.11, and 1.18, respectively, compared to those not experiencing these insomnia symptoms. There was no association between early-morning awakening and adverse events.

He said: "We found that difficulty initiating sleep, difficulty maintaining sleep, or non-restorative sleep were associated with 27%, 11%, and 18% higher risks of cardiovascular and stroke events, respectively.

"The underlying mechanisms for these links are not completely understood," continued He. "Previous studies have shown that insomnia may change metabolism and endocrine function, increase sympathetic activation, raise blood pressure, and elevate levels of proinflammatory and inflammatory cytokines – all of which are risk factors for cardiovascular disease and stroke."

Women with insomnia symptoms had a slightly higher risk of cardiovascular and stroke events than men, especially for non-restorative sleep, but the difference between sexes did not reach statistical significance.

He said: "We cannot conclude that insomnia is more dangerous for women, given the limitations of meta-analyses and the lack of a statistically significant difference between sexes. However, we do know that women are more prone to insomnia because of differences in genetics, sex hormones, stress, and reaction to stress. It may therefore be prudent to pay more attention to women's sleep health."

He concluded: "Sleep disorders are common in the general population and sleep health should be included in clinical risk assessment. Health education is needed to increase public awareness of insomnia symptoms and the potential risks, so that people with sleep problems are encouraged to seek help."

- **doi:** 10.1177/2047487317702043

Monoclonal antibody cures Marburg infection in monkeys

Scientists funded by the US National Institutes of Health have found that an experimental treatment cured 100% of guinea pigs and rhesus monkeys in late stages of infection with lethal levels of Marburg and Ravn viruses, relatives of the Ebola virus. Although the Marburg and Ravn viruses are less familiar than Ebola virus, both can resemble Ebola in symptoms and outcomes in people, and both lack preventive and therapeutic countermeasures.

The study involved giving the animals a therapeutic candidate, MR191-N, which is a monoclonal antibody derived from a person who survived Marburg disease. Monoclonal antibodies are immune system fighters designed to bind to a specific part of an invading virus or bacterium to treat disease. The authors report that two doses of MR191-N were able to confer protection of up to 100% when treatment was started up to 5 days post infection. Prior studies of different experimental Marburg treatments involved daily dosing for 7 and 14 days, respectively, with treatment beginning closer to the time of infection.

The study was led by scientists at the University of Texas Medical Branch Galveston National Laboratory and Mapp Biopharmaceutical, Inc., and included collaborators from Vanderbilt University Medical Center, the University of Natural Resources and Life Sciences in Austria, and The Scripps Research Institute. The NIH's National Institute of Allergy and Infectious Diseases (NIAID) provided project funding.

The researchers are now working with NIAID's preclinical services group to perform the additional safety testing necessary to advance the monoclonal antibody treatment to initial human clinical studies. Public health workers learned during the 2014-15 Ebola outbreak in West Africa that lack of available treatment options kept diseased and at-risk people away from treatment centres, making disease tracking and outbreak containment more difficult. They fear the same situation would develop in a large-scale Marburg outbreak.

• **doi:** 10.1126/scitranslmed.aai8711

New 'gene silencer' drug reduces cholesterol by over 50%

The first in a new class of gene-silencing drugs, known as inclisiran, has been shown to halve cholesterol levels in patients at risk of cardiovascular disease.

The findings come from the largest trial yet to test the safety and effectiveness of this kind of therapy. The technique, known as RNA interference (RNAi) therapy, essentially 'switches off' one of the genes responsible for elevated cholesterol.

Researchers from Imperial College London and their colleagues, who conducted the trial, say the twice-a-year treatment could be safely given with or without statins, depending on individual patient needs. Eventually, inclisiran could help to reduce the risk of heart attacks and stroke related to high cholesterol.

"These initial results are hugely exciting for patients and clinicians," said Professor Kausik Ray, lead author of the study from the School of Public Health at Imperial.

"We appear to have found a versatile, easy-to-take, safe, treatment that provides sustained lowering of cholesterol levels and is therefore likely to reduce the risk of cardiovascular disease, heart attacks, and stroke. These reductions are over and above what can be already be achieved with statins alone or statins plus ezetemibe, another class of cholesterol-lowering drug.

Elevated levels of low-density lipoprotein (LDL) cholesterol can lead to cardiovascular disease and blood vessel blockage, leading to an increased risk heart attacks and stroke in patients.

Statins are currently the standard treatment for high cholesterol, combined with exercise and healthy diet, as they reduce levels in the blood and therefore help to prevent heart attacks and stroke.

However, some patients are unable to tolerate the highest doses and they need.

Now, this new phase 2 clinical trial has confirmed the effectiveness of injecting inclisiran for reducing cholesterol that can be taken alone or potentially combined with statins for maximum effect.

In the study, researchers gave 497 patients with high cholesterol and at high risk of cardiovascular disease either inclisiran at varying doses, or placebo. Seventy-three per cent of these patients were already taking statins, and 31% were taking ezetimibe. Participants, who were recruited from Canada, USA, Germany, Netherlands, and the UK, were excluded if they were taking monoclonal antibodies for cholesterol lowering.

Patients were given different doses of inclisiran or placebo via subcutaneous injection, either via a single dose, or via a dose on day one and another at three months. They were followed up regularly for a subsequent eight months and tested for blood cholesterol and side effects.

The researchers found that just one month after receiving a single treatment of inclisiran, participants' LDL cholesterol levels had reduced by up to 51%.

In those on a single dose of 300 mg, cholesterol levels were reduced by 42% at six months. In the matched placebo group, cholesterol levels had increased by two per cent within that time frame.

In those on two doses of 300 mg, cholesterol levels were reduced by up to 53% at six months. Moreover, cholesterol levels had gone down for all patients in this group, and 48% of them had achieved cholesterol levels (below 50 mL/dL).

In all patients, cholesterol levels stayed lower for at least eight months. No extra side effects were seen in the study group compared to the placebo group.

The study will follow up patients for a further four months (one year total follow up). The results from this trial, known as ORION-1, are published in the *New England Journal of Medicine*.

The authors say the results show the drug acts quickly to reduce cholesterol levels by as early as two weeks post-injection, while also giving a prolonged effect when given in two doses over a year. Therefore, the next step is to conduct an extended study, using more patients and for a longer period of time, to determine whether these reductions in cholesterol translate into a reduction in heart attacks and strokes.

Aside from its effectiveness, the authors point out that because inclisiran acts on a different biological pathway to statins, the two drugs would likely be combined for the best results.

• doi: 10.1056/NEJMoa1615758

Newer medications cure HCV infections

A new analysis reveals a dramatic transformation in the care of patients infected with hepatitis C virus (HCV) as more effective and tolerable medications have become available.

In an analysis of all HCV antiviral treatment regimens (N=107,079) initiated from 1999 through 2015 in the US Veterans Affairs national healthcare system, cure rates increased steadily from 19.2% in 1999 to 36.0% in 2010 before a remarkable increase to 90.5% in 2015. The number of patients achieving sustained virologic response was 1313 in 2010, the last year of the interferon era and increased 5.6-fold to 7377 in 2014 and 21-fold to 28,084 in 2015.

"The introduction of effective direct antiviral agents together with the allocation of appropriate funds and resources allowed the VA healthcare system to treat and cure hepatitis C in unprecedented numbers. In fact, out of approximately 57,500 patients cured of hepatitis C in the VA since 1999, approximately half were cured in a single year in 2015," said Dr George Ioannou, senior author of the Alimentary Pharmacology and Therapeutics analysis.

"The question is whether we are delivering these medications to the patients who need them and what obstacles there are to treating and curing the majority of hepatitis C infected patients."

• doi: 10.1111/apt.14021 MEH

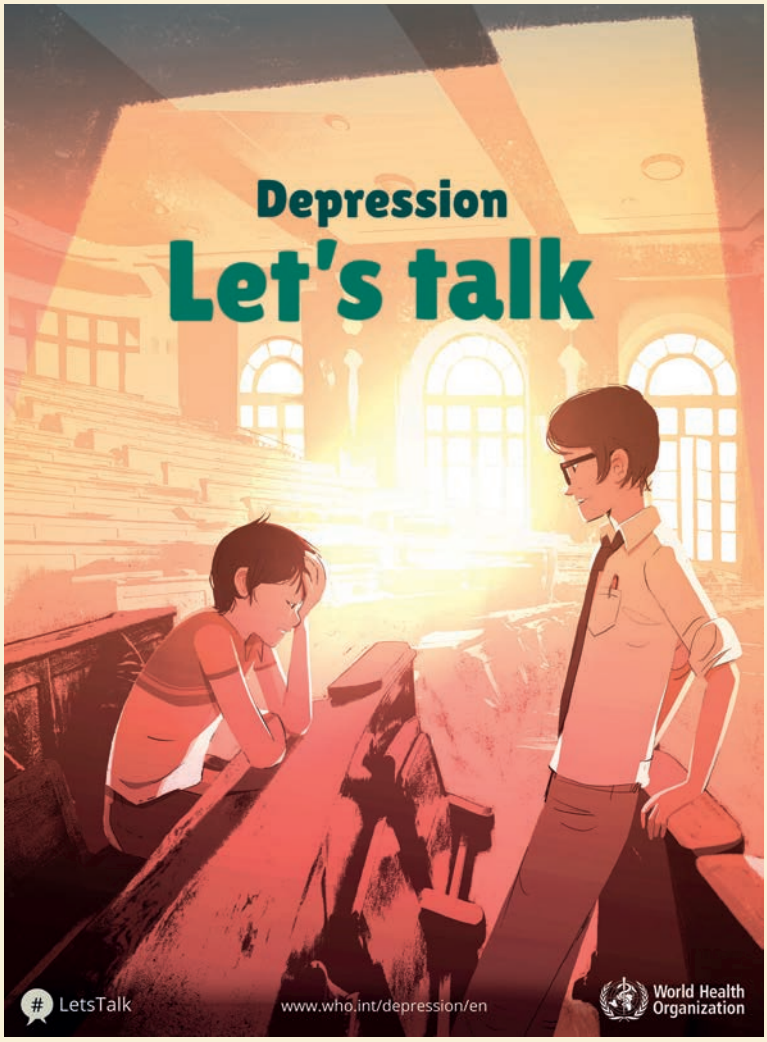
More than 300 million affected by depression worldwide

In an effort to raise global awareness of depression, it was made the core theme of the 2017 World Health Day campaign – held on 7 April.

Depression is a common illness worldwide, with more than 300 million people affected. Depression is different from usual mood fluctuations and short-lived emotional responses to challenges in everyday life. Especially when long-lasting and with moderate or severe intensity, depression may become a serious health condition. It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. Close to 800,000 people die due to suicide every year. Suicide is the second leading cause of death in 15-29-year-olds.

Although there are known, effective treatments for depression, fewer than half of those affected in the world (in many countries, fewer than 10%) receive such treatments, according to the WHO. Barriers to effective care include a lack of resources, lack of trained healthcare providers, and social stigma associated with mental disorders. Another barrier to effective care is inaccurate assessment. In countries of all income levels, people who are depressed are often not correctly diagnosed, and others who do not have the disorder are too often misdiagnosed and prescribed antidepressants.

The burden of depression and other mental health conditions is on the rise globally. A World Health Assembly resolution passed in May 2013 has called for a comprehensive, coordinated response to mental disorders at country level. MEH



What is depression?

Depression is an illness characterized by persistent sadness and a loss of interest in activities that you normally enjoy, accompanied by an inability to carry out daily activities, for at least two weeks. In addition, people with depression normally have several of the following symptoms: a loss of energy; a change in appetite; sleeping more or less; anxiety; reduced concentration; indecisiveness; restlessness; feelings of worthlessness, guilt, or hopelessness; and thoughts of self-harm or suicide.

Helping Syrians cope with depression

A psychotherapist at a mental health centre near the Syrian border shows materials she adapts when working with Syrian refugees.

"We call depression the black snowball," says B. Hussain*, a psychologist at a mental health centre in the southeastern Turkish city of Gaziantep. Hussain works with some of the nearly 3 million Syrian refugees that have escaped to Turkey and been granted shelter there since the crisis in their country began.

Like most refugees worldwide, Syrians now living in Turkey are under tremendous psychological stress. During years of conflict, many have lost loved ones, their homes, their livelihoods and certainty about their futures. After escaping bombs or sniper fire, they suffer from anxiety, post-traumatic stress disorder and other psychological illnesses.

But for some refugees, the suffering they have experienced builds up, and the black snowball gets bigger. It can lead to serious depression. For those who were already predisposed to depression before the crisis, the danger is even greater.

Isolated and withdrawn

Hussain describes a Syrian man in his early 30s who arrived in Turkey alone. "He already had a tendency to be depressed," says Hussain. "And he lost a lot of friends – they were killed in Syria. He found himself here with no friends, nothing. He became severely isolated and withdrawn."

Somehow, he made his way to the mental health centre where Hussain works. "He said, 'I'll give you 5 sessions. If it doesn't work, I'll commit suicide.'"

Helping troubled Syrians

Hussain and others have help from WHO to supplement their own education and experience. In Turkey and in northern Syria, WHO provides materials, training and other support to mental health groups and professionals.

"There are only 2 psychiatrists right now in northern Syria. It's a huge gap," says Dr Fuad Almosa, a psychiatrist based in Gaziantep who, like Hussain, is part of a WHO working group on mental health for Syrians. "So when you bring 37 trained doctors, it really helps." Almosa is referring to 37 doctors in northern Syria who were trained last year in WHO's Mental Health Gap Action Programme (mhGAP), a programme to identify and treat psychological disorders including depression. The trained doctors receive online clinical supervision and follow-up help.

WHO provides mhGAP training to Syrian doctors now living in Turkey. In parts of Turkey hosting many Syrian refugees, WHO is working to ensure that primary health care centres specifically created for the refugees are each staffed by 2 mental health experts.

"When patients come to me with psychological problems, I usually refer them," says a family physician who works near the border with Syria and who was trained in mhGAP in March 2017. "But I know sometimes people can't go to where I am referring them – they don't even have the money to take a bus. After this training, I decided that I would try to help them."

WHO also trains community members who can be a first line of defence in helping depressed Syrians. Community health workers in besieged areas of Syria have received online training in psychological first aid – in some cases, despite aerial attacks.

"With psychological first aid, the trainees are not providing therapy," explains Almosa. "But they learn about the services available nearby, and link a person to those services."

Almosa supervises mental health work in 8 clinics in northern Aleppo. For him, "the most valuable part of mhGAP training was that it 'demedicalized' mental health. We see the patient as not just a biological being, but a social one," he explains. "This reduces stigma."

Adapting mental health services to the culture

Almosa says that mental health workers in northern Syria are using approaches that are acceptable in their culture.

"Certain health approaches were not acceptable. For example, there was a mental health centre near a huge prison. That stigmatizes it. It's better when you provide service near the people," he says. "You become nearer to the community. It's not like in the past, when mental health was isolated."

As part of this approach, WHO plans to fund a mental health centre in a Syrian town called Sarmada in Idleb, as well as a mental health mobile clinic that "will reach far-flung villages", according to Dr Manuel de Lara, Public Health Officer for WHO. The centre and clinic will be staffed by trained professionals from Hussain's group, the Union of Medical Care and Relief Organizations (UOSSM), a WHO health partner. "It will be a mental health rapid response team," explains de Lara. "If there are acutely ill patients, they can be taken immediately to the mental health centre in Sarmada, or referred into Turkey itself."

In a city called Kilis, near the border with Syria, an organization that is part of WHO's working group has 10 community mental health workers who conduct door-to-door outreach. The teams often start by simply saying, "Hello, how are you?"

Planning for the future

Mental health workers also vary their approaches based on other needs. Sometimes group therapy is effective. Therapy for children must be specially tailored. In Gaziantep, another UOSSM psychologist uses cognitive behavioural therapy (CBT) when working with some depressed Syrian refugees.

Despite immense obstacles, the members of WHO's working group have been able to help thousands of people inside Syria and thousands of refugees in Turkey. The suicidal young man Hussain treated is "back to his normal life: he has plans for the future, new friends, a new job and fiancée," according to Hussain.

Challenges remain, such as how to provide the best care for depressed Syrians who live in Turkey's refugee camps. The toll of the Syrian conflict is immense and will be long-lasting, say experts. "Right now, Syrians are in survival and denial mode," says Hivin Kako of Bihar Relief. "After the conflict stops, we'll need an army of psychological experts."

De Lara agrees that the stakes are high for Syrians who have endured so much emotional suffering. "If no mental health services are provided now," he warns, "we'll lose the future."

*Full name withheld on request.

• This report was originally published by the World Health Organisation on 30 March 2017.

Gene therapy trial results in complete remission of sickle cell disease

A gene therapy trial in a 13-year-old patient with sickle cell disease has enabled complete remission of clinical signs of disease and correction of biological indicators.

Results of the trial begun in October 2014 are published in the 2 March 2017 issue of *New England Jounal of Medicine*.

Prof. Marina Cavazzana lead the team that conducted the research at Necker Children's Hospital, AP-HP and the Imagine Institute (AP-HP / Inserm / Université Paris Descartes. The study was conducted in collaboration with Prof. Philippe Leboulch (CEA / University Faculties of Medicine of Paris-Sud and Harvard University) who developed the vector used and directed preclinical studies.

Sickle cell disease is characterized by the production of an abnormal haemoglobin and deformed (sickle-shaped) erythrocytes, due to a mutation in the gene encoding the β-globin. This disease causes episodes of very severe pain caused by vaso-occlusive crises. It also causes lesions of all vital organs, sensitivity to infections, as well as iron overload and endocrine disorders. It is estimated that hemoglobinopathies affect 7% of the world population. Among them, sickle cell disease is considered the most common with 50 million people carrying the mutation.

The first phase of the trial consisted of collecting hematopoietic stem cells, enabling the production of all the lineages of blood cells, in the bone marrow of the patient. A vector1 virus carrying a therapeutic gene, already developed to treat beta-thalassemia, was then introduced into these cells.

This lentiviral vector capable of carrying long complex DNA segments, was developed by Prof Leboulch.

The treated cells were then reinjected intravenously into the young patient in October 2014. The teenager was then supported during his hospitalization in the paediatric immunohaematology service of the Necker Children's Hospital.

Fifteen months after transplantation of genetically corrected cells, the patient no longer needs to be transfused, no longer suffers from vaso-occlusive crises, and has fully resumed his physical and school activities, the researchers noted.

"We also note that the expression of the therapeutic protein from the vector, which inhibits pathological sickle cell formation, is remarkably strong and effective," said Prof Leboulch.

Prof Cavazzana said: "We hope, with this gene therapy approach, to develop future clinical trials and include a significant number of patients with sickle cell disease."

• **doi**: 10.1056/NEJMoa1609677 MEH

Sickle cell disease in Arab states

Sickle cell disease is highly prevalent in the Arab states. Some of the world's highest frequencies of the disease are seen in Saudi Arabia (5.2%), Oman (3.8%), UAE (1.9%). Lower values are observed in Yemen (0.95%), Bahrain (0.7%), and other Arab countries. Studies in population genetics revealed that the extent of clinical severity in sickle cell disease is related to the genetic back- ground (haplotype) of the affected individual. In the Arabian Peninsula, sickle cell disease occurs in association with two backgrounds: the African haplotype, a severe type, mostly occurring in patients residing in the western regions of the Arabian Peninsula, and the Arabian/Asian haplotype, a moderate type, mostly occurring in patients residing in the eastern regions of the Arabian Peninsula. The high prevalence of the disease has prompted extensive studies on it, and almost all Arab countries have undertaken vast amounts of work on the clinical features, genetics, and management of sickle cell disease. Several Arab states have taken extensive measures to reduce the rates of sickle cell disease. Screening programs are one of the most effective of such strategies. Especially in the countries of the Gulf Cooperation Council (GCC), screening of students, infants, and mandatory screening of couples before their marriage have been very effective.

• Centre for Arab Genomic Studies

1.7 million children die each year from a polluted environment

More than 1 in 4 deaths of children under 5 years are attributable to unhealthy environments. Every year, environmental risks – such as indoor and outdoor air pollution, second-hand smoke, unsafe water, lack of sanitation and inadequate hygiene – take the lives of 1.7 million children under 5 years, say two new World Health Organization (WHO) reports.

The first report, *Inheriting a Sustainable World: Atlas on Children's Health and the Environment* reveals that a large portion of the most common causes of death among children aged 1 month to 5 years – diarrhoea, malaria and pneumonia – are preventable by interventions known to reduce environmental risks, such as access to safe water and clean cooking fuels.

"A polluted environment is a deadly one – particularly for young children," says Dr Margaret Chan, WHO Director-General. "Their developing organs and immune systems, and smaller bodies and airways, make them especially vulnerable to dirty air and water."

Harmful exposures can start in the mother's womb and increase the risk of premature birth. Additionally, when infants and preschoolers are exposed to indoor and outdoor air pollution and second-hand smoke they have an increased risk of pneumonia in childhood, and a lifelong increased risk of chronic respiratory diseases, such as asthma. Exposure to air pollution may also increase their lifelong risk of heart disease, stroke and cancer.

Emerging environmental threats

"A polluted environment results in a heavy toll on the health of our children," says Dr Maria Neira, WHO Director, Department of Public Health, Environmental and Social Determinants of Health. "Investing in the removal of environmental risks to health, such as improving water quality or using cleaner fuels, will result in massive health benefits."

For example, emerging environmental hazards, such as electronic and electrical waste (e.g. old mobile phones) that is improperly recycled, expose children to toxins which can lead to reduced intelligence, attention deficits, lung damage and cancer. The generation of electronic and electrical waste is forecasted to increase by 19% between 2014 and 2018, to 50 million metric tonnes by 2018.

With climate change, temperatures and levels of carbon dioxide are rising, favouring pollen growth which is associated with increased rates of asthma in children. Worldwide, 11-14% of children aged 5 years and older currently report asthma symptoms and an estimated 44% of these are related to environmental exposures. Air pollution, second-hand tobacco smoke, and indoor mould and dampness make asthma more severe in children.

In households without access to basic services, such as safe water and sanitation, or that are smoky due to the use of unclean fuels, such as coal or dung for cooking and heating, children are at an increased risk of diarrhoea and pneumonia.

Children are also exposed to harmful chemicals through food, water, air and products around them. Chemicals, such as fluoride, lead and mercury pesticides, persistent organic pollutants, and others in manufactured goods, eventually find their way into the food chain. And, while leaded petrol has been phased out almost entirely in all countries, lead is still widespread in paints, affecting brain development.

Making places safe for children

Reducing air pollution inside and outside households, improving safe water and sanitation and improving hygiene (including in health facilities where women give birth), protecting pregnant women from second-hand tobacco smoke, and building safer environments, can prevent children's deaths and diseases.

Top 5 causes of death in children under 5 years linked to the environment

A companion report, *"Don't pollute my future! The impact of the environment on children's health"*, provides a comprehensive overview of the environment's impact on children's health, illustrating the scale of the challenge. Every year:

- **570,000 children** under 5 years die from respiratory infections , such as pneumonia, attributable to indoor and outdoor air pollution and second-hand smoke.
- **361,000 children** under 5 years die due to diarrhoea, as a result of poor access to clean water, sanitation and hygiene.
- **270,000 children** die during their first month of life from conditions, including prematurity, which could be prevented through access to clean water, sanitation and hygiene in health facilities as well as reducing air pollution.
- **200,000 deaths** of children under 5 years from malaria could be prevented through environmental actions, such as reducing breeding sites of mosquitoes or covering drinking-water storage.
- **200,000 children** under 5 years die from unintentional injuries attributable to the environment, such as poisonings, falls and drowning.

on the WEB Don't pollute my future! The impact of the environment on children's health *www.who.int/ceh/publications/don-t-pollute-my-future* MEH

One in 10 deaths worldwide due to smoking

More than one in 10 deaths worldwide (equivalent to 6.4 million deaths) are caused by smoking and half of these occur in just four countries – China, India, USA, and Russia, according to the latest estimates from the Global Burden of Disease study published in *The Lancet*.

The new estimates are based on smoking habits in 195 countries and territories between 1990 and 2015, and illustrate that smoking remains a leading risk factor for death and disability. With growing and ageing populations already heightening the burden of tobacco, it will be crucial to support more smokers to quit and stop people from starting smoking.

Since the implementation of the WHO Framework Convention on Tobacco Control in 2005, many countries have applied tobacco policies resulting in reductions in smoking prevalence, but the authors of the study warn that the war against tobacco is far from won, and argue that policy makers need renewed and sustained efforts to tackle the epidemic.

Worldwide, between 1990 and 2015, smoking prevalence decreased by almost a third (29.4%) to 15.3% in 2015, and today, one in four men (25%) worldwide smoke, as do one in 20 women (5.4%). Despite these improvements, population growth has led to an increase in the overall number of smokers, increasing from 870.4 million in 1990 to 933.1 million in 2015.

Deaths attributable to smoking increased by 4.7% in 2015 compared with 2005 and smoking was rated as a bigger burden on health – moving from third to second highest cause of disability.

"Despite more than half a century of unequivocal evidence of the harmful effects of tobacco on health, today, one in every four men in the world is a daily smoker," said senior author Dr Emmanuela Gakidou, Institute for Health Metrics and Evaluation at the University of Washington, USA. "Smoking remains the second largest risk factor for early death and disability, and so to further reduce its impact we must intensify tobacco control to further reduce smoking prevalence and attributable burden."

The 10 countries with the largest number of smokers in 2015 were China, India, Indonesia, USA, Russia, Bangladesh, Japan, Brazil, Germany and the Philippines – who together accounted for almost two-thirds of the worlds smokers (63.6%).

High smoking prevalence levels and worrying trends persist. For instance, Indonesia, Bangladesh and the Philippines saw no significant reductions in male smoking prevalence between 1990 and 2015 (2015 smoking rates were 46.7%, 38.0% and 34.5%, respectively), and in Russia, female smoking prevalence has increased (from 7.9% in 1990 to 12.3% in 2015) and comprehensive tobacco control policies were only implemented in 2014.

The authors note that Indonesia has very high smoking levels and has not yet ratified the WHO Framework Convention on Tobacco Control.

In contrast, Brazil, which has been a leader in tobacco control, showed one of the largest reductions in smoking prevalence for men and women between 1990 and 2015 – halving from 28.9% to 12.6% in men and 18.6% to 8.2% in women.

In addition, the researchers link increases in female smoking prevalence since 1990 and consistently high levels of male smokers in Eastern Europe with the tobacco industry's targeting of the area in the 1990s – for instance, Russia experienced a 56.2% increase in female smoking prevalence between 1990 and 2015 while male smoking prevalence in Latvia remained at a persistently high level, 37.3% in 1990 and 38.3% in 2015.

They warn that a similar result could happen in sub-Saharan Africa, as the tobacco industry now seeks to expand its market by exploiting the region's patchwork tobacco control regulations and its limited resources to combat the industry's marketing tactics.

For this reason, the authors note that while the WHO tobacco convention is necessary for creating policy, each country must ensure that tobacco control is tailored to their own context and needs, and that compliance and enforcement work together.

Table of smoking stats for Middle East

Country or Territory	SDI Level	2015 Female Age-Standardized Prevalence (95% UI)	2015 Male Age-Standardized Prevalence (95% UI)	Annualised Rate of Change, Female 1990-2015 (95% UI)	Annualised Rate of Change, Male 1990-2015 (95% UI)	Annualised Rate of Change, Female 1990-2005 (95% UI)	Annualised Rate of Change, Male 1990-2005 (95% UI)	Annualised Rate of Change, Female 2005-2015 (95% UI)	Annualised Rate of Change, Male 2005-2015 (95% UI)
Global		5.4 (5.1, 5.7)	25.0 (24.2, 25.7)	-1.7 (-2.0, -1.4)	-1.3 (-1.5, -1.2)	-1.6 (-2.0, -1.2)	-1.2 (-1.4, -1.0)	-1.8 (-2.4, -1.1)	-1.5 (-1.9, -1.1)
Egypt	Middle SDI	0.6 (0.4, 0.8)	31.7 (28.8, 35.0)	-0.9 (-2.9, 1.4)	0.2 (-0.4, 0.9)	-1.1 (-4.4, 2.5)	0.0 (-0.9, 0.9)	-0.6 (-5.2, 3.6)	0.6 (-0.7, 1.9)
Iran	High-middle SDI	2.1 (1.4, 3.0)	17.9 (15.3, 20.6)	-0.8 (-3.0, 1.4)	0.1 (-0.8, 1.0)	-1.6 (-4.6, 1.4)	0.3 (-0.9, 1.5)	0.3 (-3.7, 4.6)	-0.2 (-1.9, 1.5)
Iraq	Middle SDI	3.0 (2.0, 4.3)	23.8 (20.4, 27.6)	0.1 (-2.1, 2.3)	-0.4 (-1.2, 0.4)	0.5 (-2.7, 4.0)	-0.4 (-1.4, 0.7)	-0.6 (-4.7, 3.5)	-0.5 (-2.2, 1.0)
Jordan	High-middle SDI	6.8 (5.1, 8.8)	30.7 (26.9, 34.6)	-0.4 (-2.2, 1.4)	-0.1 (-0.8, 0.6)	-0.7 (-3.3, 2.0)	0.6 (-0.3, 1.7)	0.0 (-3.5, 3.3)	-1.2 (-2.5, 0.2)
Lebanon	High-middle SDI	17.9 (13.8, 22.8)	28.0 (24.5, 31.8)	-0.2 (-1.6, 1.3)	-1.7 (-2.4, -1.1)	-0.2 (-2.2, 1.9)	-2.1 (-2.9, -1.2)	-0.2 (-3.2, 2.6)	-1.2 (-2.7, 0.2)
Oman	High-middle SDI	1.5 (1.0, 2.1)	9.5 (8.0, 11.4)	0.6 (-1.6, 2.9)	-1.4 (-2.4, -0.5)	1.6 (-1.4, 4.6)	-2.2 (-3.5, -0.9)	-0.9 (-5.3, 3.5)	-0.2 (-2.2, 1.8)
Qatar	High-middle SDI	2.3 (1.7, 3.1)	12.2 (10.4, 14.0)	-3.2 (-5.2, -1.4)	-0.1 (-1.1, 0.8)	-6.0 (-9.8, -2.6)	-1.6 (-3.1, 0.1)	1.0 (-3.7, 5.8)	2.0 (-0.2, 4.2)
Saudi Arabia	High-middle SDI	1.7 (1.4, 2.0)	19.5 (18.5, 20.6)	-2.9 (-4.0, -1.9)	2.4 (2.1, 2.8)	-4.9 (-6.5, -3.2)	3.6 (2.9, 4.2)	0.0 (-2.2, 2.2)	0.7 (0.0, 1.6)
Tunisia	Middle SDI	3.0 (2.0, 4.2)	36.1 (32.0, 40.4)	-2.4 (-4.5, -0.4)	-0.5 (-1.1, 0.1)	-3.9 (-6.7, -1.0)	-0.2 (-1.1, 0.6)	-0.1 (-4.1, 3.8)	-0.9 (-2.1, 0.4)
United Arab Emirates	High SDI	1.8 (1.2, 2.6)	11.3 (9.3, 13.4)	-2.3 (-4.5, -0.2)	-0.8 (-1.8, 0.2)	-4.0 (-7.3, -0.6)	-0.3 (-1.8, 1.1)	0.1 (-4.5, 4.8)	-1.6 (-3.7, 0.5)
Yemen	Low-middle SDI	6.3 (4.3, 8.8)	18.8 (16.1, 21.8)	-0.9 (-3.1, 1.1)	-0.7 (-1.6, 0.2)	-1.0 (-3.7, 2.0)	-0.3 (-1.4, 0.9)	-0.8 (-4.8, 3.2)	-1.4 (-3.0, 0.2)

CREDIT: The Lancet

"There have been some success stories, but smoking remains the leading cause of death and disability in 100 countries in 2015," said Dr Gakidou. "Its toll will remain substantial without more concerted policy initiatives, policy compliance and enforcement, and sustained political will to offset commercial interests. Despite progress in some settings, the war against tobacco is far from won, especially in countries with the highest numbers of smokers. The staggering toll of smoking on health echoes well beyond the individual, especially as tobacco threatens to exact long-term financial and operational burdens on already resource-constrained health systems. To markedly bend the global tobacco epidemic's trajectory, a renewed and sustained focus is needed on comprehensive tobacco control policies around the world. Success is possible, but requires effective and aggressively enforced policies and laws."

The study estimates were based on the number of people who smoked every day, rather than occasional or former smokers, and did not take into account how many cigarettes a person smoked in a day nor people who used smokeless tobacco products or e-cigarettes.

Writing in a linked Comment, Professor John Britton, University of Nottingham, UK, said: "Today, the smoking epidemic is being exported from the rich world to low-income and middle-income countries, slipping under the radar while apparently more immediate priorities occupy and absorb scarce available human and financial resources. The epidemic of tobacco deaths will progress inexorably throughout the world until and unless tobacco control is recognised as an immediate priority for development, investment, and research." MEH

Expert in lung transplantation joins Baylor St. Luke's Medical Center

Dr Gabriel Loor, a cardiac surgeon whose research focuses on maximizing donor organs for lung transplant recipients, has joined Baylor College of Medicine as director of lung transplantation in the division of cardiothoracic transplantation and circulatory support in the Michael E. DeBakey Department of Surgery. He will conduct surgeries at Baylor St. Luke's Medical Center.

"I am extremely excited to join the heart and lung transplantation team at Baylor College of Medicine and Baylor St. Luke's Medical Center," Loor said. "I've been very attracted to the developments in Houston, and I've been impressed by the way everybody approaches patient care, research and everyday life. There is a high level of excellence, and the incredible collaboration between Baylor, Catholic Health Initiatives and Texas Heart Institute is sure to enhance advanced heart and lung care in the region and the world."

Dr Loor is the national principal investigator on several trials using ex vivo lung perfusion, or the process of preparing donor lungs outside of the body for transplantation. Because of a renewed interest in understanding ways to optimize donor organs, including the heart, lungs, liver and kidneys, technological innovations have enabled physicians to house donor lungs in a sterile chamber outside of the body for 12 to 24 hours. Dr Loor is credited with the first of this type of "breathing lung" transplantation in the Midwest in 2014.

TransMedics Organ Care System

The portable device, the TransMedics Organ Care System, which houses the lungs, originally was developed in Boston. It has a miniaturized ventilator system and pulsatile pump that delivers blood flow through the organ. A Bluetooth monitor allows for regular readouts of how the organ is performing. The System is in the final stages of the FDA review process following the completion of two international clinical trials.

"In the past, all we've been able to do is cool the lungs down, put them on ice and transport them, and we have a certain amount of time to do that. But with this device, we've been able to have them outside the body for up to 12 hours or longer. That amount of time lets us understand how good the quality of the lung is, deal with logistics and ensure we can get the transplant in and allows the team to operate when they are well rested," Dr Loor said. "It also gives us time to consider other types of treatment we can use to improve the quality of the organ."

The landmark international trial of this device, the INSPIRE trial, found that in those lungs where this device was used, there was a 50% reduction in graft dysfunction, a lung injury that is common after lung transplantation. Patients who received these transplants also were off the ventilator and out of the hospital sooner.

The next phase in this research, the EXPAND trial, currently is looking at why surgeons are only able to use 20% of the lungs that are offered for transplantation and exploring use of this technology to utilize more donor lungs. Dr Loor serves as the international principal investigator for this study and is credited with the first EXPAND lung transplant in the world. This work allows surgeons to offer high quality transplantation to patients suffering from diseases such as pulmonary hypertension, idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, cystic fibrosis or any end stage lung disease before they become too sick for transplant.

As co-chief of adult cardiac surgery at Baylor St. Luke's Medical Center, Dr Loor will work closely with Drs Joseph Coselli, Joseph Lamelas and Todd Rosengart to expand surgical quality initiatives. Dr Loor's expertise in adult cardiac surgery includes coronary revascularization, complex re-operative surgery, valvular repair and replacement and endovascular surgery. Dr Loor also has done work to address the issues of blood conservation and bloodless surgery and has published numerous articles on this topic.

Dr Gabriel Loor

"Dr Loor represents the first-class, cutting edge academic surgeon that we are so thrilled to have been able to recruit to the Michael E. DeBakey Department of Surgery. I have no doubt that he will make highly impactful contributions clinically and by innovation," said Dr Todd Rosengart, chair and professor of surgery at Baylor who also holds the DeBakey-Bard Chair in Surgery.

Dr Loor is a Fellow of the American College of Cardiology and member of the Society of Thoracic Surgeons and the International Society for Heart and Lung Transplantation. He is fluent in Spanish.

He will see patients at Baylor St. Luke's Medical Center Heart and Lung Clinic

■ For more information contact International Services at Baylor St Luke's Medical Center:
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Visit: *StLukesInternational.org* MEH

New investigational malaria vaccine PfSPZ shows significant protection

An investigational malaria vaccine given intravenously was well-tolerated and protected a significant proportion of healthy adults against infection with *Plasmodium falciparum* malaria – the deadliest form of the disease – for the duration of the malaria season, according to new findings published in the February 15, 2017 issue of the journal *Lancet Infectious Diseases*. The study participants live in Mali, Africa, where they are naturally exposed to the parasite.

The investigational vaccine, known as the PfSPZ Vaccine, contains live but weakened sporozoites, the form of the parasite that infects humans, and was developed by scientists at Sanaria Inc. The study was conducted by researchers from the US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, and the University of Science, Techniques, and Technologies of Bamako (USTTB), Mali, one of NIAID's International Centers of Excellence in Malaria Research.

In 2015, 212 million cases of malaria occurred worldwide, and 429,000 people with malaria died, largely African children under five years old, according to the World Health Organization.

"Considerable progress has been made in the global fight against malaria within the past decade, yet far too many people -- particularly young African children -- continue to become infected and die from the disease," said NIAID Director Anthony S. Fauci, M.D. "A safe, effective vaccine to protect against this mosquito-borne illness would greatly help efforts to bring the disease under control."

PfSPZ Vaccine generates an immune response to protect against malaria infection. Earlier research found that the experimental vaccine safe and protective against malaria infection for up to a year in healthy US adults who had not been previously exposed to malaria.

The Mali study was launched in January 2014 to provide additional safety data about PfSPZ Vaccine and determine if it could protect adults living in a malaria-endemic area against naturally occurring malaria infection. The study enrolled 109 healthy African men and non-pregnant women ages 18 to 35 years old.

Participants received either five doses of the intravenous PfSPZ Vaccine or five doses of placebo (saline) over five months of the dry season at the study's clinical site in the Donéguébougou village in rural Mali. Clinical staff then actively monitored the participants during the six-month rainy, malaria-transmission season for the presence of malaria parasites in the blood.

The investigators report that the vaccine candidate was well-tolerated and safe with no serious adverse events. Among the 40 participants who received five placebo doses, 93% developed P. falciparum malaria infections; by comparison, 66% of the participants who received five doses of the PfSPZ Vaccine developed malaria infection. Based on the primary study analysis, PfSPZ Vaccine demonstrated a 48% protective efficacy by time-to-first positive malaria blood smear and 29% efficacy by proportion of participants with at least one positive malaria blood smear during a full 20-week malaria transmission season. By both measures of protective efficacy, there was statistically significant protection in the vaccine group as compared with the placebo group.

"This level of sustained efficacy against malaria infection in a region with an intense transmission season has not been seen in previous malaria vaccine studies in Africa," said Dr Healy. "It is a very encouraging finding that we can, hopefully, build upon."

The investigators report that the intravenous delivery system for the PfSPZ Vaccine did not pose a problem to administer in a rural, malaria-endemic area -- an initial concern about the experimental vaccine's unique design.

"Direct venous inoculation is not currently used for any licensed vaccines to prevent an infectious disease," said Professor Ogobara Doumbo, M.D., Ph.D., senior scientist for the Mali malaria vaccine program and chair of the Department of Epidemiology of Parasitic Diseases at USTTB. "In this study, we administered 491inoculations in a rural setting without a problem, and the dosages were delivered in a matter of seconds. It shows that this approach is feasible from both a logistical and public health standpoint."

According to the researchers, a preventive malaria vaccine employed in mass vaccination programs to eliminate P. falciparum from geographically defined areas would need to prevent malaria infection or transmission in at least 80% of recipients throughout the malaria transmission season. Clinical trials now underway in Africa, Europe and the United States have been designed to boost PfSPZ Vaccine's efficacy by increasing dosage levels and varying the timing and number of doses. The experimental vaccine is also being examined in demographic groups other than healthy adults, including adolescents, children and infants.

• **doi:** 10.1016/S1473-3099(17)30104-4 (2017). MEH

Innovating in the brain

"Shocked," was what Laura Fernandez-Ortiz remembers feeling three years ago when an MRI revealed she had a tumour at the base of her skull. "And also very scared," she adds. The 46-year-old paediatrician had been in excellent health, running a bustling private practice in Miami, Florida. Her doctors decided to keep an eye on the tumour, but last year, when a scan showed the mass had grown, they recommended she undergo surgery. **Kate Ledger**, Mayo Clinic, reports.

Like any concerned patient, Dr Fernandez-Ortiz went online to research surgical options for olfactory groove tumours, eventually making an appointment at a local medical centre for an open craniotomy to remove the growth. Her medical training gave her reservations about the invasiveness of the procedure. "I wasn't happy about it. I knew it would involve retraction of the brain and possible cellular injury," she says. "I scheduled it, but I continued making calls."

By chance, days before her scheduled surgery, she stumbled across a video about Alfredo Quiñones-Hinojosa, M.D., and a patient of his with a skull-base tumour. Using a new technique that he pioneered, Dr Quiñones had removed the tumour through the patient's eyelid. This was exactly the type of minimally-invasive approach that Dr Fernandez-Ortiz had hoped to find. That same day, she called Dr Quiñones at Mayo Clinic in Jacksonville, Florida, a five-hour drive from her home, to see if she would be a good candidate for the same surgery.

A specialist in primary and metastatic tumours of the brain and tumours of the pituitary and brain stem, Dr Quiñones has made it his mission to improve neurosurgical techniques and the methods of diagnosing and treating tumours. One surgeon who operates with him attests: "He's constantly innovating." The author of more than 100 book chapters, 6 books, 315 papers in medical journals, and other resources including the Video Atlas of Neurosurgery, he serves as the chair of neurologic surgery and the William J. and Charles H Mayo Professor at Mayo Clinic in Florida. Today, this warm and energetic clinician-scientist focuses on addressing the most difficult tumours in ways that best help patients. As he puts it: "My goal is giving people hope."

Dr Quinones in surgery

Every brain is different

For more than a decade, Dr Quiñones has been keenly interested in advancing techniques that access tumours while sparing surrounding tissue. When it comes to removing eloquent tumours, those occurring in the speech and motor areas, he strives to keep critical regions of the brain intact. But the speech centres of the brain, and their sizes, differ between patients and even between single- and multi-language speakers. "Like every face, every brain is different," he says.

In the Operating Room and beyond

Dr Quiñones is eager to see improved diagnosis and treatment of tumours, and he believes those advances can happen right in the operating room. Currently, he's part of a team investigating whether the technology of optical coherence tomography (OCT), used since the 1990s to image the retina, can be co-opted to recognize diseased cells in the brain. Early results of the team's studies showed OCT can distinguish normal excised brain tissue from denser pathologies, like brain cancer. Used intra-operatively, the non-invasive imaging may soon be able to show neurosurgeons exactly which tissue needs to be removed so they can resect a wide margin without causing unnecessary damage to surrounding areas.

He's also interested in how best to treat brain cancers, and his patients donate tumour tissue to make the studies possible. One approach he's investigating in his basic science lab is the use of stem cells, known to have two remarkable capabilities. For one, stem cells can migrate to the site of a tumour. Additionally, they have the ability to differentiate into any type of cell. His lab is studying whether souped-up stem cells, carrying specific anti-tumour proteins, can deliver their cargo directly to a tumour. Moreover, those stem cells may be able to coax highly malignant cancer cells, like glioblastomas, to turn into less migratory, more treatable cell types, like astrocytomas. So far, the team found the cellular therapy halted tumours in mice, laying the groundwork for future studies at Mayo Clinic that will test the therapy in patients.

Dr Alfredo Quiñones-Hinojosa in the Operating Theater

Over the years, he has become a specialist in performing what's known as an "awake craniotomy". Working with a team that includes Mayo Clinic epileptologists, Dr Quiñones maps the brain during the operation, allowing the resection of a tumour and the removal of the widest possible margins around the mass, while preserving the functional cortical regions. During surgery, patients are positioned on their backs with their heads secure in stereotactic frames. Though under general anaesthesia at the beginning and end of surgery, they are sedated in a comfortable twilight state throughout the procedure, so that they can converse, answer questions, identify pictures, and respond to commands. He introduced the use of a camera in front of their faces so he can monitor facial changes as well.

The critical piece of equipment Dr Quiñones' team developed and patented is a 5X5 cm plastic screen with a grid of tiny, flat electrodes that are placed directly against the brain. A stimulator delivers a gentle pulse to each region, interrupting the normal electrical activity of that area. If patients fail to recognize a simple picture, answer a question, or follow a command to move an arm or a leg, Dr Quiñones knows to leave that part of the brain intact. Importantly, the mapping also enables what's known as a supramarginal resection, removing the maximum surrounding tissue to prevent tumour recurrence.

The awake craniotomy minimizes the use of anaesthesia, which may alter the immune system and increase recurrence of some cancers. The mapping also records electrical activity of the brain to prevent potentially devastating seizures during the craniotomy. Collecting data from his surgeries, Dr Quiñones has found the awake craniotomy, accompanied by motor and speech mapping, reduces a hospital stay from approximately 8 days to a mere 4 days. Overall, patients have higher scores on quality- and quantity-of-life assessments than those who have gone through a standard craniotomy.

Minimally invasive brain surgery

He also has devoted attention to improving the latest minimally invasive surgeries. Entering the brain through the nose has become acknowledged in the U.S. as the best means to remove pituitary tumours. Many surgeons insert a speculum in the patient's nose and employ a microscope as they access the tumour. Dr Quiñones has adapted the transsphenoidal procedure, using the endoscope, a camera slimmer than a pencil. "It's much less invasive and allows you to look deeper and around the corners," he says.

The biggest alteration, however, is that while most surgeons enter through both nostrils simultaneously, the endoscope enables Dr Quiñones to enter through just one. A resident manipulates the endoscope as Dr Quiñones operates surgical tools through the same corridor in the nose. "The nostril on the contralateral side remains completely intact," Dr Quiñones says. Significantly, his technique (used for tumours existing exclusively in the interior skull base known as the sella) does not remove the turbinates, the tiny bones in the nose that provide resistance to the air and the sensation of airflow. Patients are spared the rare consequence of endonasal surgery known as "empty nose syndrome". As he's studied his outcomes, Dr Quiñones has found patients who undergo the endoscopic approach spend less time in the operating room and typically go home sooner than those who undergo traditional endonasal surgery. He's now exploring data to determine whether the one- or two-nostril approach best maintains patients' sense of smell and taste.

Through the eyelid

Another innovation Dr Quiñones

brought to the operating room was an improvement to the minimally-invasive "keyhole" surgery, which introduces tiny cameras and microsurgical tools to the brain through an incision in the eyelid. Several years ago, he realized he could access the same supraorbital bone, and map a route to the tumour, entering through the eyelid. The approach is sometimes an alternative to endonasal surgery, as it was for one patient, a voice-over actor, who was concerned surgery through his nose would ruin his livelihood.

As it turned out, a CT scan suggested that Laura Fernandez-Ortiz was an excellent candidate for the removal of the skull-base tumour through her eyelid. "The question is the patient's frontal sinus," Dr Quiñones explains. "A large cavity can lead to infection, but I've found a small cavity to be safe."

At Mayo Clinic he operates side by side with plastic surgeon Antonio Forte, M.D. The procedure combines tumour removal with the approach of an upper blepharoplasty, the cosmetic surgery for aging eyelids. The entry point is a hidden fold within the upper eyelid, that still enables Dr Quiñones to proceed to the tumour at the skull base. Using intraoperative scans and a neuronavigational system, similar to a GPS, he's able to precisely assess anatomy and instrument placement. At the end of surgery, Dr Forte closes the site and the scar remains well hidden.

For Dr Fernandez-Ortiz, the surgery provided not only a less invasive alternative to a craniotomy, but an easier recovery. She was home within days and working fulltime at her clinic within six weeks. She's also pleased – as Dr Quiñones had hoped – that the absence of a scar means she can live her life after brain surgery with a sense of normalcy. "People who didn't know I had a tumour have no idea I've had surgery at all," she says. MEH

New guidelines for surgical ablation for patients with Atrial Fibrillation

While there is no cure for atrial fibrillation – an irregular heart rhythm that can cause an increased risk of stroke – many successful treatments are available, including surgical ablation. A growing population of patients means an increased demand for care. In an effort to provide practitioners with the most up-to-date information, the American Association for Thoracic Surgery (AATS) assembled an expert board to study the available literature and develop evidence-based guidelines and best practices on surgical ablation for the treatment of atrial fibrillation. Their consensus statement is published in *The Journal of Thoracic and Cardiovascular Surgery*, the official publication of the AATS.

AATS leadership convened a 10-member board comprised of leading experts in the field, including cardiac surgeons, biostatisticians, and a leading electrophysiologist, to make recommendations based on rigorous study of unbiased scientific data. The resulting document offers guidance about surgical ablation based on morbidity and stroke outcomes associated with the procedure, as well as information about the state of hybrid procedures, the optimal ablation tools available, and clinical training.

"These guidelines are extremely important for a few reasons," said lead author Niv Ad, MD, Professor of Surgery, Division of Cardiothoracic Surgery, West Virginia University School of Medicine. "This consensus statement demonstrates the safety of the procedure and the clear association with reduced early death compared to patients who were left with atrial fibrillation. It also clearly states that there is a reduction in late stroke and better long term survival with improved quality of life."

"Clinical practice regarding surgical ablation of atrial fibrillation varies widely. This consensus statement should guide surgeons to provide the best therapy for their patients who have atrial fibrillation," added co-author Marc Gillinov, MD, Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic, Cleveland, OH.

The guidelines offer a robust look at many facets surrounding surgical ablation and begin with morbidity, stroke risk, and quality of life outcomes for atrial fibrillation patients. For example, investigators found that concomitant surgical ablation for atrial fibrillation improves 30-day operative mortality, so it is recommended to be performed when indicated.

The recommendations also note that ablation does not increase the risk of periprocedural morbidity or early stroke/transient ischemic attack (TIA) and that late stroke/TIA is decreased by surgical ablation in a follow up longer than one year. Other topics covered include indications for off pump hybrid procedures, the recommended surgical ablation devices that are associated with reliable transmural lesions, and the importance of standardized surgeon training and education.

By creating these guidelines, the board wanted to deliver a comprehensive consensus statement on ablation with the goal that clear guidelines would encourage more surgeons and referring cardiologists to understand the operation's potential value to patients with atrial fibrillation and utilize it when appropriate. "The methodology used for the guidelines is also unique and provided the members of the committee with rigorous unbiased statistical data to support their recommendations," said Dr Ad. "This type of scientific rigor is unique compared to other guidelines published on this topic."

• **doi:** 10.1016/j.jtcvs.2017.02.027

Develop your healthcare leadership and management capability with an internationally recognised Master's Degree in Dubai

In this world of rapidly advancing knowledge it is important to keep up to date with the latest developments and be in a position to make your healthcare organisation more agile in an increasingly competitive environment.

To this end, the Royal College of Surgeons in Ireland (RCSI)-Dubai Institute of Leadership is offering two Master's Degree courses in Dubai – a Master's Degree in Health Management and a Master's Degree in Health Quality and Safety. The courses are designed to accommodate busy healthcare professionals and are a blend of online study and attendance at RCSI-Dubai in Mohammed Bin Rashid University of Medicine and Health Sciences in Dubai Healthcare City.

The courses are internationally recognised and accredited by the Commission for Academic Accreditation (CAA) in the UAE and the National University of Ireland. The Master's Degree programmes are the only UAE-based Level 9 programmes of their kind, accredited by the CAA.

Prospective candidates should be degreed healthcare professionals, including doctors, nurses, pharmacists and those in allied healthcare professions. Candidates should have a GPA (grade point average) score of 3 on a 4-point scale

RSCI have been running these courses in Dubai since 2005 and longer in Bahrain. As such they are well tuned to the specific nuances and requirements of Middle East culture.

"We think it is extremely important that healthcare professionals be involved in management and leadership in healthcare organisations – and these courses provide the necessary preparation for these roles," said Ciaran O'Boyle, Director of the Institute of Leadership at RCSI. "Our mission is to develop healthcare professionals' leadership and management capability as well as that of their organisations."

"Since we've been running these courses, we have graduated 550 healthcare professionals in the Middle East – most of whom have been promoted in their organisations soon after completing the course – and have gone on to make significant and beneficial changes to their organisations."

The Master's Degree courses are run over two years. The first year comprises six modules requiring four days in class for each module – 24 days in the year. The rest of the course is completed online. In the second year, students are required to complete a 'change project' requiring only 7 days in class during the course of the year. The 'change project' can be implemented in conjunction with the organisation where they work.

"We can take 40 students a year on each programme. Interestingly, over the past few years we have seen an increasing number of applications from pharmacists," said O'Boyle. He added that they plan to expand capacity to accommodate more students.

"Next year we will be adding an additional course – a Master's Degree in Healthcare Leadership," he said.

■ For more information, visit the RCSI-Dubai Institute of Leadership website: *www.rcsileadership.org/UAE* MEH

Facebooking your doctor's appointment

Telemedicine, which allows doctors to communicate, diagnose and even treat their patients remotely is on the rise thanks to advances in information technology. It allows healthcare workers to securely monitor patients in inaccessible parts of the world as well as providing more timely responses for patients in many situations. New research published in the *International Journal of Medical Engineering and Informatics* suggests that the world-wide social networking site, Facebook, and smart phone use could make telemedicine even more common and useful in healthcare.

Agostino Giorgio of the Politecnico di Bari, Italy, points out that, for most patients, telemedicine means fewer hospital visits, but it also provides critical services that might otherwise be unavailable. Remote heart monitoring and other diagnostic tools are quite common. Now, Giorgio has developed smart phone software, an application, that connects patient and doctor via the social networking site Facebook, although it could be adapted to work with another such networking system.

The Care-App allows private and secure communication between doctor and patient as well as offering a medication diary for the patient rescue call and clinic search and booking utility. Video connectivity makes the visit more personal but also allows a patient to show the doctor some symptoms or problems. There is also the option to use a "telestethoscope" device that connects to the smart phone headphone jack and would be provided to the patient or their carer. Giorgio and colleagues in the Cardiology department have already tested and validated a telestethoscope with this app. Other devices such as blood-oxygen saturation and pulse monitor, electrocardiogram (such as the AliveCor Heart Monitor), thermometer could also be used in conjunction with the smart phone input or in some cases simply through the video connection or a verbal/textual reporting of temperature, for instance.

"The patient also may use the Facebook share button or private message button, to send the doctor any other kind of information he may acquire and store with its own smart phone, concerning its own health status," says Giorgio. "Care-app manages all these steps, apps and operations, performed by the doctor and by the patient during the remote medical visit." Care-

Internet portal for telemedicine programs aims to change patients' lifestyles

At Medica 2016, in Dusseldorf, Germany, SYMILA, the Fraunhofer Application Center at Hamm-Lippstadt, demonstrated a telemedicine Internet portal for diabetics, which was implemented on behalf of DITG – Deutsches Institut für Telemedizin und Gesundheitsförderung. The portal, centrepiece of an E-Health intervention system, collects and evaluates the data from telemedicine devices and lets DITG coaches address each patient based on information about her/his current situation. The system meets the requirements for a "Medical Data Space (MedDS)" that guarantees a secure exchange of medical data, as specified by the Fraunhofer initiative "Industrial Data Space (IDS)".

DITG develops and implements health management programs for health insurance companies, pharmaceutical companies and organizations with an internal health management system. These programs typically aim to improve the participants' quality of life while at the same time reducing healthcare spending.

On behalf of DITG, SYMILA, the Fraunhofer Application Center powered by Fraunhofer FIT developed and implemented a telemedicine portal for monitoring type 2 diabetes patients and for advising them on health-related problems. The participants in the program are given a set of telemedicine devices like blood glucose meter, electronic balance and pedometer, whose data are collected in the portal in real time. Here they are converted to easy-to-understand charts that are available to the participants and to the coaches from DITG. When a critical parameter exceeds a pre-defined threshold, the portal sends an automatic warning. It allows the coach to intervene as appropriate and avoid situations that might pose a risk to the patient. Thus, the patient learns how to deal with her specific condition with a minimum loss of quality of life.

The portal is based on a modular, open systems architecture with flexible interfaces, so it can easily be extended to cater for other medical conditions, such as cardiac insufficiency or COPD.

This portal was developed by

App is written in HTML5/Java, and so should work on any operating system with all smart devices – smart phones, tablets, notebook and desktop computers. MEH

Fraunhofer FIT and is now operated in a computer centre of its own, in order to satisfy the requirements for data availability and data security.

"Keeping patients in control of theirvown data is a very important aim for us. ThevDITG system demonstrates convincingly how medical data can be shared securely and efficiently between patient, physician, clinic and other stakeholders", explained Prof Harald Mathis, head of both the Biomolecular Optical Systems group (BioMOS) of the Fraunhofer Institute for Applied Information Technology FIT and SYMILA.

The DITG system is based on the concept of "Medical Data Space (MedDS)" put forward by the Fraunhofer initiative "Industrial Data Space (IDS)". The Medical Data Space is a virtual data space that supports sharing and aggregating medical and health-related data from different sources, based on standards and shared models of governance. The MedDS concept aims to improve the quality of diagnostics, prevention and therapy as well as therapy monitoring.

InTouch Health and GE Healthcare start Virtual Onsite Training

InTouch Health, a US-based enterprise telehealth provider with solutions that have been used at over 1,500 locations in more than 30 countries, and GE Healthcare's Global Education Services division, have started Virtual Onsite Training, a remote presence training commercialization effort after successful completion of a two-year pilot.

The initiative begins with establishing a total of 50 InTouch Health Tech remote presence devices in rotation at more than 200 global locations to support the technical and product training of clinicians, physicians, and technicians using a variety of GE Healthcare products.

During the pilot, the InTouch Health telehealth network and remote presence devices were used to connect GE experts remotely to healthcare providers across GE's installed base around the world. More than 200 telepresence training classes occurred, involving more than 300 medical professionals, in both the proper use of GE equipment and best practices. The pilot program demonstrated that adding this remote presence training resulted in higher effectiveness than traditional training alone, and offered greater convenience to the customer through the flexibility of on-demand telepresence.

The Virtual Onsite Training device replicates face-to-face training through an attached video monitor and robotics for twoway communication and interaction.

Commenting on the initiative, Mario Lois, General Manager, GE Healthcare Global Education Services, said: "GE Healthcare provides technology to providers and patients around the world. The users who operate those devices are as impactful, if not more so, on the actual efficiency and patient outcomes as the product itself. Therefore, GE has made it a global priority to re-imagine its training and education solutions to help users achieve and maintain optimal skills and product usage. Our collaboration with InTouch Health enables network connectivity, hands on interaction, and an intuitive user experience for their online mobile remote presence training which will be foundational to reaching this goal."

The InTouch Health telehealth network is a single unified cloud infrastructure that includes data centres around the globe, covering the Americas, Asia, Africa, Europe and the Middle East. The network provides a regulatory (HIPAA) compliant, secure, scalable, and always available network hosting FDA Class II and Class I medical devices. The network architecture allows for the delivery of business intelligence and data analytics gathered from all data traffic managed on any connected device. This is the same network used by GE to deliver their customer on-demand Virtual Onsite Training.

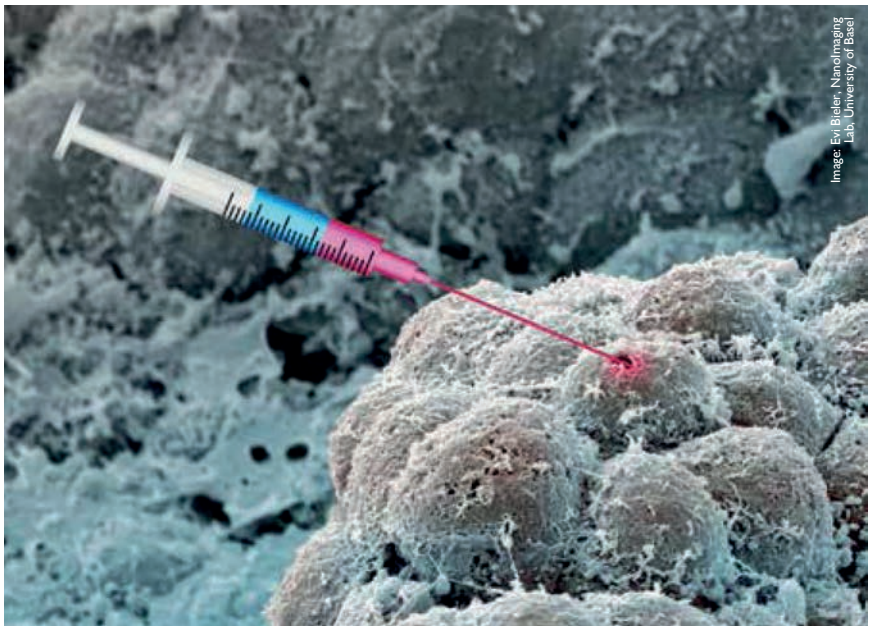


Illustration demonstrating the anti-cancer effect of the drug combination

Treating cancer with drugs for diabetes and hypertension

A combination of a diabetes medication and an antihypertensive drug can effectively combat cancer cells. The team of researchers led by Professor Michael Hall at the Biozentrum of the University of Basel has also reported that specific cancer cells respond to this combination of drugs. The results of the study have now been published in *Science Advances*.

Metformin is the most widely prescribed drug for the treatment of type 2 diabetes. Besides its blood sugar lowering effect, it also displays anti-cancer properties. The usual therapeutic dose, however, is too low to effectively fight cancer. The research team led by Prof Michael Hall, at the Biozentrum of the University of Basel, has now made an unexpected discovery: The antihypertensive drug syrosingopine potentiates the anti-cancer efficacy of metformin. Apparently, this drug combination drives cancer cells to programmed "suicide".

Drug cocktail kills tumour cells

At higher doses, the antidiabetic drug inhibits the growth of cancer cells but could also induce unwanted side effects. Therefore, the researchers screened over a thousand drugs for whether they can enhance the anticancer action of metformin. A favourite emerged from this screening: Syrosingopine, an antihypertensive drug. As the study shows, the cocktail of these two drugs is effective in a wide range of cancers. "For example, in samples from leukaemia patients, we demonstrated that almost all tumour cells were killed by this cocktail and at doses that are actually not toxic to normal cells," says the first author, Don Benjamin. "And the effect was exclusively confined to cancer cells, as the blood cells from healthy donors were insensitive to the treatment."

Drugs block "juice" supply to cancer cells

In mice with malignant liver cancer, enlargement of the liver was reduced after the therapy. Also the number of tumour nodules was less – in some animals the tumours disappeared completely. A glance at the molecular processes in the tumour cells explains the drug combination's efficacy: Metformin lowers not only the blood glucose level, but also blocks the respiratory chain in the energy factories of the cell, the mitochondria. The antihypertensive drug syrosingopine inhibits, among other things, the degradation of sugars. Thus, the drugs interrupt the vital processes which provide energy for the cell. Due to their increased metabolic activity and rapid growth, cancer cells have a particularly high energy consumption, which makes them extremely vulnerable when the energy supply is reduced.

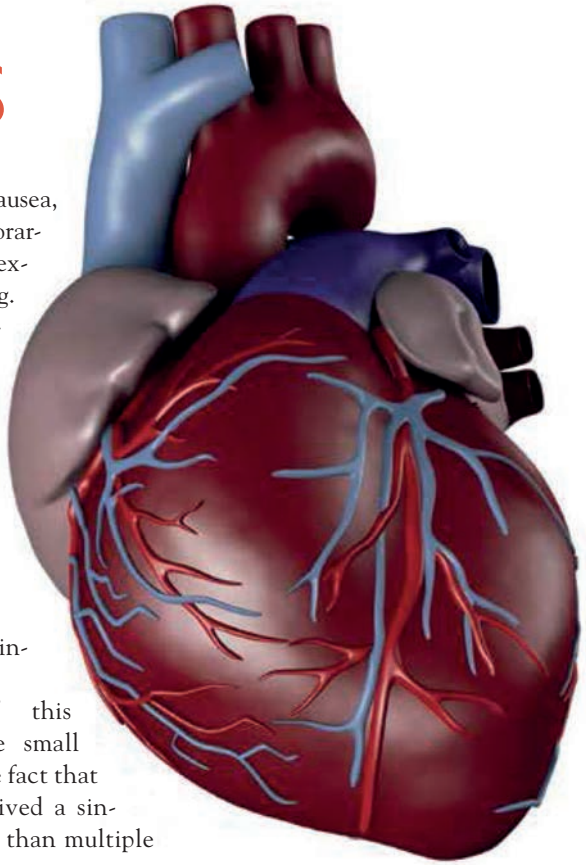
Groundbreaking step towards clinical application

By testing a range of other compounds with the same mode of action, the scientists could demonstrate that the inhibition of the respiratory chain in the mitochondria is a key mechanism. These also reduced cancer cell growth in combination with the antihypertensive drug.

"We have been able to show that the two known drugs lead to more profound effects on cancer cell proliferation than each drug alone," explains Benjamin. "The data from this study support the development of combination approaches for the treatment of cancer patients." This study may have implications for future clinical application of combination scenarios targeting the energy needs of tumour cells.

• **doi:** 10.1126/sciadv.1601756 MEH

Novel drug may help repair failing hearts



Cimaglermin, a new experimental drug, may help restore cardiac function after heart failure, according to a first-in-man study published in *JACC: Basic to Translational Science*.

Heart failure, characterized by a loss of cardiac function, is among the leading causes of death worldwide. A significant portion of heart failure patients, particularly those with severe left ventricular systolic dysfunction, do not sufficiently respond to current medical therapy.

Researchers examined the safety and efficacy of a single infusion of cimaglermin, which acts as a growth factor for the heart, helping the structural, metabolic and contractile elements of the heart to repair itself following injury. The study enrolled 40 heart failure patients who were taking optimal medical therapy for at least three months prior to the trial. Compared to patients who received a placebo, patients who received a high dose of cimaglermin had a sustained increase in left ventricular ejection fraction, or pumping capacity, through 90 days after dosing, with the maximum increase reached at day 28.

"These findings support continued clinical development of the investigational drug cimaglermin, including further safety evaluations and detailing the potential improvement on clinical heart failure outcome measures," said Daniel J. Lenihan MD, from the division of cardiovascular medicine at Vanderbilt University and the lead author of the study. "As with all experimental therapeutics, additional studies will be required and subject to regulatory review to determine if the relative risks and benefits of cimaglermin warrant approval."

The most common side effects were headache and nausea, which were temporarily associated with exposure to the drug. One patient receiving the highest planned dose of cimaglermin experienced an adverse reaction that met the stopping criteria of Federal Drug Administration guidance for drug induced liver injury.

Limitations of this study include the small sample size and the fact that patients only received a single infusion rather than multiple doses.

"Although the results of the study must be regarded as provisional because of the small numbers of patients, the results of this study are nonetheless very exciting," said Douglas L. Mann, MD, FACC, editor-in-chief of JACC: Basic to Translational Science. "Instead of blocking the fundamental mechanisms that lead to cardiac injury, the early results with cimaglermin suggest that it may also be possible to administer therapeutics that allow the failing heart to repair itself using its own repair mechanisms. If the results of this study can be replicated and translated into improvements in clinical outcomes in larger numbers of patients in phase II and III clinical trials, it will represent a paradigm shift in the way in which clinicians treat patients with heart failure."

• **doi**: 10.1016/j.jacbts.2016.09.005 MEH

Although the results of the study must be regarded as provisional because of the small numbers of patients, the results of this study are nonetheless very exciting. Instead of blocking the fundamental mechanisms that lead to cardiac injury, the early results with cimaglermin suggest that it may also be possible to administer therapeutics that allow the failing heart to repair itself using its own repair mechanisms.

Radiology Information System market set to grow to $941 million by 2022

The Radiology Information System market is forecast to grow to US$941 million globally by 2022 registering a compound annual growth rate (CAGR) of 5.9% during the period 2016-2022, according to Allied Market Research.

The integrated radiology information systems segment held over three-fifths share of the total market in 2015, according to the report.

Radiology Information Systems (RIS) are a computer networked system used to organize and manage the workflow of medical imagery and radiology departments, supporting business analysis in a department. RIS is widely used along with Picture Archiving and Communication Systems (PACS) and vendor neutral archives to manage billing, record keeping, and image archives.

The integrated radiology information systems held the largest share in 2015 and is expected to grow at the highest CAGR of 6.0% during the analysis period. This is owing to the surging adoption and demand of integrated healthcare information technology platforms in various healthcare organizations for easy operations to curb over expense and provide quality health.

The services component segment held the largest market share with more than three-eighths share in 2015 due to improving healthcare infrastructure in the emerging markets such as Brazil and the Middle East. The software segment is expected to grow at the highest CAGR during the analysis period owing to the increase in the demand of RIS software in radiology and imaging laboratories.

The web-based deployment segment dominated the RIS market in 2015 and

accounted for three-fifths of the overall RIS market. However, the cloud-based segment is expected to grow at the fastest CAGR of 7.8% during the analysis period, due to an increase in demand for cloud-based services because they reduce operational costs for healthcare organizations.

Key findings of the RIS market report:

- Integrated radiology information systems was the leading segment in 2015
- North America is projected to grow at a CAGR of 5.5%
- Asia-Pacific is expected to grow at the highest CAGR during the analysis period
- Hospitals held the largest market share of the total RIS market in 2015
- The global cloud-based market is expected to grow at a CAGR of 7.8% during the study period

Geographically, North America accounted for the largest market share in 2015, due to well-established healthcare systems in the region, higher adoption of healthcare information technologies, and an increase in the number of chronic diseases. However, Asia-Pacific is expected to emerge as the area with maximum growth potential due to a focus of key players in the emerging economies and improving healthcare infrastructure.

The report provides a comprehensive analysis of some of the key players operating in this market including Epic Systems Corporation, MedInformatix, GE Healthcare, Carestream Health, Cerner Corporation, merge Healthcare Incorporated, All scripts Healthcare Solutions, McKesson Corporation, Philips, and Siemens.

The PACS market

According to a market study by Technavio, the global Picture Archiving and Communication Systems (PACS) is expected to grow at a CAGR of close to 6% through 2021.

This research report titled 'Global Picture Archiving and Communication System (PACS) Market' provides an in-depth analysis of the market in terms of revenue and emerging market trends.

> The rise in adoption of mini PACS in emerging markets is due to the rise in the number of small hospitals and government initiatives moving toward centralized healthcare IT systems.

The market research analysis categorizes the global PACS market into three major product segments. They are:

- Global mini PACS market;
- Global mid-end PACS; and
- Global enterprise PACS market.

Global mini PACS market

The global mini PACS market is expected to grow at a steady pace due to the increase in adoption rate. In most developed countries, small hospitals are being acquired by large medical facilities. These small hospitals have limited infrastructure and investment in PACS helps in their development as reference laboratories. The rise in adoption of mini PACS in emerging markets is due to the rise in the number of small hospitals and government initiatives moving toward centralized healthcare IT systems.

According to Srinivas Sashidhar, a lead analyst at Technavio for medical imaging research: "The Americas has recorded increased installations of mini PACS in the recent years. However, it is expected that during the forecast period APAC [Asia-Pacific] would lead the global mini PACS market. Cost reduction by vendors would increase the affordability of these PACS in the emerging markets of APAC and EMEA [Europe, the Middle East and Africa]."

Global mid-end PACS

The global mid-end PACS market is expected to grow at a rapid pace, due to an increase in adoption rate and growing demand for integrated teleradiology network. The improvement in the healthcare information technology (IT) sector has triggered the installation of integrated systems. Mid-end PACS helps in connecting multi-modality departments and small hospitals, which helps in the enhancement of patient care. Hospitals with 250-500 beds and department-specific diagnostic centers are the primary end-users of mid-end PACS. These medical facilities have a sound infrastructure with moderate patient inflow in both emerging and developed markets.

Global enterprise PACS market

The global enterprise PACS market is expected to grow at a steady pace due to a moderate rise in adoption rate. The change in the healthcare IT sector triggers the installation of integrated systems. PACS radiology helps in connecting multi-modality departments and hospitals, which, in turn, helps in the enhancement of patient care. The adoption rate is expected to increase during the forecast period with the reduction in cost by vendors.

"Cloud-based applications are beneficial in collating medical imaging data in enterprise PACS. These PACS help in connecting one medical facility to another. The huge inflow of data is controlled by these PACS, allowing data sharing and management," said Srinivas.

The top vendors highlighted by Technavio's healthcare and life sciences market research analysts in this report are:

- GE Healthcare;
- Philips;
- Agfa-Gevaert;
- McKesson; and
- Fujifilm MEH

Philips showcases its latest connected health system at HIMSS17

Philips showcased a broad range of population health management, acute healthcare informatics and personal health solutions, fully integrated in a highly secure, cloud-based ecosystem at the 2017 Healthcare Information and Management Systems Society (HIMSS) conference and exhibition (HIMSS17) in February in Orlando, United States.

The company displayed their suite of interoperable intelligent solutions that provide advanced data and analytics to help support decision-making from the hospital to the home.

Prominently featured was Philips HealthSuite, a cloud-enabled connected health ecosystem of products, programs and services that seamlessly work together to empower personalized health and continuous care across the health continuum from prevention and healthy living, to diagnosis and treatment and home care.

Personal and population health management solutions were also featured and included the latest in population health analytics, chronic disease prevention and management, predictive analytics, enterprise telehealth, home monitoring, and sleep and respiratory care.

With the acquisition of Wellcentive, Philips brings expertise in aggregating and analysing patient data to improve health outcomes inside and outside the hospital walls.

The company is also enhancing its personal health programs with the launch of Jovia Coach, a smartphone app that combines technology with human coaching for people at-risk of type 2 diabetes. The program supports participants to adopt the dietary, lifestyle and exercise habits that could help to prevent type 2 diabetes; and Philips continuous care and home monitoring solutions help patients stay healthier at home, and connected to caregivers around the clock. They include Philips Lifeline medical alert device and Philips CareSage predictive analytics technology to support discharged patients in their home.

Healthcare Informatics

Philips also showcased their Healthcare Informatics Solutions. These provide actionable insights to support more confident clinical decision support and improved diagnostics. They include adap-

IntelliSpace Enterprise Edition

Philips introduced IntelliSpace Enterprise Edition, a managed service for hospital-wide healthcare informatics. The platform integrates Philips IntelliSpace portfolio into a scalable solution for clinical informatics and data management.

The platform offers a full suite of interoperable healthcare informatics applications and services for hospitals and integrated health networks. It helps health enterprises further improve quality of care while meeting the evolving challenges of budget constraints and the management, interoperability, security and value maximization of health data and information technology (IT) platforms.

For a manageable upfront cost based on pay-per-use, IntelliSpace Enterprise Edition provides Philips' extensive IntelliSpace portfolio and enhances it with an end-to-end managed service delivery model. The IntelliSpace portfolio consists of clinical tools for radiology, cardiology and oncology departments, intervention suites, as well as dose and data management solutions. The managed service offering provides many benefits to the IT administration, as well as for clinical teams. The solution ensures interoperability with cross-industry connectivity standards, single sign-on and integrated workflows.

With a known total cost of ownership, clinicians enjoy regular updates and always have access to the latest clinical tools and innovations. As part of the managed services, Philips provides continuous remote monitoring, as well as data backup and restore. This is further enhanced with benefits like the convenience of one 24/7 sup-

tive intelligence, integrated healthcare informatics, critical care analytics, automated early warning scoring, radiation dose management, and precision medicine solutions for oncology, including genomics.

IntelliVue

Philips IntelliVue Guardian Solution is designed to aid clinicians in the early detection of subtle signs of patient deterioration in the general care ward. It can be used with the Philips Wearable Biosensor, a medical-grade, self-adhesive, single patient-use wireless device worn discreetly on the chest that automatically and continuously measures key vital signs, including respiratory rate to alert caregivers to intervene quickly;

IntelliSpace Genomics

Philips IntelliSpace Genomics provides a secure healthcare informatics solution that integrates genomic information with full patient context to empower clinicians with precision diagnostics and therapeutics across hospitals. The solution, powered by Philips HealthSuite, delivers real-time, actionable diagnostic information – including raw sequencing data, up-to-date in silico genomic databases, clinical data and knowledge databases, longitudinal patient records, medical images and pathology data – to physicians and specialists for therapy planning at the point of care; and

Illumeo

Philips Illumeo is a newly launched imaging and informatics technology with adaptive intelligence that enhances how radiologists interpret and share medical images. The company said the intelligent software is the first to combine contextual awareness capabilities with advanced data analytics to augment the work of the radiologist. MEH

port line, one contract and a dedicated Customer Success Manager.

Philips IntelliSpace Enterprise Edition's pay-per-use model ensures the healthcare informatics portfolio always meets the healthcare enterprises' current IT needs. Usage elasticity can be scaled up and down as demand for care changes. Combined with clear performance indicators, such as guarantees on system uptime that come with IntelliSpace Enterprise Edition's partnership approach, it decreases financial risk for healthcare enterprises as they invest in their IT infrastructure.

IntelliSpace Enterprise Edition builds on and leverages the success of Philips' Picture Archiving and Communication System (PACS) managed service model.

Configured as a scalable and modular solutions platform, the initial launch of the secure, connected and intelligent IntelliSpace Enterprise Edition offers a harmonized managed service solution for the following applications:

- **IntelliSpace PACS** – Enables physicians to more efficiently manage their work without compromise, through connected images and information, secured patient data and intelligent work flow;
- **IntelliSpace Portal** – Advanced visual analytics to support complex interpretations across many clinical disciplines, including cardiology, oncology and neurology. Integrates with both IntelliSpace PACS and IntelliSpace Cardiovascular to deliver a seamless workflow experience for radiologists and cardiologists;
- **IntelliSpace Universal Data Manager** – a scalable, secure, interoperable data management solution that supports healthcare enterprises in organizing large datasets, including millions of images and other data from multiple sources, and quickly delivering them to virtually any clinician throughout their health network;
- **Illumeo with adaptive intelligence** – Clinically intelligent software that augments the skills of clinicians and redefines how they currently interface with images. Designed to empower radiologists and work for them, it provides the technology and tools that enhance their expertise and efficiency – all within a single workspace;
- **IntelliSpace Cardiovascular** – Provides access to advanced cardiovascular informatics applications, brings multimodality images and clinical tools together in a single workspace for integrated clinical decision support. It seamlessly integrates with IntelliSpace ECG and the Philips Xper Information Management cath lab workflow solution; and
- **Philips DoseWise** – Helps health systems manage patient and staff radiation exposure with a comprehensive suite of tools that collect, measure, analyze, and report dose exposure across departments and train care professionals in realizing a low-dose culture.

The solution will initially be available in North America.

dicomPACS – The perfect PACS for your hospital

dicomPACS® is a contemporary and actively maintained, high-tech solution for intelligent image management from Northern Germany. Thousands of satisfied customers in private practices, clinics and large hospitals around the world use this 'Made in Germany' PACS.

An ever-increasing number of hospitals optimise workflow with the help of computers. Staff quickly come to appreciate and rely on fully automated documentation and instant access to images and files. These developments improve many aspects of the daily routine, and result in significant savings in time and money. Our PACS can be customised to your individual needs. In hospitals, large numbers of medical imaging devices including X-ray, CT, magnetic resonance tomography and ultrasound machines can be integrated using our system. Special analysis and computing stations can be established. Multiple authorised users at different work stations can concurrently access the same images. The results of several examinations pertaining to a single patient can be combined, processed and viewed on the same monitor. All images are linked to the appropriate digital patient record. New findings can quickly be compared with previous observations.

Solutions

dicomPACS® is a smart choice for today and a wise investment for the future. The system is standardised, modular, and can be expanded as well as updated. Your data and archives are structured according to DICOM standards. The *dicomPACS*® software was developed by OR Technology in cooperation with medical specialists. The result is a well-designed and user-friendly tool for daily diagnostic tasks.

The *dicomPACS*® connects, directs and administers all processes having to do with images and documents: from admissions to diagnosis, data archiving and communication. Depending on the manufacturer, the system can comprise a wide array of features, including electronic faxes, document management, operative reports and X-ray histories. Software solutions for 3D reconstruction, surgical planning, voice recognition, and statistics can also be integrated.

The system can process image files from all medical imaging modalities, regardless of manufacturer.

With *dicomPACS*®, all images as well as diverse documents including admission notes, medical findings, medical histories and faxes are stored in a digital patient record and readily accessible. Modern medical care involves many different examinations that rely on imaging techniques and produce large data volumes on a daily basis. This information must be accessible online and securely archived for many years. The PACS data storage capacity can be increased upon demand.

dicomPACS® can easily be adapted to existing patient and image information management systems. Interfaces with radiology information systems (RIS) and hospital information systems (HIS) are straightforward. The image management system can accommodate established workflows and demands no changes in daily routine.

dicomPACS® can exchange data with all common standard interfaces (e.g., HL7, GDT, BDT) as well as proprietary and customised interfaces.

Images and documents in the DICOM format can be shared worldwide via internet and email. Online access to images is becoming increasingly important in all branches of clinical medicine.

ORCA – the cloud solution

ORCA (OR Technology Cloud Archiving) is a platform for storing, viewing and exchanging medical images and documents. ORCA offers two exciting applications: *ORCA Archive* and *ORCA Share*. Image files from direct sources and from PACS are stored in the cloud using *ORCA Archive*. At the same time, ORCA is a platform for communicating with external partners. Using *ORCA Share*, images and medical findings can be exchanged with colleagues, specialists and patients.

Diagnostic tools

The image management software *dicomPACS*® offers diverse special functions, including Chiro and NUCCA tools. These image processing functions were developed with American and Canadian specialists for chiropractic, orthopaedic and surgical applications. The software tools improve diagnosis and treatment planning.

- For further information, visit: *www.or-technology.com*
- Or email: *info@or-technology.com* MEH

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Extensive references in the MENA area are available.

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Global guidelines for HPV vaccination for cervical cancer prevention

The American Society of Clinical Oncology (ASCO) has issued a clinical practice guideline on human papillomavirus (HPV) vaccination for the prevention of cervical cancer. This is the first guideline on primary prevention of cervical cancer that is tailored to multiple regions of the world with different levels of socio-economic and structural resource settings, offering evidence-based guidance to healthcare providers worldwide.

The guideline includes specific recommendations according to four levels of resource settings: basic, limited, enhanced and maximal. The levels pertain to financial resources of a country or region, as well as the development of its health system – including personnel, infrastructure and access to services. The guideline complements ASCO's two other global, resource-stratified guidelines on cervical cancer, also stratified to these four levels of resources.[1,2]

Key guideline recommendations:

- In all environments and independent of the resource settings, two doses of human papillomavirus vaccine are recommended for girls ages 9 to 14 years, with an interval of at least 6 months and up to 12 to 15 months between doses.
- Girls who are HIV positive should receive three doses.
- For maximal and enhanced resource settings:
  - o If girls are 15 years or older and have received their first dose before age 15, they may complete the two-dose series;
  - o If they have not received the first dose before age 15, they should receive three doses;
  - o In both scenarios vaccination may be given through age 26 years.
- For limited and basic resource settings: if sufficient resources remain after vaccinating girls 9 to 14 years, girls who received one dose may receive additional doses between ages 15 and 26 years.
- Vaccination of boys: in all settings, boys may be vaccinated, if there is at least a 50% coverage in priority female target population, sufficient resources, and such vaccination is cost effective.

Cervical cancer is the fourth most common cancer among women worldwide, with less developed regions suffering a disproportionate burden from the disease. In fact, 85% of cervical cancer diagnoses and 87% of cervical cancer deaths occur in less developed regions, including parts of Africa and Latin America.

"Because resource availability varies widely, both among and within countries, we need to adjust strategies to improve access to HPV vaccination everywhere," said Silvia de Sanjosé, MD, PhD, co-chair of the Expert Panel that developed the guideline and head of the Cancer Epidemiology Research Program at Institut Català d'Oncologia in Barcelona, Spain. "This guideline is unique in offering cervical cancer vaccination recommendations that can be adapted to different resource levels and we expect it to have a major impact on the global health community."

HPV infection causes virtually all cervical cancers in the world. Although it may also lead to genital warts and certain other cancers, cervical cancer is by far the most common severe condition related to HPV infection. Unlike other existing HPV vaccination guidelines, ASCO's guideline focuses on the use of HPV vaccination specifically for the prevention of cervical cancer.

"Although HPV vaccine has been around for more than a decade, the uptake of the vaccine has been less than ideal in many places, including in high-resource countries such as the United States," said Silvina Arrossi, PhD, co-chair of the Expert Panel that developed the guideline

Academics call for greater research into endometriosis and the treatments available to patients

A new study has raised concerns over women's experiences gaining treatment for endometriosis - with many forced to live with painful side-effects and some reporting that medical staff don't take their concerns seriously.

The findings, which highlight the ongoing challenges experienced by many women living with the condition, were shared as part of Endometriosis Awareness Week in March in the United Kingdom by researchers at Birmingham City University's Faculty of Health, Education and Life Sciences.

Many reported the ongoing failure of treatments and described an array of negative side-effects including weight gain, hair loss, abnormal hair growth and depression. Women also felt that there is a lack of understanding about the condition from medical staff; whilst others spoke of their 'desperation' in searching for treatment options to help alleviate their pain.

Endometriosis is a condition where cells similar to those found in the lining of the womb are found elsewhere in a woman's body. It can cause painful periods, tiredness, bowel and bladder problems, and in some severe cases it can even lead to infertility. It is the second most common gynaecological condition in the UK, affecting 1.6 million women, a figure similar to the number of women affected by diabetes.

The study, which forms part of a larger research trial, looked at the experiences of women living with endometriosis and the various medical treatments available to them, including the pill, the coil and the injection.

Women described the frustration of trying to get a diagnosis. One woman stated: "I feel like the times that I was referred to the hospital – you really weren't taken seriously… I'm 22 and it was like when I was speaking to them they were like, 'You're just a young girl it's fine, you've had the symptoms for a while, you know, it's nothing serious.' It was like people just weren't really willing to listen."

Another commented: "I think you get to the point where you're so desperate. It's so hard to get people to take endometriosis seriously anyway."

After receiving the diagnosis, a woman describes the merry-go-round of ineffective treatments she'd been given to manage her endometriosis symptoms: "They started me on Depo-Provera, and that made it really, really bad… Then they put the coil in me and that, for a year and a half, was agonisingly painful. And they stopped that, and then they put me back on Depo-Provera actually. And then my symptoms got worse again, and then I was like, 'I can't do this.' So then they put me on the pill. They tried that for six, seven months, and it didn't do anything. Then they put me back on the coil for a month!"

Currently there is no cure for the condition and treatment options vary but can include surgery, hormone treatment, nutrition, and pain management.

Researcher Dr Annalise Weckesser said: "Endometriosis has long been a neglected area of research and funding. We know that the average waiting time for women to receive a diagnosis is seven years, which is unacceptable. Our pilot study shows that even once women receive a diagnosis, for some their struggle with managing their symptoms has only begun."

Professor Emeritus Elaine Denny, who was also part of the team of researchers said: "As there is no definitive treatment for endometriosis, many women will be prescribed a range of medical treatments with distressing side effects, such as symptoms of the menopause. Yet their effectiveness may be short lived or non-existent, and they may temporarily impact on fertility. We desperately need more research into the condition to help the millions of women who are living with the condition." MEH

and an official and researcher at the Instituto Nacional del Cancer in Buenos Aires, Argentina. "As an organization of cancer doctors, ASCO continues to endorse HPV vaccination programs and efforts to help spare more women around the world from this very difficult cancer."

Guideline methodology

The guideline recommendations were developed by a multinational and multidisciplinary panel of oncology, obstetrics/gynecology, public health, cancer control, epidemiology/biostatistics, health economics, behavioural/implementation science, and patient advocacy experts, including some of the world's foremost research leaders on HPV and HPV vaccines.

The Expert Panel reviewed relevant literature published from 1966 to 2015, including systematic reviews, existing guidelines, and cost-effective analyses. This guideline reinforces selected recommendations offered in the World Health Organization (WHO) guideline, US Centers for Disease Control and Prevention (CDC) guidelines, National Advisory Committee on Immunization guideline (Canadian), German guidelines, and Immunise Australia guideline.

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on the WEB The Primary Prevention of Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline
www.asco.org/rs-cervical-cancer-primary-prev-guideline MEH

Why fertility declines with age

Researchers at the University of Montreal Hospital Research Center (CRCHUM) have discovered a possible new explanation for female infertility. Thanks to cutting-edge microscopy techniques, they observed for the first time a specific defect in the eggs of older mice. This defect may also be found in the eggs of older women.

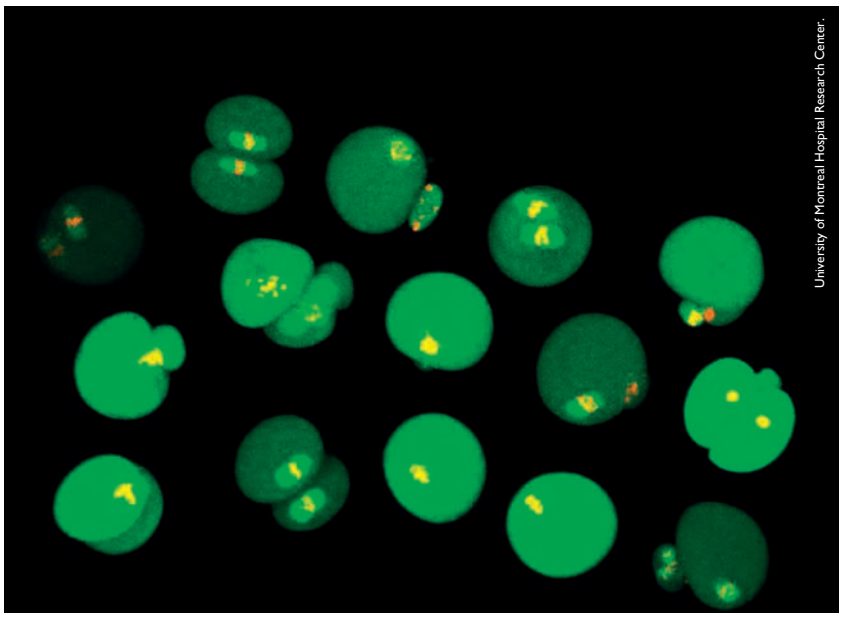
The defect causes the choreography of cell division to go awry, and leads to errors in the sharing of chromosomes. These unprecedented observations are published in *Current Biology*.

"We found that the microtubules that orchestrate chromosome segregation during cell division behave abnormally in older eggs. Instead of assembling a spindle in a controlled symmetrical fashion, the microtubules go in all directions. The altered movement of the microtubules apparently contributes to errors in chromosome segregation, and so represents a new explanation for age-related infertility," said CRCHUM researcher and Université of Montreal professor Greg FitzHarris.

Women – and other female mammals – are born with a fixed number of eggs, which remain dormant in the ovaries until the release of a single egg per menstrual cycle. But for women, fertility declines significantly at around the age of 35.

"One of the main causes of female infertility is a defect in the eggs that causes them to have an abnormal number of chromosomes. These so-called aneuploid eggs become increasingly prevalent as a woman ages. This is a key reason that older women have trouble getting pregnant and having full-term pregnancies. It is also known that these defective eggs increase the risk of miscarriage and can cause Down's syndrome in full-term babies" explained Prof FitzHarris.

Scientists previously believed that eggs are more likely to be aneuploid with age because the "glue" that keeps the chromosomes together works poorly in older eggs. This is known as the "cohesion-loss" hypothesis.



The choreography of cell division goes awry in the eggs of older mice and causes errors in the sharing of chromosomes.

"Our work doesn't contradict that idea, but shows the existence of another problem: defects in the microtubules, which cause defective spindles and in doing so seem to contribute to a specific type of chromosome segregation error," said Prof FitzHarris.

Microtubules are tiny cylindrical structures that organize themselves to form a spindle. This complex biological machine gathers the chromosomes together and sorts them at the time of cell division, then sends them to the opposite poles of the daughter cells in a process called chromosome segregation.

"In mice, approximately 50% of the eggs of older females have a spindle with chaotic microtubule dynamics," said Prof FitzHarris.

The researchers conducted a series of micromanipulations on the eggs of mice between the ages of 6 and 12 weeks (young) and 60-week-old mice (old).

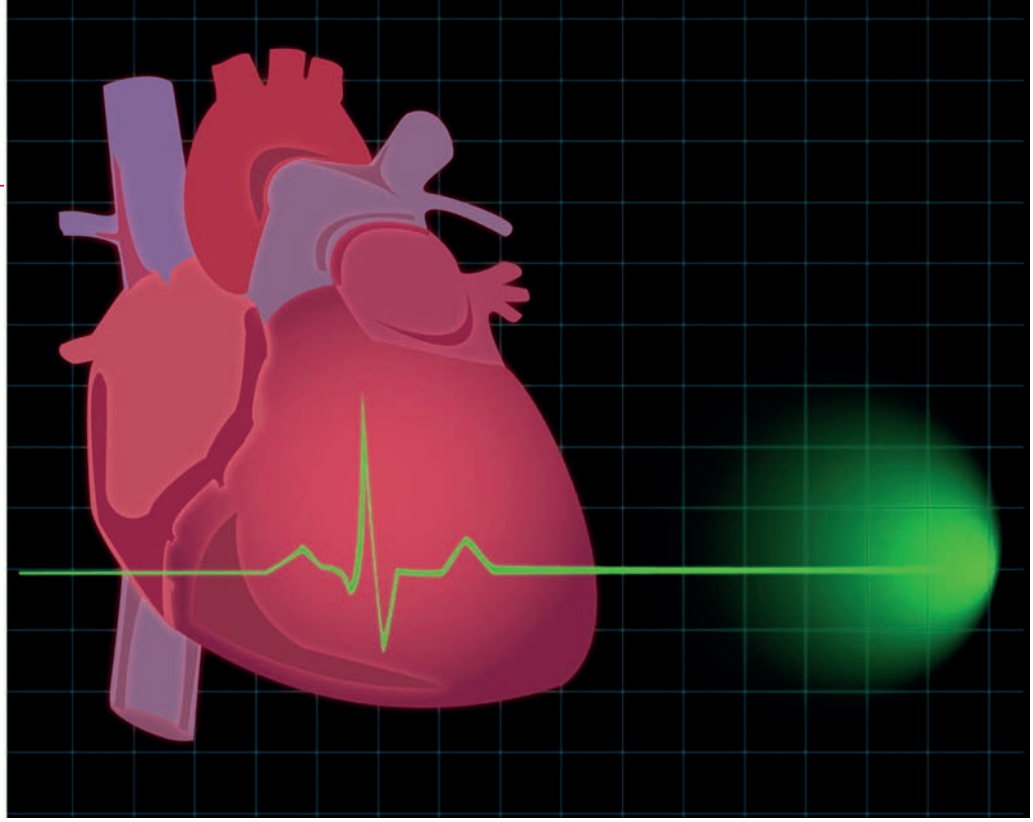
"We swapped the nuclei of the young eggs with those of the old eggs and we observed problems in the old eggs containing a young nucleus," explained Shoma Nakagawa, a postdoctoral research fellow at the CRCHUM and at the Université de Montréal. "This shows that maternal age influences the alignment of microtubules independently of the age of the chromosomes contained in the nuclei of each egg."

Prof FitzHarris's team notes that spindle defects are also a problem in humans. In short, the cellular machinery works less efficiently in aged eggs, but this is not caused by the age of the chromosomes.

This discovery may one day lead to new fertility treatments to help women become pregnant and carry a pregnancy to term.

"We are currently exploring possible treatments for eggs that might one day make it possible to reverse this problem and rejuvenate the eggs," explained Prof FitzHarris.

• **doi:** 10.1016/j.cub.2017.02.025 MEH



Big women have nearly threefold greater risk of atrial fibrillation

Big women have a nearly threefold greater risk of atrial fibrillation than small women, according to research presented at EuroPrevent 2017. The study included 1.5 million women who were followed-up for more than 30 years.

Atrial fibrillation is the most common heart rhythm disorder, with a 20% lifetime risk. It occurs most often in people over 60 years of age and increases the risk of stroke and heart failure.

"Our research has previously shown that a large body size at age 20, and weight gain from age 20 to midlife, both independently increase the risk of atrial fibrillation in men," said author Professor Annika Rosengren, professor of internal medicine at the Sahlgrenska Academy, University of Gothenburg, Sweden. "In this study we investigated the impact of body size on atrial fibrillation risk in women."

The study included 1,522,358 women with a first pregnancy aged 28 years on average. Data on weight early in pregnancy, height, age, diabetes, hypertension and smoking were obtained from the Swedish Medical Birth Registry. Information on hospitalisation with atrial fibrillation was collected from the Swedish Inpatient Registry.

Body surface area (BSA) in m2 was calculated by a standard formula based on weight and height. Women were divided into four groups according to BSA: 0.97–1.61, 1.61–1.71, 1.71–1.82, and 1.82–3.02 m2.

During a maximum follow up of 33.6 years (16 years on average) 7,001 women were hospitalised with atrial fibrillation at an average age of 49 years. Compared to women in the lowest BSA quartile, those in the second, third, and fourth (highest) quartiles had a 1.16, 1.55 and 2.61 times increased risk of atrial fibrillation, respectively, after adjustment for age at first pregnancy, diabetes, hypertension and smoking.

"We found that bigger women have a greater risk of atrial fibrillation," said Professor Rosengren. "There was a stepwise elevation in risk with increasing body size. The group with the highest body surface area had nearly three times the risk as those with the lowest body surface area."

BSA is influenced by both height and weight. Compared to women with the lowest BSA, those with the highest BSA were 9 cm taller (161 versus 170 cm), 28 kg heavier (54 versus 82 kg), and had a higher body mass index (BMI: 21 versus 28 kg/m2).

"Atrial fibrillation is the result of obesity-related metabolic changes but there is also a second cause," said Professor Rosengren. "Big people – not necessarily fat, but big – have a larger atrium, which is where atrial fibrillation comes from. People with a bigger atrium have a higher risk of atrial fibrillation."

"Generally it's better to be tall because you have less risk of stroke and heart attack, and better survival," continued Professor Rosengren. "Taller people are often are better educated, have higher socioeconomic status, and may have received better nutrition at a young age and in the womb. But in this case being tall is less desirable because it alters the structure of the heart in a way that may be conducive to atrial fibrillation."

Professor Rosengren pointed out that the absolute risk of atrial fibrillation in these young women, regardless of weight, height or BSA was very low (less than 0.5%). "In general young women need not worry about their risk of atrial fibrillation, whatever their body size," she said. "For older women and men, being big could be an indicator that you are at increased risk of atrial fibrillation. In the clinic I have seen many big people with atrial fibrillation."

She concluded: "If you are very tall, I think that it could be a good idea to avoid accumulating excess weight. That would apply to both men and women." MEH

Neena and her boys

Creating a different future for people with JMC

Expert care coming from Nemours/Alfred I. duPont Hospital for Children

Thanks to Dr. MacKenzie at Nemours/Alfred I. duPont Hospital for Children in Wilmington, Delaware, Neena received care for her Jansen metaphyseal chondrodysplasia (JMC). For Neena, however, the road to Nemours/Alfred I. duPont Hospital for Children began in Dubai.

Born in Dubai, Neena was sick and spent most of her time as an infant in the NICU. Her bones were soft and there was little, if any, cartilage, causing her legs and arms to be bowed and turned inward. As a result, she was delayed developmentally, and didn't begin walking until she was almost 4 years old. Doctors diagnosed her with rickets, then polio, and treated Neena with a variety of medications – but nothing helped. She was confined to a wheelchair for 10 years, but despite the overwhelming amount of pain and more than 30 surgeries, Neena persevered.

After graduating from college, Neena got a job and began living on her own. She ultimately met Adam online. Adam was living in Nebraska and they communicated online for 10 months. Finally, Adam flew to Dubai to meet Neena. They were married two weeks later and have been married 10 years.

Doctors said Neena would likely never have children and, if by some chance she did, the baby would not go to term. Neena did carry a baby boy, Arshaan, to term without any complications. However, when Arshaan was 2 and Neena was pregnant with her second son, Neena noticed Arshaan's legs were beginning to turn outward, just like hers did. Then at her four-month checkup, the limb measurements of her unborn child were off. A pediatric geneticist tested Arshaan, and he was diagnosed with nephrocalcinosis, a condition doctors never detected in Neena.

Diagnosed with Jansen metaphyseal chondrodysplasia

Blood work was then sent to Germany and Jansen metaphyseal chondrodysplasia (JMC) was confirmed as the diagnosis. Jansen type metaphyseal chondrodysplasia (JMC) is an extremely rare progressive disorder in which portions of the bones of the arms and legs develop abnormally with unusual cartilage formations and abnormal bone formation at the bulbous end portions (metaphyses) of these long bones (metaphyseal chondrodysplasia). As a result, affected individuals exhibit unusually short arms and legs and short stature, findings that typically become apparent during early childhood. Abnormal cartilage and bone development may also affect other bones of the body, particularly those of the metacarpals and metatarsals. During childhood, affected individuals may begin to show progressive stiffening and swelling of many joints and/or an unusual waddling gait and squatting stance.

Neena, Arshaan and Neena's second son, Jahan, are three of just 30 people in the world with JMC. Following their diagnosis, Neena and her family moved from Dubai to the United States so they could receive care from Dr Mackenzie at Nemours/Alfred I. duPont Hospital for Children. Arshaan and Jahan have each had four surgeries in Wilmington, Delaware: osteotamies with ring fixators to straighten and support their legs, followed by extensive physical therapy. For the boys, ages 6 and 8, the toughest part has been relearning how to walk after each surgery.

With the intention of finding a cure for JMC, Neena established the Jansen's Foundation. In partnership with a prominent researcher from Boston, the concept behind a cure is that this condition could be managed as a chronic illness similar to the way diabetes is managed via an insulin pump. For JMC, when calcium levels drop too low, a pump would infuse calcium to keep the bones strong. If all goes as planned, Neena will be the first person to try this experimental cure, followed by her sons.

Since the creation of the Jansen's Foundation, Neena was contacted by a girl from Paraguay with JMC. Neena and Adam hope they can bring her to Nemours/Alfred I. duPont Hospital for Children to meet Dr Mackenzie. MEH

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BEST CHILDREN'S HOSPITALS
U.S.News & WORLD REPORT
ORTHOPEDICS 2016-17

Meet Evelyn, Gabby and Zoey. Diagnosed with achondroplasia and patients of Nemours, these strong little girls were all smiles when they reconnected at a Little People of America Regional Conference, hosted by the Nemours skeletal dysplasia team.

At Nemours, we partner with families every step of the way to build lasting relationships. To understand the unique needs of each child—not just the condition. And to provide the most advanced quality of care from world-renowned orthopedic and genetic experts. It's all part of our promise to help kids everywhere have a better chance of growing up healthy and happy.

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Hamburg-based private fertility clinic offers advanced expertise in 'oasis of calm'

Fertility Clinic Valentinshof is a private fertility clinic in Hamburg, Germany, where couples wishing to have a child but struggling with infertility problems find expertise and professionalism. In this pure and welcoming practice there is an "oasis of calm" – a place where couples can catch their breath and relax, because they know that they and their needs are the focus of our practice.

The team consists of five highly skilled doctors and biologists. That is Dr Anja Dawson, gynaecologist and obstetrician, with specialization in reproductive medicine and prenatal medicine; Dr Nuray Aytekin, gynaecologist and obstetrician, with specialization in reproductive medicine; Dr Ulrich Knuth, gynaecologist and obstetrician, with specialization in reproductive medicine and andrology, as well as; Dr Elke Leuschner, reproductive biologist and Dr Andreas Schepers, reproductive biologist and senior clinical embryologist, who run the IVF laboratory.

Fertility Clinic Valentinshof has exceptional success in pregnancy rates, especially in couples who have 'given up'. Their highly experienced doctors, embryologists, the advanced technology they use and the quality of their laboratory as well as the empathy they offer, are all reasons for this success.

Fertility Clinic Valentinshof offers a complete range of fertility treatments – from optimizing the body's natural cycle to assisted or in-vitro fertilization (IVF/ICSI).

Their holistic approach is also focussed on the male partner: He is directly included in the therapy. They know from discussions with their patients that couples appreciate this approach. They also work with partners in associated disciplines such as nutrition, osteopathy, psychology, TCM and urology.

They draw information on the latest fertility treatments from international congresses and publications. Any significant developments that they find worthy are directly integrated into their work.

> Fertility Clinic Valentinshof has exceptional success in pregnancy rates, especially in couples who have 'given up'.

"We work with the most modern equipment in our own IVF laboratory. In constructing our practice, we paid special attention to using clean, low-pollutant materials throughout," says Dr Dawson.

They guarantee their patients the greatest possible discretion, keep the waiting times as short as possible and they offer individual rooms in their consultation area.

"We are an independent clinic that is not bound to any health or laboratory company. We are only bound by our service to you, and by the traditional values of the medical profession," says Dr Dawson. MEH

Women suffer from asthma symptoms more frequently and more severely than men

Women suffer more frequently and more severely from pollen and food allergies and therefore also from asthma, according to Erika Jensen-Jarolim from MedUni Vienna's Institute of Pathophysiology and Allergy Research.

She explains that female sex hormones increase the risk and symptoms of asthma and allergies and, adds that hormone preparations such as the contraceptive pill play a role.

These factors should be given more consideration than was previously the case, says Jensen-Jarolim.

Up until the age of 10, boys are more likely to suffer from allergies and asthma and to have more severe symptoms. But the increased production of the sex hormone oestrogen associated with the onset of sexual maturity and puberty means that girls become much more susceptible. Jensen-Jarolim explains: "Oestrogens cause inflammatory cells, such as the mast cells, for example, to react more sensitively to allergens. Conversely, the male hormone testosterone seems to exert a kind of protective function."

This phenomenon accompanies women through the waves of hormone production in their respective life phases – from their first period to the taking of contraceptives, pregnancy through to hormonal replacement therapy at the menopause. In addition to that, they become more sensitive to environmental pollutants, especially smoking.

Nowadays, taking hormones is almost unavoidable because of life and family planning and also to avoid falling hormone levels, which play a significant role in the development of osteoporosis, for example.

"Such hormone treatments can trigger hypersensitivities, which, on top of that, are characterised by atypical symptomatology," explains Jensen-Jarolim. These atypical symptoms include migraines, joint pain, eczema, worsening of acne and breathing difficulties. "We still do not pay enough attention to these links in the interaction between allergology and gynaecology." Hormone treatments also play an increasing role in transgender medicine and must be borne in mind.

Hormonal factors in allergies

"Where am I in my cycle? Am I taking hormone preparations? Do I already suffer from asthma?" – these questions should be considered and discussed between doctor and patient, advises Jensen-Jarolim. Especially if the woman is pregnant. "The hormone balance changes again in pregnancy. Asthma can worsen in one third of pregnant women – and an asthma attack during pregnancy represents a serious risk to mother and child." It is therefore advisable to have an allergy diagnosed at an early stage, preferably before pregnancy – because an untreated allergy is the first step towards asthma.

A field of research that is still in its infancy but is becoming increasingly important and affects women is that of allergy to hormones themselves, that is to say a "hormone allergy" in connection with contraceptives, which can lead to miscarriage. The scientists at MedUni Vienna believe there is a pressing need not only to initiate research in this area but also to improve diagnostics together with the gynaecologists. MEH

Bariatric surgery – more than merely weight loss

For years the Berlin-based specialists Prof. Dr. Jürgen Ordemann and Prof. Dr. Michael Ritter have been successfully treating obese patients conservatively and surgically. They are aware of the prejudices and restrictions which those affected have to struggle with. Obesity is a transboundary problem: no other disease spreads so strongly and quickly – the WHO refers to a global obesity epidemic. In some countries, a normal weight has already become an exception and overweight has become the rule. "The consequences are catastrophic", says Professor Ordemann, "mortality is rising while life expectancy is decreasing, and concomitant diseases such as type 2 diabetes mellitus, sleep apnoea syndrome, infertility as well as cardiovascular and tumour diseases are increasing." Obese patients often no longer manage to reduce their weight on a long-term basis. "From a considerable extent of overweight, genetic causes and metabolic changes bring about a poor prognosis, not the 'weakness of character' or 'laziness' of those affected. Today we know that surgical measures can break the cycle", explains Professor Ritter. Numerous studies show that surgical therapy constitutes the only effective and above all sustainable treatment for obesity. Metabolic sequelae are substantially improved, frequently even healed – this explains why the medical discipline is also called 'metabolic surgery'. "According to our experience, the quality of life among operated patients increases immediately, while mortality decreases substantially compared to obese patients who did not have the surgery", says Ordemann. The most common bariatric surgery procedures are the following:

Experts place the gastric bypass in a minimally invasive procedure

First a small stomach pouch (20-30 ml) is placed on the cardia and separated from the remaining stomach. The small intestine is subsequently severed in the upper segment and connected with the stomach pouch. Food enters this significantly shortened section of the small intestine, whereby the nutrient absorption otherwise occurring in another section is omitted. Instead, only bile and digestive enzymes from the pancreas are transported here. Further below the loop is reconnected to the small intestine. The weight loss anticipated through the gastric bypass is up to 80% of excess weight. In addition, hormonal and neuronal changes are decisive for the success.

The placement of a sleeve gastrectomy also occurs laparoscopically

In the process, two thirds of the stomach are resected, i.e. removed. The remaining stomach encompasses about 80-120 ml, has the shape of a sleeve and roughly the size of a banana. The sleeve gastrectomy extends from the oesophagus to the pyloric orifice and is further accessible by means of endoscopic examination methods. With the removal of stomach tissue, not only a reduction in the size of the stomach occurs, but also an appetite-curbing effect. Neuronal control elements – which have a direct influence on the pivotal metabolic centres – also seem to be activated with the procedure. The operation takes 30 to 60 minutes and is performed under general anaesthesia. Patients can lose up to 75% of their excess weight. Among those affected from warmer countries, the necessarily increased intake of fluids is to be heeded. That is why the sleeve gastrectomy is usually preferred to the gastric bypass in a common conversation.

Both procedures reduce the size of the stomach (restriction) and ensure a desired maldigestion (malabsorption). The origins of bariatric surgery were solely designed to reduce the energy intake of patients and thereby to enable a severe weight loss. "Meanwhile we know that the effect of an operation is considerably more comprehensive. Clinical and experimental studies push restriction and malabsorption into the background. Complex physiological mechanisms are more important", emphasises Professor Ordemann. "The altered digestive anatomy leads to diverse biophysiological processes. Thus an altered release or the blockage of specific intestinal hormones – which seem to have an exclusive role in the hunger and satiety system – comes about. Immediately after the operation, patients have less appetite and rapidly have the feeling of satiety." Despite less hunger, most patients experience an increase in their energy turnover. "After a surgical procedure, diets are no longer perceived as an ordeal, but as a normal condition", adds Professor Ritter. All these mechanisms lead to the fact that seriously ill, obese patients can reduce their weight for the first time on a long-term basis – this enables active participation in life, while self-esteem and quality of life are considerably enhanced.

Professor Dr. Jürgen Ordemann heads the Centre for Obesity and Metabolic Medicine at HELIOS Hospital Berlin-Buch.

Professor Dr. Michael Ritter heads the Department of Diabetology and Endocrinology at HELIOS Hospital Berlin-Buch.

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Or visit: *www.helios-international.com*
Or discover: *www.heliosaktuell.de/en/international-news* MEH

Region's healthcare leaders gather in Dubai to learn latest developments in diagnostics

The 4th annual "Roche Days" medical conference brought together more than 300 medical experts to exchange knowledge, and discuss challenges and solutions in diagnostics – focusing on serology, cardiovascular diseases, and women's health.

Improving turnaround time for laboratory results, testing for imminent heart attacks and detecting cervical cancer are just some of the important topics discussed at the 4th annual Roche Days conference. Roche Days, presented by Roche Diagnostics Middle East, is a platform for key opinion leaders throughout the region. More than 300 of the region's medical experts in the in-vitro diagnostics (IVD) industry in the Middle East were hosted from 11-13 March 2017.

The conference was inaugurated by Sheikha Rasha Al Qassimi, Phd, Food Science & Technology (UK) and Assistant Director General of Public Health and Central Laboratories, Sharjah Municipality, assisted by Harald Wolf, General Manager, Roche Diagnostics Middle East. Roche Days was held as part of Roche Diagnostics' commitment to providing continued medical education and highlighting regional expertise to share knowledge and discuss challenges as well as solutions in diagnostics particularly in the areas of cardiovascular diseases and women's health, such as cervical cancer, and laboratory automation.

"Through our Roche Days, we were able to cascade the many benefits of laboratory automation in the industry and allow for cross-border collaboration to bring together the brightest minds in the region to discuss challenges and solutions. We live in a fast-paced period when technology continues to bring greater benefits for us. Roche Diagnostics leads the way in in-vitro diagnostics in terms of research and innovation to provide the broadest range of laboratory solutions which dramatically improve turnaround time for tests and results, provide efficiency, quality and safety," said Mr. Wolf.

A focus of this year's Roche Days was on laboratory automation and more efficient laboratory procedures to release diagnostic information to physicians faster while also reducing error and sample contamination. With automation, Dr Amid Abdelnour, Chief Executive Officer, Biolab, Jordan, noted that a remarkable increase in patient safety as well as productivity and capacity are being observed with the implementation of automation in laboratories.

Innovations in diagnostics also paved the way for testing heart attacks faster with more precise and reliable results. It is estimated that 23.6 million people will die by 2030 from cardiovascular diseases and accurate early detection and intervention is crucial. With high-sensitivity assays, doctors are now able to improve the speed of detection of myocardial injury and can help identify risks associated with cardiovascular diseases and predict adverse outcomes.

Dr Rabih Azar, Professor of Medicine, St. Joseph University, Chief of Cardiology Research, Division of Cardiology, Hotel Dieu de France Hospital, Lebanon, noted that with available high-sensitivity tests, a safe and rapid diagnosis can be done within one hour of observation, which is faster than the usual 3-6 hours of observation using the conventional diagnostic approach. This was discussed extensively during the acute coronary diseases panel session, which included Dr Laila Abdel-Wareth of Cleveland Clinic Abu Dhabi, among others.

In terms of women's health, cervical cancer remains a challenge across the region due to lack of awareness among women and, until recently, the lack of a specific diagnostics tests or screening. While cervical cancer is preventable, although around 500,000 new cases worldwide are diagnosed every year. However, with the advanced diagnostic tools available, doctors can now detect cervical cancer early and prevent progression of the disease.

To this end, Dr Hisham Shams, Group Medical Director at Alborg Medical Laboratories, Saudi Arabia, brought to light new tools and new thinking in addressing cervical cancer. The past limitations on cervical cytology have been replaced with improved methods to detect the presence of Human Papillomavirus (HPV), the principal cause of cervical cancer in women. Using HPV molecular diagnostics instead of the conventional methods, the sensitivity of detection is increased by 50%.

"The conference provided a platform to change the view of diagnostics being just a tool for diagnosis. From prevention to monitoring, diagnostics is now an integral part of decision making along the healthcare continuum," said Mr. Wolf. MEH

Surviving war, and what comes after

By **Dr Gregory Keane**

I first noticed him as I looked through the broken windows at the gathering crowd. We were near the town of Baharka, north of Erbil, Kurdistan. It was afternoon, on the 10th of August 2014. He was about 12, thin and a little taller than his mates. Apart from the fact he was without shoes, he was dressed for the bright sky and 40°C heat. He was kicking a football around in the dust outside the medical clinic, hastily set up by MSF in a derelict building in the quickly thrown together camp. Occasionally, he would peer through the window then return to his game.

In the sudden crisis of that week I had been drawn away from my usual role as psychiatrist working in refugee camps with Syrians escaping their own war. Under the supervision of our senior physician, I helped out in the medical clinic. Looking around the clinic room, what you would have seen was a crowd of people – mostly women, children and elderly; huddling, sweating, around plastic tables and chairs. A makeshift partition providing some semblance of privacy. There were bottles of water for people thirsty with heat and some carpet rolled out to make the place feel more welcoming: small attempts to provide the tiniest bit of dignity and show some respect to people who had just lost their homes and livelihoods. In the previous hours, following the push by ISIS from Mosul toward Erbil, a huge exodus of humanity – some 500,000 people – had rapidly departed the eastern part of Ninewah province. The boy and his family, like the other people waiting in the clinic queue, had suddenly left villages like Qaraqosh, a town 30km east of Mosul.

The story of this family is familiar to many Iraqis. Their flight from danger had certainly not been the family's first. Earlier that summer in the first few days of June 2014, they had fled eastward out of Mosul to escape the brutality of ISIS. At the very end of the clinic that day, after the last of more than 100 patients had been seen for their basic medical needs, the boy approached my table. He had a shy smile, hands behind his back, eyes pointed toward the ground. When I asked what we could do to help, he pointed to his calves and explained that they hurt. Hot and tired myself, but missing the extra moments I would usually have with my patients as a psychiatrist, I offered him a seat. We spent a few moments together. He explained that the night before he had fled Qaraqosh with his family. In the enormous traffic jam that night, surrounded by the fleeing city, their car could go no further. While his mother and father carried their other children, the boy carried his baby brother the extra kilometres across the border to safety in Kurdistan.

Psychiatric care

MSF's mental health teams currently work in 'hot spot' provinces across Iraq and the Kurdistan region of Iraq. The teams are composed mostly of people employed locally – many being the survivors of war and displacement themselves. With the failure of public health systems in Mosul over the last two years, care for people with chronic conditions, including those with psychotic disorders, has often been unavailable for long periods. Their symptoms may have relapsed, leading to distress and placing a huge burden upon them and their families. MSF provides psychiatric care for these people with our Syrian and Iraqi psychiatrists, medical doctors and other therapists working in IDP camps each day.

Stress support & psychological care

There is little to be said when faced with the immediacy of situations such as those faced by Iraqis at the moment. What has been done cannot be undone. In the aftermath, however, when relative safety is reached and an uncertain future awaits, the mental health clinician's job is to identify how much the person might have been affected by the stress of their situation, and consider approaches to support the survivor's return to effective functioning. As well as recruiting the person's own internal strengths and social supports, MSF uses various psychological approaches, including cognitive-behavioural and narrative

MSF UAE

MSF has been in UAE since 1992 under the patronage of Sheikh Nahyan Bin Mubarak Al Nahyan, the UAE Minister of Culture, Youth, and Community Development. MSF in UAE consists of Executive, Finance, HR & Administration, Communications & Fundraising, Logistics and Desks (program manager, HR, Finance, logistics and medical referent).

Visit: *www.msf-me.org*

therapies. Therapeutic interventions that can help manage symptoms of trauma are also used. Working out of containers, tents and mobile clinic vehicles, our therapists and psychiatrists in 12 camps in Ninewah carry out more than 700 individual consultations each week.

More than a million displaced

As of March 2017 more than a million people have been displaced from Mosul – many in the numerous IDP camps scattered across Ninewah and in Kurdish controlled territory. Thousands continue to leave Mosul each day. Each has their own story of loss and survival – like the boy and his family from Qaraqosh. The world's responsibility is the same now as it was in 2014: To ensure safety first, then water, food, shelter and medical care. Once acute needs are met, the mental health clinician's role is first to listen and act as witness. Observing the hurt, fear, loss and uncertainty. Using psychological interventions, clinicians can then help people understand their troubling symptoms of stress and seeing them as very normal responses to shockingly abnormal events. We also observe the resilience and strength that emerges, by necessity. We note a survivor's courage in the face of fear, and action in the face of danger. MEH

The Author

Dr Gregory Keane is a psychiatrist and works in the Middle East for Médecins Sans Frontières (MSF).

Syrian hospital supported by MSF bombed

A hospital in northern Syria supported by Médecins Sans Frontières (MSF) has been hit in an aerial attack, MSF said in a statement on 31 March..

At around 6 pm on 25 March, Latamneh hospital in northern Hama governorate was targeted by a bomb dropped by a helicopter, which hit the entrance of the building. Information collected by the hospital medical staff suggests that chemical weapons were used.

Immediately after the impact, patients and staff reported suffering severe respiratory symptoms and burning of mucous membranes – symptoms consistent with an attack using chemicals.

Two people died as a result of the attack, including Dr Darwish, the hospital's orthopaedic surgeon. Thirteen people were transferred for treatment to other facilities.

"The loss of Dr Darwish leaves just two orthopaedic surgeons for a population of around 120,000," says Massimiliano Rebaudengo, MSF's head of mission in northern Syria.

Following the attack, the hospital went out of service for three days, after which the emergency room reopened.

Latamneh hospital is located a few kilometres from the frontline between government and opposition forces, and provides medical care for a population of around 8,000. Prior to the attacks, the hospital had an emergency room and inpatient department, and provided general and orthopaedic surgery.

"Bombing hospitals, although banned by international humanitarian law, remains common practice in Syria, and health services are severely affected by these repeated attacks," says Rebaudengo.

Despite a new round of peace talks between warring parties, which began in January, increased fighting is taking place on several fronts. In northern Hama governorate, 40,000 people have fled their homes due to the fighting.

Over the past year, MSF has received reports of at least 71 attacks on at least 32 different health facilities which it runs or supports in Syria. On 22 February, an MSF-supported health facility in Idlib governorate was hit by rockets, killing six and wounding 33.

MSF directly operates four health facilities in northern Syria and provides support to more than 150 health facilities countrywide. MEH

Revolutionary non-surgical bone conduction hearing solution launched in UAE

A new innovative technology offering a non-surgical bone conduction solution for conductive hearing loss, will soon be available in the UAE. MED-EL, the leading provider of hearing implant solutions in the Middle East, announced the launch of the next generation of bone conduction hearing solutions: ADHEAR. The new hearing system has no age limitation, meaning that infants right through to the elderly with conductive hearing loss or single sided deafness "SSD" are expected to obtain benefit.

ADHEAR is an excellent option for people with conductive hearing loss who are unsuitable for, or not wishing to undergo, bone conduction implant surgery. The novel system has two external components: an adhesive adaptor and an audio processor. The audio processor picks up sound waves, converts them into vibrations and transmits them onto the bone via an advanced adhesive adaptor worn behind the ear. The bone then transfers the vibrations through the skull to the inner ear where they are processed as normal sound. Bone conduction uses the skull bone to transmit sound waves directly to the inner ear and may be an appropriate option for people who have hearing loss due to problems with the eardrum, ear canal or middle ear.

Notably, ADHEAR fills an unmet need for a viable non-surgical bone conduction solution on the market, one that is both aesthetically pleasing and comfortable to wear, yet does not sacrifice sound quality.

• For more information, visit: *www.medel.com*

About ADHEAR

ADHEAR is an easy-to-use and comfortable-to-wear system that provides consistent access to sound and can be worn discretely behind the ear. The device is available in three colours: Simply Black, Terra Brown and Dove Silver.

Audio Processor

Height	15mm
Width	35mm
Weight including battery	15g

Adhesive Adaptor

Height	6mm
Width	30mm
Weight	1g

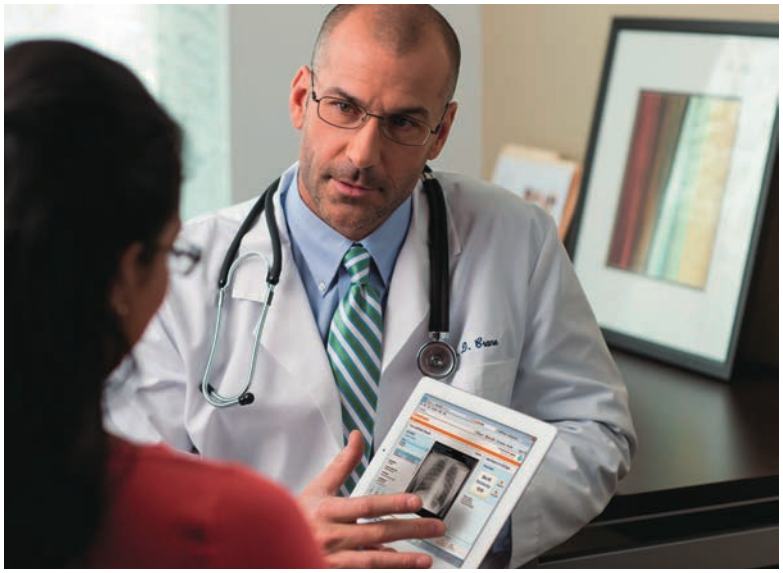
Power Supply

One non-rechargeable size 13 zinc-air button cell with a nominal 1.4 volt supply, offering a battery lifetime of approximately two weeks

Connectivity

ADHEAR can be connected to audio devices (mobile phones, etc.), Bluetooth streamers and accessories, FM receivers, telecoil receivers

Carestream launches new Vue Clinical Collaboration Platform



Carestream's new Vue Clinical Collaboration Platform (CCP) delivers next-generation enterprise clinical content management to help medical professionals achieve higher productivity and enhanced patient care. This platform delivers comprehensive, patient-centered views of clinical images and data across departments and sites.

Carestream's CCP supports an advanced radiology diagnostic viewer and powerful multimedia reporting with images and interactive hyperlinks. The Carestream Vue platform is vendor-neutral and interoperable with existing IT ecosystems.

• For more information, visit: *www.caresteam.com*

Timesco a leader in reusable and single-use laryngoscopes

Timesco Healthcare Ltd, England, has been at the forefront of laryngoscopes design, manufacture and innovative developments in intubation for over five decades.

Timesco manufactures the world's number one single use disposable fibre optic laryngoscopes system "Callisto", which is complemented with Callisto single use and Optima reusable LED handles.

Complete ranges of single use, "Callisto", "Europa" and reusable "Optima", "Sirius" laryngoscopes systems covering from neonate to adult intubation, as well as specialist, Robert Shaw, Seward, and difficult intubation "Eclipse" tilting tip blades are available.

The Timesco Laryngoscope programme is also available with a new Rechargeable system. Timesco has also added innovative, award winning, energy savings systems for extended battery life, EES and ION.

The Timesco Laryngoscope programme is part of Timesco product ranges which cover all disciplines of surgery. Timesco surgical and medical ranges cover premium O.R. quality Surgical Instruments, Dental, Electro surgery, Diagnostic, EMS etc.

Timesco has been established since 1964 and is one of the largest privately owned quality surgical and medical companies in UK. We are approved suppliers to many MOH's throughout the world including the NHS in UK.

We have regional distribution in the Middle East and have an office in Dubai, manager Mr Misbah Jabbar, email: *misbah.jabbar@timesco.com*, phone: 00971 508 451019.

Timesco is an ISO, FDA, CE and SFDA registered company.

• For more information please visit: *www.timesco.com*

Getinge launches the new Advanta V12 – 32mm Balloon Expandable Covered Stent

Getinge has introduced the Advanta V12 32mm length balloon expandable covered stent. This is a much-needed addition to the Advanta V12 product offering and will allow clinicians additional treatment options for optimal patient outcomes.

With over 200 clinical publications and close to 500,000 patients successfully treated worldwide, this latest product line extension will add to the rapidly growing body of evidence supporting the safety and efficacy of Getinge's covered stent technology.

The Advanta V12 covered stent is a low profile, pre-mounted balloon expandable covered stent made of a radial expandable 316L stainless steel that is completely encapsulated with a patented one-piece PTFE covering technology. Getinge's proprietary covering technology creates a microporous PTFE layer that completely encapsulates the stainless steel stent and allows for uniform expansion without ridges or folds in the material being formed. V12 is customizable with the ability to post dilate to meet each patient's anatomical needs. MEH

Hill-Rom introduces Monarch Airway Clearance System

Hill-Rom Holdings has introduced the Monarch Airway Clearance System. Building on decades of leadership with The Vest Airway Clearance System, the Monarch system represents Hill-Rom's debut in mobile therapy and the next chapter in the company's patient-centred respiratory care solutions.

The Monarch system is a mobile device that provides high frequency chest wall oscillation (HFCWO) therapy in a mobile vest with a customizable, personalized fit. With its sporty design and stylish shells, the Monarch system uses Pulmonary Oscillating Discs (PODs) that provide targeted kinetic energy and HFCWO to the lungs to thin mucus and generate airflow, moving mucus up and out of the lungs. The Monarch system allows a patient to be active and productive while receiving therapy.

"We know that consistent respiratory therapy improves lung function," said Alton Shader, president, Front Line Care at Hill-Rom. "The Monarch system gives patients more control to fit therapy into their lives and to actively stay on track to meet their therapy goals."

Up until now, HFCWO therapy was primarily delivered by a vest connected to a generator with the patient seated in a chair. Hill-Rom's revolutionary POD technology delivers similar therapy, while allowing patients to move freely.

"I wanted to create a portable, long-lasting battery-powered device that clears the lungs so patients are free to be outside, go camping, live a fuller, higher quality of life," said Marten DeVlieger, inventor and cystic fibrosis patient who collaborated with Hill-Rom to design the Monarch system.

The Monarch system also incorporates LTE or WiFi technology to keep patients wirelessly connected to their care team using Hill-Rom's VisiView Health Portal.

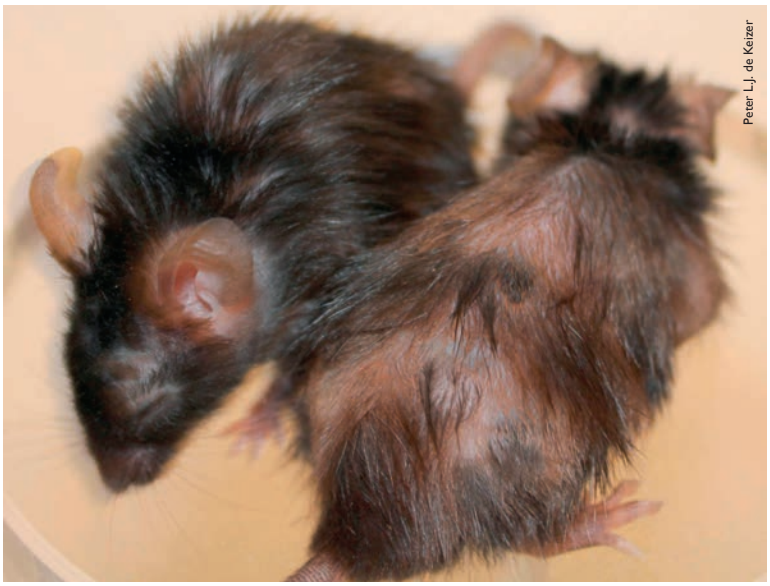
• For more information, visit: *www.respiratorycare.hill-rom.com*

Researchers reverse ageing in mice

Researchers have managed to reverse the effect of ageing in a proof-of-concept study in mice. The scientists used regular infusions of a peptide that can selectively seek out and destroy broken-down cells that prevent proper tissue renewal, called senescent cells. By doing this they found evidence of improving healthspan in naturally-aged mice and mice genetically engineered to rapidly age. They showed that the anti-senescent cell therapy could reverse age-related loss of fur, poor kidney function, and frailty.

The research – Targeted Apoptosis of Senescent Cells Restores Tissue Homeostasis in Response to Chemotoxicity and Aging – is published in the March 23, 2017 issue of *Cell*.

It is currently being tested whether the approach also extends lifespan, and human safety studies are being planned.



This photograph shows two fast-aging mice. The mouse on the left was treated with a FOXO4 peptide, which targets senescent cells and leads to hair regrowth in 10 days. The mouse on the right was not treated with the peptide.

The peptide took over four years of trial and error to develop and builds on nearly a decade of research investigating vulnerabilities in senescent cells as a therapeutic option to combat some aspects of ageing.

It works by blocking the ability of a protein implicated in senescence, FOXO4, to tell another protein, p53, not to cause the cell to self-destruct. By interfering with the FOXO4-p53 crosstalk, the peptide causes senescent cells to go through apoptosis, or cell suicide.

"Only in senescent cells does this peptide cause cell death," says senior author Peter de Keizer, a researcher of aging at Erasmus University Medical Center in the Netherlands. "We treated mice for over 10 months, giving them infusions of the peptide three times a week, and we didn't see any obvious side effects. FOXO4 is barely expressed in non-senescent cells, so that makes the peptide interesting as the FOXO4-p53 interaction is especially relevant to senescent cells, but not normal cells."

Results appeared at different times over the course of treatment. Fast-aging mice with patches of missing fur began to recover their coats after 10 days. After about three weeks, fitness benefits began to show, with older mice running double the distance of their counterparts who did not receive the peptide. A month after treatment, aged mice showed an increase in markers indicating healthy kidney function.

Senescent cell therapy is one of several strategies being tested in mice aimed at reversing aging or lengthening healthspan. In 2015, the Valter Longo laboratory at the University of Southern California reported that mice on a calorie-restricted diet that mimics fasting benefited from a longer life, a reduction in inflammatory disease, and improved memory (*Cell Metabolism*, 10.1016/j.cmet.2015.05.012). And last December, Juan Carlos Izpisua Belmonte at the Salk Institute of Biological Science and colleagues made headlines with their discovery that cellular reprogramming of epigenetic marks could extend lifespan and improve health in fast-aging mice (*Cell*, 10.1016/j.cell.2016.11.052).

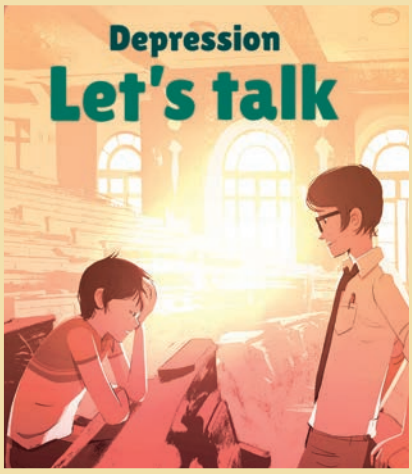
"This wave of research on how we can fight ageing is complementary, and not in competition," says de Keizer. "The common thread I see for the future of anti-ageing research is that there are three fronts in which we can improve: The prevention of cellular damage and senescence, safe therapeutic removal of senescent cells, to stimulate stem cells – no matter the strategy – to improve tissue regeneration once senescence is removed."

• **doi:** 10.1016/j.cell.2017.02.031

Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

Event	Date / City	Contact
■ May 2017		
Advanced Diabetes Conference	19 – 20 May, 2017 Abu Dhabi, UAE	*www.icldc.ae/event/advanced-diabetes-conference-2017*
25th European Congress of Obstetrics and Gynaecology 2017 (EBCOG 2017)	17 – 21 May, 2017 Antalya, Turkey	*www.ebcog2017.org*
Medlab Dubai 2017	6 – 9 February 2017 Dubai, UAE	*www.medlabme.com*
■ September 2017		
8th Arab Diabetes Forum	20-22 September, 2017 Cairo, Egypt	*www.arabicdiabeticforum.com*
International Conference on Fungal Diseases & Control	25 – 27 September, 2017 Dubai, UAE	*www.fungalinfections.conferenceseries.com*
11th Global Ophthalmologists Annual Meeting	25 – 27 September, 2017 Dubai, UAE	*http://annualmeeting.conferenceseries.com/ophthalmologists*
10th World Pediatric Congress	28 – 29 September, 2017 Dubai, UAE	*www.pediatriccongress.conferenceseries.com/*
23rd World Nurse Practitioner Conference	28 – 29 September, 2017 Dubai, UAE	*http://nursepractitioner.nursingconference.com/middleeast*
■ October 2017		
7th International Conference and Exhibition on Traditional & Alternative Medicine	3 – 6 October, 2017 Dubai, UAE	*www.traditionalmedicine.conferenceseries.com*
3rd World Congress on Climate Change and Global Warming	16 - 17 October, 2017 Dubai, UAE	*www.climatechange.conferenceseries.com/asiapacific*
4th International Conference on Rhinology and Otology	18 – 20 October, 2017 Dubai, UAE	*www.otolaryngology.conferenceseries.com*
14th Global Obesity Meeting	23 – 24 October, 2017 Dubai, UAE	*www.obesitymeeting.conferenceseries.com*



Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

Event	Date / City	Contact
10th International Conference on Neuropharmacology and Neuropharmaceuticals	23 – 24 October, 2017 Dubai, UAE	*www.neuro.pharmaceutical conferences.com/middleeast/*
2017 ISAM (International Society of Addiction Medicine) Conference: Addiction Medicine New Frontier	26 – 20 October, 2017 Abi Dhabi, UAE	*www.isam2017abudhabi.ae*
November 2017		
8th Global Obesity Conference	14 – 15 November, 2017 Dubai, UAE	*www.obesitymeeting. conferenceseries.com*
8th World Congress on Healthcare and Medical Tourism	17 – 18 November, 2017 Dubai, UAE	*www.healthcare.global-summit. com/middleeast/*
5th International Conference on Physiotherapy	27 – 28 November, 2017 Dubai, UAE	*www.physiotherapy. conferenceseries.com*
International Conference on Cancer Diagnostics	27 – 28 November, 2017 Dubai, UAE	*www.cancerdiagnostics. conferenceseries.com/middleeast*
22nd Global Vaccines & Vaccination Summit	30 November- 1 December, 2017 Dubai, UAE	*www.vaccines.global-summit.com/ middleeast*
December 2017		
Global Cancer Meet and Expo	4-6 December, 2017 Dubai, UAE	*https://globalcancermeet.com*
29th World Psychiatrist Meet	7-9 December, 2017 Dubai, UAE	*http://psychiatrist. conferenceseries.com*
25th Global Diabetes Summit and Medicare Expo	11 – 12 December, 2017 Dubai, UAE	*www.diabetesexpo.com/ middleeast*
10th International Conference on Gastroenterology	14 – 15 December, 2017 Dubai, UAE	*www.gastroenterology. conferenceseries.com/asiapacific*
7th International Society of Nephrology	13-16 December, 2017 Dubai, UAE	*www.nephrology.emanuae.com*

List your conference:
If you have upcoming conference/exhibition details which you would like to list in the agenda, please email the details to the editor: *editor@MiddleEastHealthMag.com*

Special features* in the next issue of *Middle East Health*:

- Paediatrics
- Imaging – MRI
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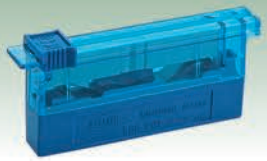

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