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May - June 2019

Traffic-related air pollution and asthma

Kuwait, UAE top list of most cases of childhood asthma linked to traffic-related air pollution, says new global report

US leads the way

NIH's massive $39 billion medical research fund ensures scientific knowledge proliferates

Brain research

Scientists restore activity in pig brain post mortem

In the News

- WHO announces major reforms to modernize organization
- New global influenza strategy to improve preparedness for pandemic flu
- Researchers begin first-in-human trial of universal flu vaccine
- New protocol offers hope for sickle cell disease, beta thalassemia cure

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Prognosis

Air pollution and childhood asthma

Kuwait and the UAE have come out top of the list of the number of cases in a shocking report linking traffic-related air pollution and child asthma. The report published recently in the *Lancet Planetary Health* journal provides the first global estimates of their kind which suggest that more than one in ten childhood asthma cases could be linked to traffic-related air pollution every year. According to the WHO, asthma is the most common non-communicable disease among children globally.

The report's findings indicate that the country with the highest rate of traffic pollution-related childhood asthma is Kuwait (550 cases per 100,000 children each year), followed by the United Arab Emirates (460 per 100,000), and Canada (450 per 100,000). The authors note that policy initiatives to alleviate traffic-related air pollution can lead to improvements in children's health and also reduce greenhouse gas emissions. Read more about this report in this issue.

Also, in this issue of *Middle East Health*, we report on a new imaging system that is helping surgeons remove tiny ovarian tumours and we look briefly on a series of papers published by *The Lancet* which brings together global evidence detailing the role of surgery in the opioid crisis, in which the authors say that inappropriate pain management after surgery is one of the major causes of the crisis.

In our international report we look at the United States and its leading role in advancing medical research for the benefit of, not only Americans, but all people around the world. The latest data from the National Institutes of Health indicate that this medical research agency is investing nearly $39 billion annually in medical research with a growing proportion going to brain research through the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative.

In the news, we report on a new global influenza strategy which aims to improve preparedness for pandemic flu; a new mobile app launched by the WHO, called hearWHO, which helps detect hearing loss; and major reforms announced by the WHO to modernize this important global organization.

As in each issue, you will find a wide range of news, research reviews and interviews to inform you.

Ramadan Kareem to all our Islamic readers.

Callan Emery
Editor
editor@MiddleEastHealthMag.com

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Publisher
Michael Hurst
michael@middleeasthealthmag.com

Editor
Callan Emery
editor@middleeasthealthmag.com

Editorial and Production
Trident Communications
www.TridentComms.media

Editorial Consultants
Dr Gamal Hammad, Dr Peter Moore, Harry Brewer

Middle East Editorial Office
PO Box 72280, Dubai, UAE
Telephone: (+9714) 391 4775
editor@middleeasthealthmag.com

Marketing Manager
Foehn Sarkar
Telephone: (+9714) 391 4775 ▮ Fax: (+9714) 391 4888
marketing@middleeasthealthmag.com

Subscription & Admin Manager
Savita Kapoor
Telephone: (+9714) 391 4775 ▮ Fax: (+9714) 391 4888
savita@middleeasthealthmag.com

Advertising Sales
PO Box 72280, Dubai, UAE
marketing@middleeasthealthmag.com

Americas, France
Joy Sarkar
P O Box 72280, Building No.2
2nd Floor, Dubai Media City
Dubai, United Arab Emirates
Tel: +971 4 391 4775 Fax: +971 4 391 4888
joy@middleeasthealthmag.com

Japan
Mr Katsuhiro Ishii
Ace Media Service Inc
12-6, 4-chome, Adachi-ku, Tokyo 121-0824, Japan
Tel: +81-3-5691-3335 ▮ Fax:+81-3-5691-3336
Email: *amskatsu@dream.com*

China
Miss Li Ying
Medic Time Development Ltd,
Flat 1907, Tower A, Haisong Building, Tairan 9th Road,
Futian District, Shenzhen, China 518048
Tel: +86-755-239 812 21 ▮ Fax: +86-755-239 812 33
Email: *medic8@medictime.com*

Taiwan
Larry Wang
Olympia Global Co Ltd
7F, No.35, Sec 3, Shenyang Rd, Taichung
Taiwan 40651 ▮ P O Box: 46-283 Taichung Taiwan 40799
Tel: +886- (4)-22429845 ▮ Fax:+886- (4)-23587689
Email: *media.news@msa.hinet.net*

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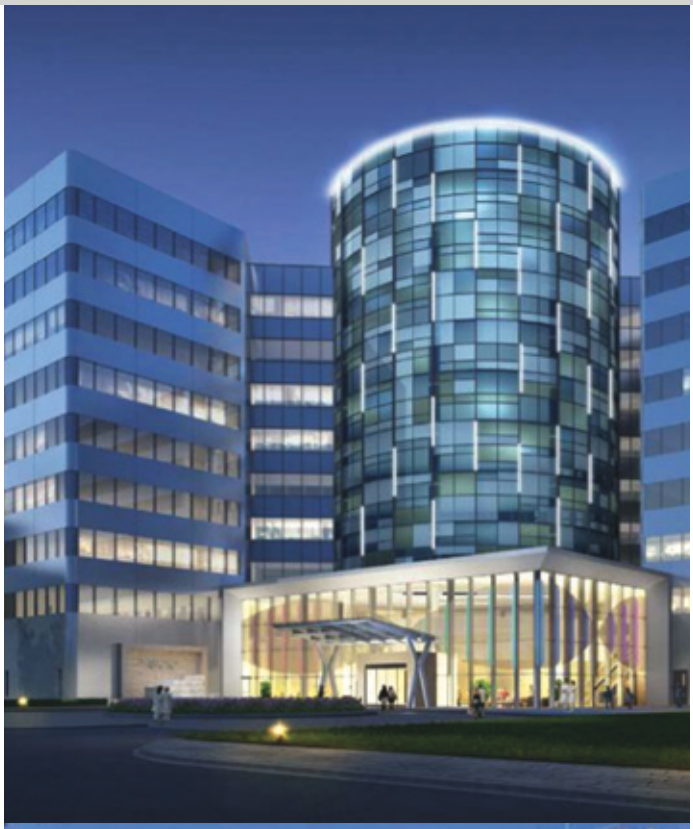

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- First in the metropolitan D.C. area to hold a CMS **5-star rating** from the U.S. Government (CMS.gov)

- We rank among the **top 5 percent of hospitals nationwide**, according to the online rating organization Healthgrades

- Inova is one of only **four health systems in the United States to hold an AA+ bond rating** from both Moody's and Standard & Poor's of non-acute health care sector distribution, indicating strong financial stability

- Participant in national research studies with organizations such as the **U.S. National Institutes of Health** and other organizations and multi-million dollar research grant recipient

- Inova is a teaching hospital with full time medical residency affiliated with George Mason University, Georgetown University, George Washington University, Howard University, University of Virginia

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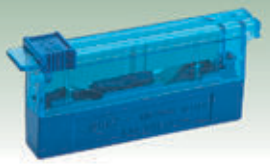

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middle east monitor

Update from around the region

Dr Hiba Ahmad Ghannam, dermatology specialist at Healthpoint.

Dermatologists use artificial intelligence to diagnose skin cancer

Artificial intelligence is helping save lives at leading Abu Dhabi specialty hospital Healthpoint, with doctors now using digital photography to diagnose and treat skin cancer.

The new technology is an innovative skin visualization and analysis tool used to monitor moles, lesions and other blemishes for abnormalities.

"In the Gulf region, strong sunshine and high levels of ultraviolet radiation makes people especially vulnerable to skin cancer, especially if they have fair skin or spend a lot of time outdoors," said Dr Hiba Ahmad Ghannam, dermatology specialist at Healthpoint.

"The unprecedented clarity offered by this innovation will help our physicians to detect pathological changes as early as possible, with potentially life-saving consequences."

The machine documents the whole surface of the body, enabling dermatologists to track individual moles over time. Unlike conventional 'mole mapping' systems, it utilizes what is known as the 'two-step method' for digital analysis, an approach recommended by key opinion leaders worldwide for monitoring high-risk patients.

Using a process called automated total body mapping, full-body photography is combined with 'digital dermoscopy'. The computerized equivalent of a powerful magnifying glass, it gives physicians exceptionally clear, detailed imagery, with the help of high-definition screens. Scans taken in the past can be compared with the new photographs instantly, providing at-a-glance indicators of any changes.

While the 'mole mapping' machine is principally used in the prevention and diagnosis of skin cancer, the system has numerous clinical and aesthetic applications.

Children that fled ISIS-held areas show signs of severe psychological distress

Thousands of Syrian and foreign children who have moved from ISIS-held areas into displacement camps in North East Syria show signs of psychological distress, and many will likely need long-term mental health and psychosocial support to recover from their experiences, said Save the Children.

In Al Hol camp, where most of the people displaced by the offensive to recapture ISIS-held areas have arrived, Save the Children has set up recreational spaces for children, as well as a centre for unaccompanied children.

"Across all of these facilities, our teams report that children are showing signs of psychological distress, including nervousness, withdrawal, aggression, nightmares and bedwetting, especially among children aged 10 to 14 years old," Save the Children said.

Save the Children said that more than 2,500 foreign children from more than 30 countries were living in three camps for people displaced in North-East Syria, including 38 who are unaccompanied in three camps Al Hol (more than 40,000 people), Ain Issa (more than 12,000 people) and Roj (more than 1,500 people).

Children who have fled ISIS-held areas are likely to have witnessed acts of brutality and lived under intense bombardment and deprivation in the last enclave held by the group.

Mai*, 11, lived for several years under ISIS with her family. Currently in a camp in the North East, she remembers witnessing beheadings and other acts of violence. Her older brother was detained by ISIS four years ago when he was seventeen and the family hasn't seen him since.

She recalls life under ISIS: "They burned our home to the ground to force us out. When ISIS was there, we weren't allowed to go to school or learn and they raised the price of vegetables, so we were all going hungry. Whenever they saw a woman talking with a man they would stone them, and they would behead prisoners in front of their family. I always tried not to look when there were beheadings, I would hide behind my mum."

Hassan*, a member of Save the Children's Child Protection team said: "Boys we work with show a fear of others and a lack of trust. When we ask them about their life in recent years, they refuse to talk. They remain withdrawn and have a hard time socializing. When night falls, the children express their fears because for them darkness is synonymous with airstrikes and shelling. So they can still not dissociate those memories from the fact that they are in a camp where there is no fighting."

In order to accelerate their healing, children who have experienced conflict, violence and traumatizing events need sustained access to mental health and psychosocial services in a protective environment. Family unity and education are also vital for children's wellbeing.

Save the Children's Syria Response Director, Sonia Khush, said: "Many children arriving in Al Hol have been displaced multiple times with their families, and dozens have arrived on their own. They have moved from shelter to tent,

from town to camp, and their sense of home and belonging has been lost. For months, and sometimes years, they are likely to have missed out on regular schooling, proper nutrition and health services. While we are responding to the needs as best as we can, much more needs to be done to help these children recover. That includes funding and access for case management and protective services, and for foreign children repatriation to their countries of origin."

* These children's names have been changed to protect their identity.

ICLDC supports Diabetes Standard Set to improve value-based care

Imperial College London Diabetes Centre (ICLDC) has contributed to the definition of outcome measures that matter most to patients living with type 1 and type 2 diabetes, with the International Consortium for Health Outcomes Measurement (ICHOM).

The Diabetes Standard Set, which was released following a year-long partnership with ICHOM, is a global standard set that defines health outcomes focused on the results that matter most to type-1 and type-2 diabetes patients. It serves as a data collection guide for physicians, who can incorporate it into each patient's diabetes management plan to achieve value-based care that is centred on his or her needs.

"We are very proud to be part of such an important initiative which contributes to the improvement of diabetes management both here in the UAE and around the globe, in line with Vision 2021," said Dr Safdar Naqvi, Medical Director and Consultant Physician & Endocrinologist at ICLDC.

"At ICLDC we are at the forefront of developing a value-based approach that has the potential for positive change in clinical practices. The standard set will enable healthcare providers that measure it to pool our resources and expertise together for the best possible outcome. We will ultimately be able to learn from our results and each other's, as well as improve the care we provide to our diabetes patients using evidence-based medicine, in a safe, effective manner and at a reasonable cost."

Mona Khalid, Vice President, Outcomes Research & Development at ICHOM said: "We are pleased that Imperial College London Diabetes Centre has supported this important initiative. Their commitment, in providing expertise and funding to help establish these measures, will bring consistency and transparency to the measurement of outcomes for people who live with type 1 and type 2 diabetes worldwide. The Diabetes Set is the first step towards standardizing data collection internationally which will allow us to benchmark and identify opportunities to improve care for people living with the condition."

The outcomes defined, were determined by the 28 members of ICHOM Diabetes Working Group. Based in 19 countries and including medical experts, outcome researchers and patients, they discussed and voted on each outcome following a well-defined and structured process. The final list of outcomes was codified in the standard set and validated by 176 experts from 22 countries and 128 patients who live with diabetes from four countries.

The outcomes are a mix of clinical and Patient Reported Outcome Measures (PROMs) based on patients' priorities. They include psychological wellbeing, diabetes distress, depression, glycemic control, diabetic ketoacidosis, and chronic complications, including those of the nervous and circulatory systems. Other outcomes were related to health services such as financial barriers to treatment and healthcare utilization. The standard set also includes defined instruments and time points for measurement for each outcome.

"The ultimate aim of this initiative is not only to drive value in healthcare but also improve the experience of each and every diabetes patient," added Dr Safdar Naqvi.

Dr Safdar Naqvi, Medical Director and Consultant Physician & Endocrinologist at ICLDC

"This is a continuous exercise and the next step is for institutions around the world to join this project and start measuring and benchmarking the outcomes defined."

Imperial College London Diabetes Centre (ICLDC), part of Mubadala's network of world-class healthcare providers, is a state-of-the-art outpatient facility that specialises in diabetes treatment, research, training and public health awareness. In just over a decade, the Centre has gained international renown for its holistic approach to the treatment of diabetes and related complications that enables patients to receive the full spectrum of care they need in one place.

The International Consortium for Health Outcomes Measurement (ICHOM) was founded in 2012 by leaders at Harvard Business School, the Boston Consulting Group, and the Karolinska Institute to catalyse the global development of value-based health care.

To support the move towards value, ICHOM defines "Standard Sets" as standard measures by condition or popula-

tion sub-group, of essential outcomes and case-mix factors. Standard Sets include a combination of patient-reported and clinical measures and are developed through the volunteer contributions of clinical experts and patient advocates globally. ICHOM has developed 27 Standard Sets so far.

Royal Hospital for Women & Children opens in Bahrain

The Royal Hospital for Women & Children (RHWC), a new specialized healthcare facility located in Bahrain, opened on 21 March 2019.

The hospital currently offers outpatient care, but plans to offer an extensive range of medical services centred around women and children, including maternity and neonatal care with NICU levels 1, 2 and 3, assisted reproductive treatment (IVF), gynaecology, paediatrics, invasive and minimally invasive surgery, and women-oriented wellness and aesthetic treatments.

The facility includes advanced operating theatres, labour and deliver rooms, intensive care units, and day-care and minor procedure rooms. The hospital covers 10,000 sqm and offers spacious suites and private rooms.

Amanat, one of the region's largest integrated healthcare and education companies, which acquired a 69.3% stake in the hospital last year, said it has worked closely with its operating partners to secure top medical talent to deliver the highest standards of care.

Sanofi opens new logistics and distribution centre in Dubai Logistics District

Biopharmaceutical company, Sanofi, has inaugurated its new logistics hub in the region at Dubai Logistics District.

One of the largest facilities of its kind in the Middle East pharmaceutical industry, the 2,740 sq ft distribution centre will serve as the company's new regional logistics headquarters and facilitate the delivery of over 22 million packs of medicines every year to treat patients in the UAE, Kuwait, Bahrain, Jordan and Iraq.

His Excellency Dr Al Amiri said: "An efficient supply chain is fundamental to ensuring access to quality treatment for many. This is an important priority for the UAE, and we applaud Sanofi for its efforts and contribution towards the continued achievement of this goal in the country."

The distribution centre is equipped with the latest warehousing and cold chain technologies that adhere to the strictest global quality standards required to preserve the integrity of medication before it reaches pharmacies and patients.

Speaking on the inauguration of the distribution centre, Jean-Paul Scheuer, Country Chair and General Manager of Sanofi Gulf, said that moving to the new facility has enabled the company to increase its storage capacity by 68%.

He added: "Beyond expanding operationally, this investment, more importantly, translates into a faster ability to respond to patients' needs, delivering innovative treatments and fostering better access to healthcare. The realization of this commitment, for which Sanofi stands very strongly, is possible because of the world-class healthcare infrastructure that the UAE offers. We thank the Ministry of Health and Prevention for its leadership and unwavering partnership over the years."

Sanofi began its operations in the Gulf in the 1970s and established its very first affiliate in 1987 in the UAE.

Saudi German Hospital to open Dh300-million facility in Ajman

Saudi German Hospitals Group – one of the largest private hospital groups in the MENA region – has announced their world class, state-of-the-art, Dh300-million healthcare facility in Ajman, UAE. The tertiary-care speciality and sub-speciality facility will be the biggest hospital in Ajman, designed to cater to the growing population across all northern emirates, while offering a wide range of medical services. Spanning over 41,062 square meters, the 200-bed hospital will commence operations soon.

With 46 OPD clinics and over 20 specialities, Saudi German Hospital, Ajman, will be the Group's third healthcare facility in the UAE, and 10th across the MENA region.

Commenting on the occasion, Dr Reem Osman, CEO of Saudi German Hospitals (SGH) Group – UAE, said: "Everyone is entitled to proper healthcare and at SGH we are committed to providing superior quality services to our patients, their families and community as a whole. Saudi German Group has a very well-thought out expansion programme to reach out to maximum number of patients in the UAE and the new state-of-the-art facility in Ajman is part of the plan. With two hospitals successfully running in Dubai and Sharjah, we aim to simulate the same international standards in SGH-Ajman that we have adopted in our other facilities. Moreover, the emirate is strategically positioned in close proximity to all the other emirates, which allows SGH-Ajman to treat patients from across the UAE".

Designed with a futuristic view, SGH-Ajman can grow in all directions, both vertically and horizontally. The hospital will offer a wide range of medical services including all kinds of specialities, sub-specialities and critical care units of the highest international standards. Sub-speciality facilities include ICU, CCU, NICU, Open Heart, Oncology, Neurosurgery, ENT, Maxillo-facial surgery, Obs/Gyn and IVF centers, Laparoscopic and Laser surgeries, among others.

"Our aim is not just to provide healthcare through our hospitals, but to have a significant role in providing the UAE health sector with scientifically qualified and highly efficient medical staff. The hospital is the first phase of our expansion; in the second phase, we plan to build Centres of Excellence, medical colleges and staff accommodation, among other features. Together they will make up the Batterjee Medical City, work for which has already begun in Dubai. These, and many such features will be the legacy of the Saudi German Hospitals Group strengthening its footprint in the UAE and the MENA region," added Dr Osman.

Besides providing quality medical services, SGH-Ajman also aims to introduce several CSR initiatives, community engagements and provide wellness education to the people of Ajman and beyond. The Group has been actively involved in many humanitarian projects across the world. MEH

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Update from around the globe

Researchers make inexpensive 3D-printed hi-res microscope

Researchers have used 3D printing to make an inexpensive and portable high-resolution microscope that is small and robust enough to use in the field or at the bedside. The high-resolution 3D images provided by the instrument could potentially be used to detect diabetes, sickle cell disease, malaria and other diseases.

"This new microscope doesn't require any special staining or labels and could help increase access to low-cost medical diagnostic testing," said research team leader Bahram Javidi from the University of Connecticut. "This would be especially beneficial in developing parts of the world where there is limited access to health care and few high-tech diagnostic facilities."

The researchers describe their new microscope, which is based on digital holographic microscopy, in The Optical Society (OSA) journal Optics Letters. The portable instrument produces 3D images with twice the resolution of traditional digital holographic microscopy, which is typically performed on an optical table in a laboratory. In addition to biomedical applications, it could also be useful for research, manufacturing, defense and education.

"The entire system consists of 3D printed parts and commonly found optical components, making it inexpensive and easy to replicate," said Javidi. "Alternative laser sources and image sensors would further reduce the cost, and we estimate a single unit could be reproduced for several hundred dollars. Mass production of the unit would also substantially reduce the cost."

In traditional digital holographic microscopy, a digital camera records a hologram produced from interference between a reference light wave and light coming from the sample. A computer then converts this hologram into a 3D image of the sample. Although this microscopy approach is useful for studying cells without any labels or dyes, it typically requires a complex optical setup and stable environment free of vibrations and temperature fluctuations that can introduce noise in the measurements. For this reason, digital holographic microscopes are generally only found in laboratories.

The researchers were able to boost the resolution of digital holographic microscopy beyond what is possible with uniform illumination by combining it with a super-resolution technique known as structured illumination microscopy. They did this by generating a structured light pattern using a clear compact disc.

"3D printing the microscope allowed us to precisely and permanently align the optical components necessary to provide the resolution improvement while also making the system very compact," said Javidi.

The researchers evaluated the system performance by recording images of a resolution chart and then using an algorithm to reconstruct high-resolution images. This showed that the new microscopy system could resolve features as small as 0.775 microns, double the resolution of traditional systems. Using a light source with shorter wavelengths would improve the resolution even more.

Additional experiments showed that the system was stable enough to analyze fluctuations in biological cells over time, which need to be measured on the scale of a few tens of nanometers. The researchers then demonstrated the applicability of the device for biological imaging by acquiring a high-resolution image of a green algae.

Worldwide estimates suggest that nearly half of all children with cancer are undiagnosed and untreated

A modelling study published in *The Lancet Oncology* journal estimates that there are almost 400,000 new cases of childhood cancer annually, while current records count only around 200,000.

The new model makes predictions for 200 countries and estimates that undiagnosed cases could account for more than half of the total in Africa, South Central Asia and the Pacific Islands. In contrast, in North America and Europe only three per cent of cases remain undiagnosed. If no improvements are made, the study authors estimate that nearly three million further cases will be missed between 2015 and 2030.

"Our model suggests that nearly one in two children with cancer are never diagnosed and may die untreated," says study author Zachary Ward from the Harvard T.H. Chan School of Public Health, USA. "Accurate estimates of childhood cancer incidence are critical for policy makers to help them set healthcare priorities and to plan for effective diagnosis and treatment of all children with cancer. While under-diagnosis has been acknowledged as a problem, this model provides specific estimates that have been lacking."

Previous estimates for the total incidence of global childhood cancer have been based on data from cancer registries, which identify cases in defined populations. However, 60% of countries worldwide do not have such registries and those that do only cover a small fraction of the overall population. Many patients are not diagnosed and are therefore not recorded. This can occur due to lack of access to primary care, with patients dying undiagnosed at home, or due to misdiagnosis.

The new model developed for this study, the Global Childhood Cancer microsimulation model, incorporates data from cancer registries in countries where they exist, combining it with data from the World Health Organisation's Global Health Observatory, demographic health surveys and household surveys developed by Unicef. The model was calibrated to data from public registries and adjusts for under-diagnosis due to weaknesses in national health systems.

The study authors provide estimates of under-diagnosis for each of the 200 countries. They estimate that in 2015 there were 397,000 childhood cancer cases globally, compared to 224,000 that were recorded as diagnosed. This suggests that 43% (172,000 cases) of global childhood cancer cases were undiagnosed. There was substantial regional variation, ranging from 3% in both Western Europe (120 undiagnosed cases out of 4,300 total new cases) and North America (300 of 10,900 cases) to 57% (43,000 of 76,000 new cases) in Western Africa.

In most regions of the world, the number of new childhood cancer cases is declining or stable. However, the authors estimate that 92% of all new cases occur in low and middle-income countries, a higher proportion than previously thought.

The most common childhood cancer in most regions of the world in 2015 was found to be acute lymphoblastic leukaemia, with the notable exception of sub-Saharan Africa. There were around 75,000 new cases globally, including nearly 700 in North Europe, over 1,500 in West Africa, over 3,500 in East Africa and nearly 30,000 in South Central Asia. In East and West Africa, Burkitt's lymphoma was more common, with over 4,000 cases in East Africa and over 10,000 in West Africa. For example, there were around 1,000 cases in the Democratic Republic of the Congo and Ethiopia, while only around 20 in the UK.

"Health systems in low-income and middle-income countries are clearly failing to meet the needs of children with cancer. Universal health coverage, a target of United Nations Sustainable Development Goals, must include cancer in children as a priority to prevent needless deaths," says senior author Professor Rifat Atun, Harvard University, USA.

Taking population growth into account, the authors estimate that between 2015 and 2030 there will be 6.7 million new cases of childhood cancer worldwide. Of these, 2.9 million cases will be missed if the performance of health systems does not improve. The authors hope that their findings will help guide new policies in health systems to improve diagnosis and management of childhood cancers.

The authors found that barriers to access and referral in health systems result in substantial under-diagnosis of childhood cancer in many countries. They argue that current healthcare models, which concentrate treatment in a few specialised hospitals, are not enough. By strengthening health systems more widely, well-functioning healthcare delivery networks could develop, reducing the number of undiagnosed children with cancer.

"As the hidden incidence of childhood cancer starts to come to the fore, stronger health systems are needed for timely diagnosis, referral and treatment," says Ward. "Expanding cancer registration will be important so that progress can be tracked."

The authors highlight that their results might be affected by limited data availability in some countries.

Disease, violence and inequality threaten more adolescents worldwide than ever before

In the first study to track recent global changes to adolescent health, published in *The Lancet*, researchers estimate that, compared with 1990, an additional 250 million adolescents in 2016 were living in countries where they faced a triple burden of infectious disease, non-communicable diseases including obesity, and injuries – including from violence.

Between 1990 and 2016, a decrease in adolescent disease burden in many countries was offset by population growth in countries with the poorest adolescent health.

The authors of the study tracked progress in 12 indicators of adolescent health in 195 countries, including risk factors such as smoking and obesity, and social issues that impact on health such as child marriage and access to secondary education. The findings highlight a slow pace of change in health, education and legal systems, leaving adolescent needs unmet. The study calls for comprehensive investments in adolescent health and for responses that extend beyond health systems, for example in education. Given that the population of people aged 10-24 years is now the largest in history, at 1.8 billion in 2016, it is timely to focus attention on improving their chances to lead healthy and productive lives.

"Adolescence is a formative phase of life during which patterns of growth, development, and behaviour lay a foundation for health in later life and for the next generation," says corresponding author Dr Peter Azzopardi from the Burnet Institute, Australia.

"A burgeoning adolescent population in many low-income and middle-income countries could provide an unprecedented opportunity to drive socioeconomic development. Adolescent health and wellbeing could be central to achieving sustainable development goals and to poverty reduction. However, many young people in these settings carry a large disease burden, are disadvantaged in the social determinants of health, and are exposed to increasing health risks."

The authors recommend that the 12 indicators could be used to agree new targets to improve adolescent health: "Despite improvements in many settings, the adolescent health challenge is greater today than it was 25 years ago. The case for comprehensive and integrated investments in adolescent health, growth, and development has never been stronger," says Professor George Patton from the Murdoch Children's Research Institute and University of Melbourne (Australia) [1], who, in 2016, led The Lancet Commission on adolescent health and wellbeing.

Decline in disease overshadowed by rise in global inequalities

Between 1990 and 2016, population growth was greatest in the countries where adolescent health is poorest. This demographic shift has heightened global inequalities. By 2016 an additional 250 million young people were living in "multi-burden" countries, which are also characterised by high levels of poverty. [Multi-burden countries were defined as those in which more than 2500 disability-adjusted life years (DALYs) were lost per 100,000 adolescents due to communicable, maternal and nutritional disease.]

In 2016, non-communicable diseases (NCDs) were the leading contributor to disease in adolescents. Multi-burden countries accounted for 55% of NCDs. A quarter of the total disease burden was due to communicable, maternal and nutritional disease. However, almost all of this disease burden is borne by adolescents living in 70 low and ▶

middle-income countries. In the US, poor health caused by injury was higher than in similar high-income countries.

Nutrition, alcohol and tobacco in adolescent health

Nutritional health risks became more prominent between 1990 and 2016. In 2016, 324 million – or almost one in five – of the world's adolescents were overweight or obese, a 120% increase from the 147.3 million in 1990. An even higher proportion of US adolescents were found to be obese or overweight (44% of young women and 45% of young men). Of note, being overweight or obese was the one indicator where the prevalence is increasing for adolescents in almost every setting. Young Chinese women experienced an annual increase of nearly 5% while young Indian women experienced an annual increase of nearly 9%.

Dr Azzopardi says: "Given that recovery from adolescent obesity is rare once established, the consequences on health in later life and for the next generation could be great."

During the same period, population growth saw the number of adolescents with anaemia increase by 20% from 357 million to 430 million, with 77% of cases in multi-burden countries. Anaemia was more common in young women than in young men. In multi-burden countries, over 40% of young women (188 million of 467 million) had anaemia in 2016. In some countries - including Bhutan, Yemen and India – prevalence in young women was over 50%.

Globally, the number of teenagers aged 15-19 who binge drink changed little from 1990: from 41 million boys and 26 million girls in 1990 to 44 million boys and 27 million girls in 2016. The countries with the highest levels of young women binge drinking - with prevalence over 55% - included Ireland, Denmark, New Zealand and Finland. It was even higher in teenage boys in Austria, Denmark, and Finland. In contrast, prevalence in both sexes in Bangladesh, Pakistan and Egypt was under 1%.

The global number of adolescent daily smokers decreased by around 20%, from 174 million in 1990 to 136 million in 2016. However, the proportion in multi-burden countries increased substantially. Global prevalence among boys and young men aged 10–24 years was still over 10% in 2016. There was a small annual increase of just over 1% among girls and women in multi-burden countries.

Disproportionate number of girls and young women left behind

Gender inequality remains a powerful driver for poor adolescent health, especially in low-income countries. Child marriage remains common, reflecting harmful gender norms. An estimated 66 million women aged 20–24 years reported marrying before turning 18.

Globally, the number of 15-24-year-olds not in education, employment or training (NEET) is estimated to be around three times higher for young women (175 million) than young men (63 million). In India, the prevalence is over 15 times higher in young women than in young men (nearly 54% compared to 3.5%). High prevalence of NEET among young women in multi-burden countries could be explained by high rates of adolescent livebirths, which disrupts education and in turn restricts prospects for employment.

In the US, a relatively high proportion of adolescents were NEET, with over 17% of young women and nearly 16% of young men aged 15–24 years in this category, compared to around 4% for both sexes in the Netherlands and around 11% in the UK. At the same time, a relatively low proportion of young American women have their demand for contraception satisfied (70.9% compared to 87% in the UK).

"Achieving gender equity in determinants of adolescent health and wellbeing will require action on many fronts, including employment and economic empowerment, better access to essential health care including contraception, implementation of legislative frameworks to protect girls from early marriage, and changes in community norms," says Professor Patton.

This study used modelled estimates to help fill data gaps and to provide as complete a picture of adolescent health as possible. In some instances, primary data were limited, for example for prevalence of binge drinking, child marriage and the number of adolescents not in education, training or employment. As part of a comprehensive response to adolescent health, there must also be an investment in quality data collection.

Writing in a linked Comment, Professor Helen Weiss from the London School of Hygiene and Tropical Medicine, UK, says: "The quality of the data depends on the primary data collected, and ten of the 12 indicators were populated using modelled data, with wide uncertainty estimates indicating the lack of primary data, especially for binge drinking, child marriage, and injuries associated with conflict and war. Nonetheless, the Article is based on data with far higher coverage than previous estimates. This study is an evidence-based call to action to the global health community."

India, China, Brazil and Mexico: causes of death among 5-14 year olds

India and China together account for a third of the global population of adolescents. A second article in *The Lancet*, published at the same time, focuses on causes of death in 5-14-year-olds in India, China, Brazil and Mexico.

In these countries, more than 200,000 in this age group die every year and the researchers found that most deaths arose from preventable or treatable conditions. In 2016, India had the highest death rates in nearly every category, including from communicable diseases. In China, injuries accounted for the greatest proportion of deaths (20,970 of the estimated 39,430), primarily as a result of drowning (6,130 deaths in boys and 2,600 deaths in girls). Deaths from transport injuries, drowning, and cancer were common in all four countries, with transport accidents among the top three causes of death for both sexes in all countries, except for Indian girls, and cancer in the top three causes for both sexes in Mexico, Brazil, and China. MEH

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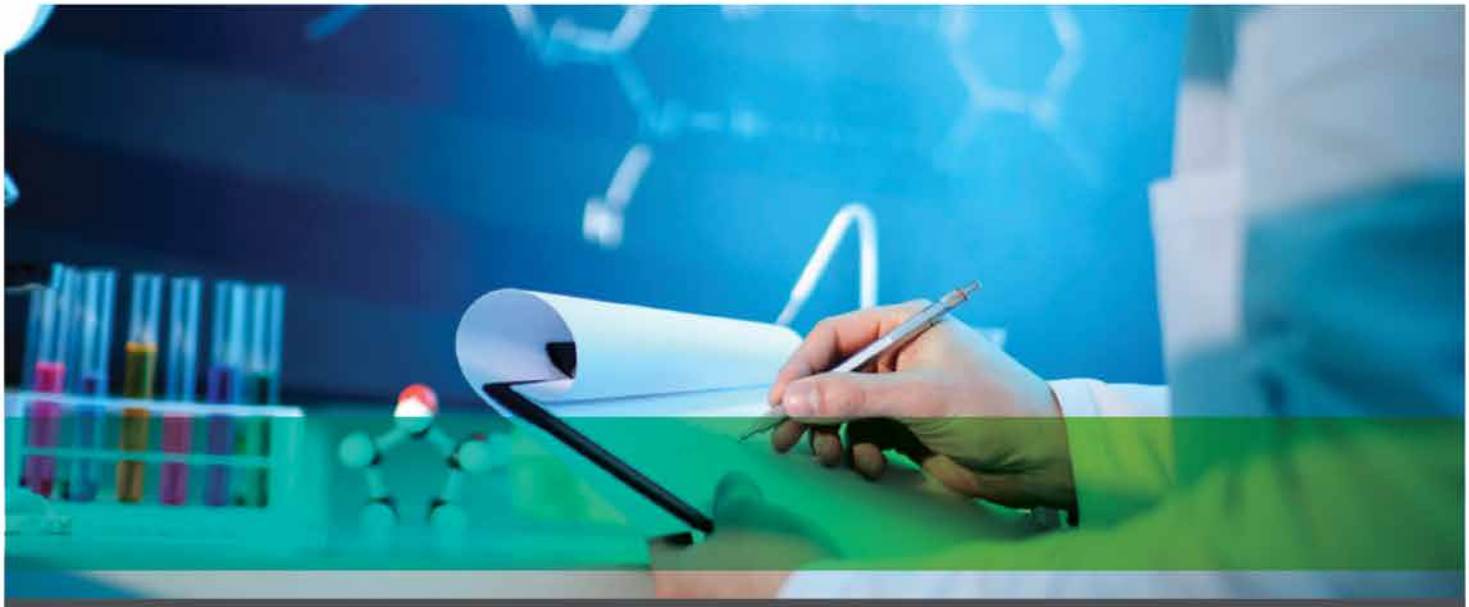

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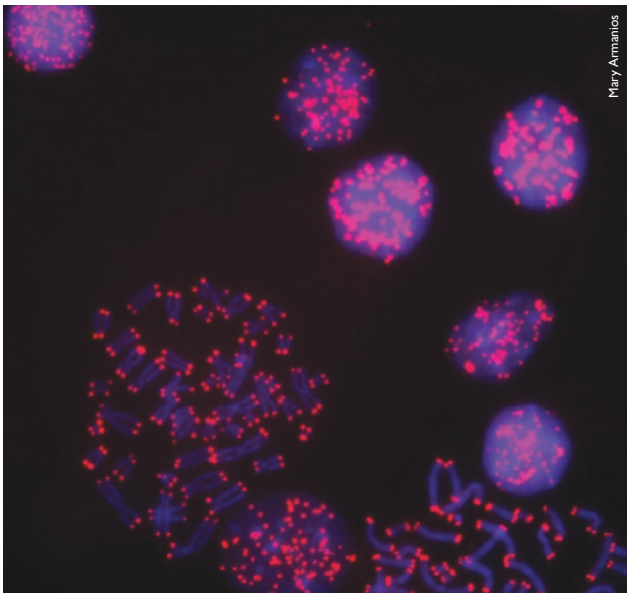


Image of human telomeres in cells. Each telomere is shown by red dots in resting nuclei of cells (circles) and cells that are dividing (separated linear chromosomes).

Immune cells age and die prematurely in people with very short telomeres

Scientists at Johns Hopkins say they have found that people born with abnormally short chromosome endcaps, or telomeres, have immune system cells that age and die prematurely. Their short-lived immune system cells also share some of the same characteristics of immune cells in much older people without the telomere disorder.

Telomeres protect genetic information within chromosomes. As people age, telomeres of all cells wear away and shrink, limiting the cells' ability to divide and multiply. However, some people are born with abnormally short telomeres, which may cause bone marrow problems and lung disease later in life.

"Our research provides evidence that short telomere length can cause a variety of conditions, including immune system abnormalities, in addition to bone marrow problems and lung disease," says Mary Armanios, M.D., professor of oncology at the Johns Hopkins Kimmel Cancer Center and clinical director of the Telomere Center at Johns Hopkins.

For the study, described in the December 2018 issue of *The Journal of Clinical Investigation*, Armanios looked to information collected for a study she began in 2005 to understand diseases caused by short telomeres. Among 28 people younger than 60 who had abnormally short telomeres and who were born with mutations in the components that regulate telomere length, she noticed that nine of them had developed infections that are more commonly seen in people with damaged immune systems, such as those who receive certain types of cancer therapies. All nine people who had developed the infections and eight of 17 other people with short telomeres had abnormally low numbers of T-cells, which are part of the immune system.

T-cells recognize and remember invaders, such as viruses, and trigger defences quickly when they try to infect the body again. Faulty or low numbers of T-cells can put people at higher risk for infections and make it more difficult for the immune system to rid the body of the infections.Armanios and her colleagues examined T-cells in 16 young people (average age 21) with short telomeres, including some of the nine patients from the 2005 study who developed infections. They compared these T-cells to those in 18 young people with normal telomeres and 12 older adults whose telomeres had shortened naturally with age and were an average of 73 years old.

In the three groups, the researchers looked at how many T-cells were recently made in the thymus, a gland that sits in the middle of the chest and makes new T-cells for fighting newly encountered infections. Young people with short telomeres and the older adults pumped out half of the number of these new T-cells that young people with normal telomeres produced.

In addition, young people with short telomeres and older adults had fewer T-cells able to recognize foreign substances called antigens, including 23 of the most common ones. Also, when their T-cells were chemically stimulated in the laboratory to mount an immune response, many of the cells died rather than lined up to attack.

"The T-cells of young people with short telomeres looked more like the T-cells of people 50 years older," says Armanios.

Despite the similarities between T-cells of young people with short telomeres and those of older healthy people, Armanios and her colleagues found some differences in the T-cells between the two groups.

When the researchers compared T-cell gene expression among the two groups, the researchers found differences in the way their T-cells were prone to die.

"A balance between survival and death programs in T-cells is needed for a healthy immune response, as well as for preventing cells from over-activation and attacking other antigens indiscriminately," says Armanios.

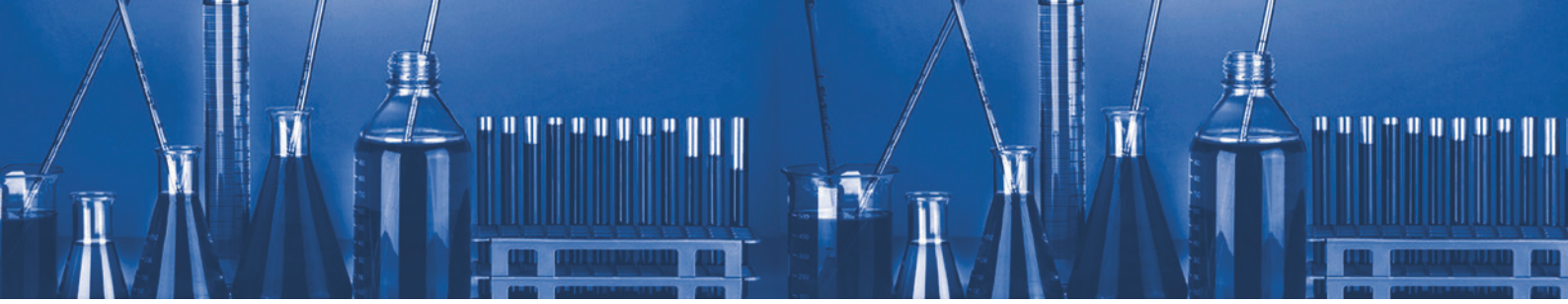
Young people with short telomeres had T-cells with more gene expression of cell death signals linked directly to damaged telomeres. Older healthy people had T-cells with a different type of cell death signal: higher levels of cell-surface proteins known as programmed cell death 1 (PD-1).

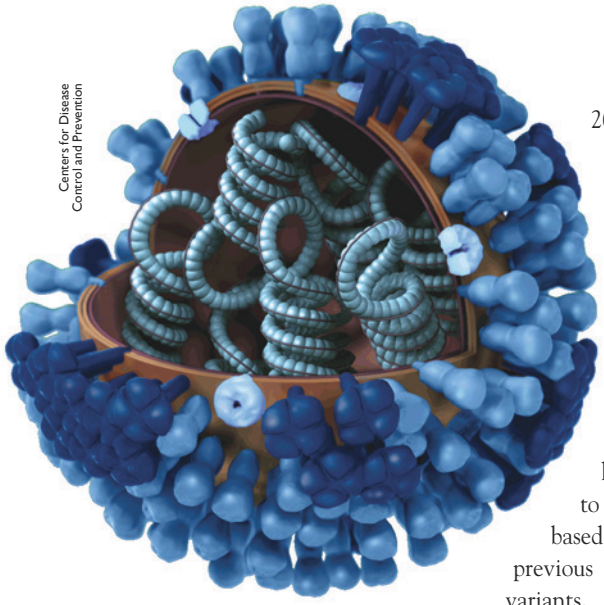
Armanios says that the differences between how T-cells die in the two groups suggests that short telomeres may not be the sole cause of T-cell aging. "This result paints a rich picture about the variety of molecular causes of aging in different individuals and suggests that mechanisms in addition to telomere shortening contribute to T-cell aging," Armanios says.

• **doi**: 10.1172/JCI120216

Researchers begin first-in-human trial of a universal influenza vaccine

The first clinical trial of an innovative universal influenza vaccine candidate is examining the vaccine's safety and tolerability as well as its ability to induce





Graphic representation of a generic flu virus

an immune response in healthy volunteers. Scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, developed the experimental vaccine, known as H1ssF_3928.

H1ssF_3928 is designed to teach the body to make protective immune responses against diverse influenza subtypes by focusing the immune system on a portion of the virus that varies relatively little from strain to strain. The vaccine candidate was developed as part of a broader research agenda to create a so-called "universal" influenza vaccine that can provide long-lasting protection for all age groups from multiple influenza subtypes, including those that might cause a pandemic.

"Seasonal influenza is a perpetual public health challenge, and we continually face the possibility of an influenza pandemic resulting from the emergence and spread of novel influenza viruses," said Anthony S. Fauci, M.D., NIAID Director. "This Phase 1 clinical trial is a step forward in our efforts to develop a durable and broadly protective universal influenza vaccine."

The clinical trial is being conducted at the NIH Clinical Center in Bethesda, Maryland. It is being led by Grace Chen, M.D., of NIAID's Vaccine Research Center (VRC) Clinical Trials Program. The trial will gradually enrol at least 53 healthy adults aged 18 to 70 years. The first five participants will be aged 18 to 40 years and will receive a single 20-microgram (mcg) intramuscular injection of the experimental vaccine. The remaining 48 participants will receive two 60-mcg vaccinations spaced 16 weeks apart. They will be stratified by age into four groups of 12 people each: 18 to 40 years, 41 to 49 years, 50 to 59 years, and 60 to 70 years. Investigators hope to understand how participants' immune responses to the experimental vaccine may vary based on age and the likelihood of their previous exposure to different influenza variants.

The VRC expects the clinical trial to complete enrolment by the end of 2019 and hopes to begin reporting results in early 2020.

Study participants will be asked to record their temperature and any symptoms on a diary card for one week after each injection. They also will be asked to visit the clinic to provide blood samples at various time points. Investigators will test the samples in the laboratory to characterize and measure levels of anti-influenza antibodies, which are potentially indicative of immunity against influenza. Participants will return for nine to 11 follow-up visits over 12 to 15 months. They will not be exposed to any influenza virus as part of the clinical trial.

"This Phase 1 clinical trial is the culmination of years of research and development made possible by the unique collaborative setting that the VRC offers by bringing together top scientists, manufacturing expertise, and an outstanding clinical team," said VRC Director John Mascola, M.D.

A team of VRC scientists developed the universal influenza vaccine prototype. It displays part of hemagglutinin (HA), an influenza protein, on the surface of a microscopic nanoparticle made of nonhuman ferritin. Ferritin is a natural protein that can be found in cells from all living species. It is useful as a vaccine platform because it forms particles that can display multiple influenza HA spikes on its surface, mimicking the natural organization of HA on the influenza virus.

HA, which enables the influenza virus to enter a human cell, is composed of a head and stem region. The body can mount an immune response to both regions, but most of the response is directed toward the head. Influenza vaccines must be updated each year because the HA head constantly changes – a phenomenon called "antigenic drift". The new vaccine candidate consists of the HA stem only. The stem is more constant than the head among influenza strains, and thus less likely to need to be updated every season. Many scientists predict that targeting the HA stem without the distraction of the HA head could induce broader and longer lasting immunity.

Scientists used the stem of an H1N1 influenza virus to create the candidate vaccine. H1 refers to the HA subtype of the virus and N1 refers to the neuraminidase (or NA, another influenza surface protein) subtype. Although there are 18 known HA subtypes and 11 known NA subtypes, only H1N1 and H3N2 circulate among people seasonally. However, H5N1 and H7N9 and other strains have caused a handful of deadly outbreaks and have the potential to cause a pandemic if they become more easily transmissible.

This H1N1 candidate vaccine protected animals from infection of H5N1, a different influenza subtype, indicating that the antibodies induced by the vaccine can protect against other influenza subtypes within "group 1", which includes both H1 and H5. In future clinical trials, the VRC plans to evaluate a vaccine that is designed to protect against "group 2" influenza subtypes, which include H3 and H7.

Initial data from an earlier VRC clinical trial evaluating a ferritin nanoparticle vaccine that included both hemagglutinin head and stem showed that the platform is safe and well-tolerated in humans. As with all clinical trials, a protocol safety review team will regularly assess study data to monitor safety of the participants in this Phase 1 study.

- For more information about the trial, visit ClinicalTrials.gov and search identifier NCT03814720 <https://clinicaltrials.gov/ct2/show/NCT03814720>.

Better mouse model built to enable precision-medicine research for Alzheimer's

Incorporating genetic diversity into a mouse model of Alzheimer's disease resulted in greater overlap with the genetic, molecular and clinical features of this pervasive human disease, according to a study funded by the National Institute on Aging (NIA), part of the US National Institutes of Health. The study also suggests that adding genetic diversity may be key to improving the predictive power of studies using mouse models and increasing their usability for precision medicine research for Alzheimer's. This research comes out of the newly established Resilience-Alzheimer's Disease Consortium (Resilience-AD) and was published online December 27, 2018 in the journal *Neuron*.

"This is the first study to show that you can replicate many of the molecular features of Alzheimer's disease in a genetically diverse mouse model," said NIA Director Richard J. Hodes, M.D. "It points to a strategy for better use of mouse models for precision medicine research – both basic and translational – for Alzheimer's disease."

Alzheimer's disease – the most common form of dementia – is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills and, eventually, the ability to carry out simple tasks.

A key tool among the multiple efforts to find a treatment or cure for Alzheimer's, mouse models allow researchers to explore genetic, molecular and even behavioural aspects of disease that can't be done in humans. The researchers, led by Catherine C. Kaczorowski, Ph.D., an associate professor and Evnin Family Chair in Alzheimer's Research at the Jackson Laboratory, Bar Harbor, Maine, and her graduate student, first author Sarah Neuner, noted that mouse models with Alzheimer's mutations are important for defining high-risk as well as protective genes and disease mechanisms, and to efficiently test new potential interventions and therapeutics.

In this study, the researchers tested the idea that including more real-world genetic variation into a mouse model of Alzheimer's would improve the translatability of the model – meaning that findings would be more likely to parallel the many complex features of the human disease. To do this, they combined a well-established mouse model of familial Alzheimer's (5XFAD) with a genetically diverse set of mice. All members of this family of transgenic mice therefore carry the high-risk human familial Alzheimer's genes but otherwise have very different genetic make-up. The detailed analysis of this new panel of mice (referred collectively as AD-BXD), showed a high degree of overlap with the genetic, molecular, pathologic and cognitive features of Alzheimer's. Moreover, in the presence of identical Alzheimer's risk genes, the differences in genetic background led to profound differences in the onset and severity of the pathologic and cognitive symptoms of Alzheimer's.

Through a series of comparative analyses, the research team also discovered that one mouse strain, C57BL/6J, commonly used to generate Alzheimer's transgenic mouse models, harbours resilience factors that lessen the impact of Alzheimer's risk factor genes. This new finding has two important implications. First, it suggests that Alzheimer's mouse models with this genetic background may not be suitable for testing of novel therapeutic agents and may explain the poor predictive power of drug screening studies using the current Alzheimer's transgenic mouse models. Second, by using the AD-BXD panel, the protective genes from the C57BL/6J strain and their mechanisms can be precisely identified leading to new candidate targets for Alzheimer's prevention.

The authors noted that the AD-BXD panel represents a new tool for better understanding the heterogeneous nature of normal aging and Alzheimer's, and for precisely identifying molecular factors that lead to resilience to genetic and environmental disease risk factors.

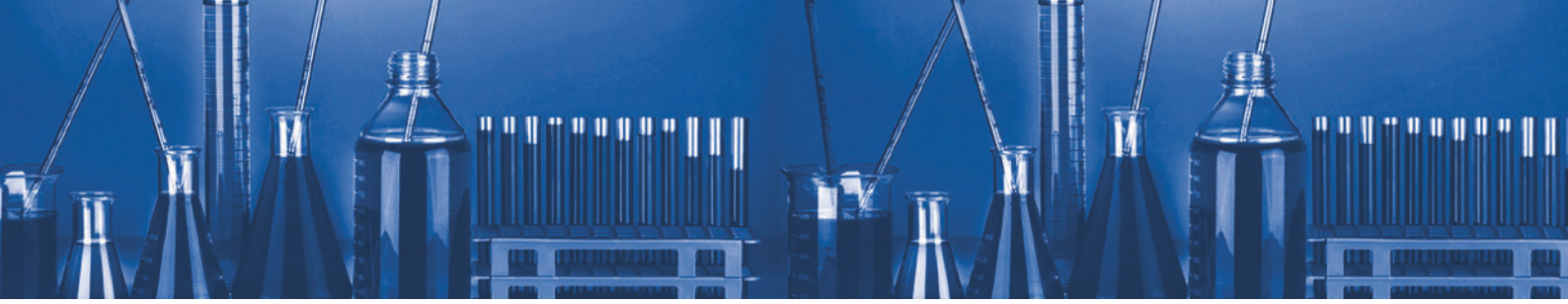
"The ability to model genetic diversity and its impact on multiple aspects of disease risk and resilience in transgenic mice in a robust and reproducible way will enable the research community to learn a lot more about the complex nature of Alzheimer's a lot faster," said Suzana Petanceska, Ph.D., program director in the NIA Division of Neuroscience, who oversees the Resilience-AD program. "This new resource adds to the series of new NIA/NIH programs generating data, analytical and research tools needed to enable more efficient and predictive drug development for Alzheimer's."

Kaczorowski's team is one of 10 multidisciplinary and multi-institutional research teams supported through the Resilience-AD program, one of a series of NIA-supported open-science consortia. Resilience-AD, launched in 2017, aims to address why and how some individuals remain dementia-free despite being at high genetic or biomarker risk of Alzheimer's. The program was developed to generate deeper mechanistic understanding of how genetic and environmental factors interact and lead to cognitive resilience in individuals who are at high risk for Alzheimer's disease and to identify novel therapeutic targets for pharmacologic and nonpharmacologic prevention strategies.

New protocol offers hope for sickle cell disease, beta thalassemia cure

Doubling the low amount of total body radiation delivered to patients undergoing bone marrow transplants with donor cells that are only "half-matched" increased the rate of engraftment from only about 50% to nearly 100%, according to a new study by Johns Hopkins researchers. The findings, published online March 13 this year in *The Lancet Haematology*, could offer a significantly higher chance of a cure for patients with severe and deadly inherited blood disorders including sickle cell anaemia and beta thalassemia.

"These results are really exciting as we're approaching a 90% cure rate for sickle cell and beta thalassemia," says Robert Brodsky, M.D., professor of medicine and oncology research at the Johns Hopkins University School of Medicine, director of the Division of Hematology, and a member of the Johns



Hopkins Kimmel Cancer Center. "Bone marrow transplants are not just for patients with a perfectly matched donor. A half-match is definitely good enough."

In the late 1980s, explain study leaders Javier Bolaños-Meade, M.D., associate professor of oncology at the Johns Hopkins Kimmel Cancer Center, and Brodsky, researchers discovered that bone marrow transplants could potentially cure sickle cell disease, a condition with few effective treatments and one that typically kills patients in their 40s. However, this treatment has only been used sparingly since then. Until recently, it required bone marrow donors and recipients to fully match each other in a set of proteins known as human leukocyte antigens that are displayed on cells. Without a complete match, Brodsky says, the recipient's body recognizes donor cells as foreign and launches a destructive attack.

Since finding a full match is difficult in this patient population – fewer than 15% have fully matched siblings free of the same genetic defect that causes sickle cell disease, and less than a quarter have full matches in unrelated registries – Johns Hopkins researchers developed a protocol, published in 2012, that allows patients to receive transplants from relatives who are only half-matched. This advance significantly expanded the pool of potential donors, Brodsky says, but the resulting transplants only engrafted to produce healthy new blood about 50% of the time.

Seeking to increase the odds of engraftment for these half-matches, Bolaños-Meade and his colleagues tested a new protocol for bone marrow transplants in patients with severe sickle cell disease and beta thalassemia, two related blood disorders known as hemoglobinopathies that are caused by defects in the same beta-globin gene. They recruited 17 patients for the study: 12 with sickle cell disease and five with beta thalassemia, with a median age of 16. Each of these patients had a relative who could serve as a half-match for a bone marrow transplant – siblings, mothers, fathers and one aunt.

As in the previous protocol, all received doses of chemotherapy and total body irradiation to knock down their immune response to the donor bone marrow before transplant. Rather than receiving 200 centigray (cGy), the low dose of radiation delivered in the previous protocol, patients in the new study received 400 cGy – still a relatively small amount of radiation that was well-tolerated. After their transplants, all received a dose of cyclophosphamide, a drug that has proved critical to avoiding a potentially deadly condition known as graft versus host disease that is particularly prevalent with half-matches.

Over the next 30, 60, 180 and 360 days, and yearly after that, the researchers tested the patients' blood for chimerism, the amount of DNA present from their donors that signals that a successful engraftment has taken place. They found that all the patients, except one with sickle cell disease, had successfully engrafted – a rate significantly higher than that seen with the previous protocol. Although five developed graft versus host disease, the condition resolved in each of these patients.

At the time of the study's publication, only three patients still needed to take immunosuppressive medications. All of those with successful engraftment had either extreme reduction or no symptoms of their disease – the sickle cell disease patients no longer had the pain crises that are hallmarks of their condition. Similarly, the beta thalassemia patients were no longer dependent on blood transfusions.

"These latest findings add to an extensive and growing body of evidence supporting the safety and effectiveness of half-matched bone marrow transplants," says Richard Jones, M.D., director of the Johns Hopkins Kimmel Cancer Center bone marrow transplantation program. "We have performed more than 1,000 half-matched bone marrow transplants, and our clinical studies have proved so successful, with safety and toxicity comparable to matched transplants, that half-identical transplants must be made available to more patients as a curative option."

Only mild, low-dose (or "mini") therapy is needed to allow the transplant to take, making the transplant potentially safer for patients with sickle cell disease and thalassemia who are often unable to tolerate the high-dose (myeloablative) therapy needed for gene therapies to take, Jones says.

New protocol could ease diagnosis of bacterial infections in infants

A new protocol could help emergency room physicians to rule out life-threatening bacterial infections among infants up to 2 months of age who have fevers, potentially eliminating the need for spinal taps, unnecessary antibiotic treatments or expensive hospital stays. Researchers from the Pediatric Emergency Care Applied Research Network (PECARN) developed the protocol from a study of more than 1,800 infants seen at 26 emergency departments around the United States.

The new protocol measures the levels of bacteria in urine, of procalcitonin (a substance produced in response to bacterial infection) in serum, and of neutrophils (an infection-fighting white blood cell). The researchers ruled out serious bacterial infection (SBI) if tests showed low levels of bacteria and procalcitonin and a normal neutrophil count. They were able to accurately rule out all but three of the 170 cases of SBI ultimately detected, including all cases of meningitis. The authors note that their findings need to be verified in a larger sample before they can be applied to medical practice.

Previous studies suggest that 8 to 13 percent of infants up to 2 months of age who have a fever may have a SBI. These include urinary tract infections, bacteremia (bacteria in the blood) and bacterial meningitis (bacterial infection of the membrane housing the brain and spinal cord). Often, a physician will need to confirm a diagnosis with a spinal tap (lumbar puncture), in which a small amount of fluid is extracted from the spinal canal. Although complications of the procedure are rare, they include inflammation of the spinal canal, bleeding and headache. In addition, an infant may be given antibiotics when a bacterial infection is suspected and may be admitted to a hospital for observation.

- The findings appear in JAMA Pediatrics.

doi: 10.1001/jamapediatrics.2018.5501

New Global Influenza Strategy to improve preparedness for pandemic flu

The World Health Organization (WHO) has released a Global Influenza Strategy for 2019-2030 aimed at protecting people in all countries from the threat of influenza. The goal of the strategy is to prevent seasonal influenza, control the spread of influenza from animals to humans, and prepare for the next influenza pandemic.

"The threat of pandemic influenza is ever-present," said WHO Director-General Dr Tedros Adhanom Ghebreyesus. "The on-going risk of a new influenza virus transmitting from animals to humans and potentially causing a pandemic is real. The question is not if we will have another pandemic, but when. We must be vigilant and prepared – the cost of a major influenza outbreak will far outweigh the price of prevention."

Influenza remains one of the world's greatest public health challenges. Every year across the globe, there are an estimated 1 billion cases, of which 3 to 5 million are severe cases, resulting in 290,000 to 650,000 influenza-related respiratory deaths. WHO recommends annual influenza vaccination as the most effective way to prevent influenza. Vaccination is especially important for people at higher risk of serious influenza complications and for health care workers.

The new strategy is the most comprehensive and far-reaching that WHO has ever developed for influenza. It outlines a path to protect populations every year and helps prepare for a pandemic through strengthening routine programmes. It has two overarching goals:

1. Build stronger country capacities for disease surveillance and response, prevention and control, and preparedness. To achieve this, it calls for every country to have a tailored influenza programme that contributes to national and global preparedness and health security.

2. Develop better tools to prevent, detect, control and treat influenza, such as more effective vaccines, antivirals and treatments, with the goal of making these accessible for *all* countries.

"With the partnerships and country-specific work we have been doing over the years, the world is better prepared than ever before for the next big outbreak, but we are still not prepared enough," said Dr Tedros. "This strategy aims to get us to that point. Fundamentally, it is about preparing health systems to manage shocks, and this only happens when health systems are strong and healthy themselves."

To successfully implement this strategy, effective partnerships are essential. WHO will expand partnerships to increase research, innovation and availability of new and improved global influenza tools to benefit all countries. At the same time WHO will work closely with countries to improve their capacities to prevent and control influenza.

The new influenza strategy builds on and benefits from successful WHO programmes. For more than 65 years, the Global Influenza Surveillance and Response System (GISRS), comprised of WHO Collaborating Centres and national influenza centres, have worked together to monitor seasonal trends and potentially pandemic viruses. This system serves as the backbone of the global alert system for influenza.

Important to the strategy is the on-going success of the Pandemic Influenza Preparedness Framework, a unique access and benefit sharing system that supports the sharing of potentially pandemic viruses, provides access to life saving vaccines and treatments in the event of a pandemic and supports the building of pandemic preparedness capacities in countries through partnership contributions from industry.

The strategy meets one of WHO's mandates to improve core capacities for public health, and increase global preparedness and was developed through a consultative process with input from Member States, academia, civil society, industry, and internal and external experts.

WHO launches hearWHO app for mobile devices to help detect hearing loss

Ahead of the annual World Hearing Day (3 March), the World Health Organization (WHO) has launched "hearWHO", a free application for mobile devices which allows people to check their hearing regularly and intervene early in case of hearing loss. The app is targeted at those who are at risk of hearing loss or who already experience some of the symptoms related to hearing loss.

Among those who will particularly benefit from this new tool include people who are often exposed to high levels of sound, such as those who listen to loud music or work in noisy places; people who use medicines that are harmful to hearing; and people aged above 60 years. Symptoms indicating the onset of hearing loss include a ringing sensation in the ear, known as tinnitus; frequently missing parts of a conversation; or a tendency to increase the volume of television, radio or audio devices.

Early detection of hearing loss is crucial to identify risky behaviours that need to be changed and ascertain the most appropriate intervention needed to address hearing loss. Such interventions are identified by hearing care professionals and can range from captioning and sign language to hearing aids and cochlear implants. Interventions to prevent, identify and address hearing loss are cost-effective.

"Many people with hearing loss are unaware of it and as such they miss out on educational, professional and everyday-life opportunities," said Dr Etienne Krug, Director of the WHO Department for the Management of Noncommunicable Diseases, Disability, and Violence and Injury Prevention. "Regular hearing checks ensure that hearing loss is identified and addressed as early as possible."

The hearWHO app is based on a validated digits-in-noise technology: users are asked to concentrate, listen and enter

into their mobile devices a series of three numbers when prompted. These numbers have been recorded against varying levels of background sound, simulating listening conditions in everyday life. The app displays the users' score and its meaning and stores the outcome of the test so that the user can monitor hearing status over time. Reminders to take the test regularly can be set by users. The app can be used by individuals as well as health providers with a view to facilitating hearing screening especially in low-resources settings.

on the WEB hearWHO
www.who.int/deafness/hearWHO

New recommendations to accelerate progress on TB

The World Health Organization has issued new guidance to improve treatment of multidrug resistant TB (MDR-TB). WHO is recommending shifting to fully oral regimens to treat people with MDR-TB. This new treatment course is more effective and is less likely to provoke adverse side effects. WHO recommends backing up treatment with active monitoring of drug safety and providing counselling support to help patients complete their course of treatment.

The recommendations are part of a larger package of actions designed to help countries increase the pace of progress to end tuberculosis (TB).

The WHO notes that since 2000, 54 million lives have been saved, and TB deaths fell by one-third. But 10 million people still fall ill with TB each year, with too many missing out on vital care.

The WHO package is designed to help countries close gaps in care ensuring no one is left behind. Key elements include:

- An accountability framework to coordinate actions across sectors and to monitor and review progress
- A dashboard to help countries know more about their own epidemics through real-time monitoring – by moving to electronic TB surveillance systems.
- A guide for effective prioritization of planning and implementation of impactful TB interventions based on analyses of patient pathways in accessing care.
- New WHO guidelines on infection control and preventive treatment for latent TB infection
- A civil society task force to ensure effective and meaningful civil society engagement

"This is a set of pragmatic actions that countries can use to accelerate progress and act on the high-level commitments made in the first-ever UN High Level Meeting on TB last September," said Dr Tereza Kasaeva, Director WHO's Global TB Programme.

TB is the world's top infectious disease killer, claiming 4500 lives each day. The heaviest burden is carried by communities facing socio-economic challenges, those working and living in high-risk settings, the poorest and marginalized.

Experts set out targets to eliminate tuberculosis within a generation

A world free of tuberculosis (TB) is possible by 2045 if increased political will and financial resources are directed towards priority areas including providing evidence-based interventions to everyone, especially to high risk groups, and increasing research to develop new ways to diagnose, treat, and prevent TB. Funding this response will require substantial investments, and accountability mechanisms will be necessary to ensure that promises are kept and targets are reached, according to *The Lancet* on TB.

The Commission says there are significant financial benefits of reducing TB mortality – the savings from averting a TB death are estimated to be three times the costs, and may be much greater in many countries.

"This report is optimistic about ending TB – a disease that is preventable, treatable and curable. However, there is no room for complacency in our work, and we must act quickly and strategically to save the next generation from TB," says lead Commissioner Dr Eric Goosby, UN Special Envoy on Tuberculosis, University of California San Francisco, USA. "In the wake of the UN High-Level Meeting on TB, the Commission views this report as a roadmap to help keep high-burden countries accountable for defeating this deadly disease."

TB remains the leading infectious killer of our time, responsible for 1.6 million deaths worldwide in 2017, with drug-resistant forms of TB threatening control efforts in many parts of the world. In addition, in 2017, around a quarter of the world's population were living with TB infection.

The World Health Organization (WHO) first declared TB a public health crisis in 1993, and in 2018 the first-ever UN High-Level Meeting (UNHLM) on TB made ending the disease a global priority. This included ambitious goals to treat 40 million people, and to prevent 30 million new cases between 2018-2022.

The Lancet Commission on TB makes policy and investment recommendations to countries with high levels of TB and their development partners. The report is the work of 37 commissioners from 13 countries, and includes economic analyses, and modelling of interventions to counter treatment challenges (drug-resistant TB, HIV co-infection, and treatment within private health systems), which are published in detail in an accompanying research paper in *The Lancet Global Health* journal.

Scaling up existing interventions

The first priority for most high burden countries is to ensure that high quality diagnostic tests and treatments are available for all people with active TB.

Many people with TB, especially the poorest, cannot access or afford services, and health systems are often slow to identify and investigate cases, meaning patients do not complete treatment or recover. Currently more than a third of TB cases (35%) are not diagnosed or treated. The authors call for universal access to drug susceptibility testing at diagnosis to ensure that all patients are given appropriate treatment, including access to second-line treatment for drug-resistant TB.

However, private health care is often the main route to diagnosis and treatment for patients in high-burden countries, meaning countries and donors must engage with the sector to improve care.

Identifying groups at high risk of TB infection (including people with HIV, people living in the same house as someone with TB, migrants, prisoners, health care professionals, and miners) and bringing them into care will be vital, including offering TB prevention, such as treating latent TB. This is particularly important in people with HIV, where risk of co-infection is high and TB is the leading cause of death.

Once high-risk populations and those already in care have access to affordable, high quality services, introducing universal health coverage is needed to help countries find remaining TB cases.

Investing in TB

However, even if current treatments were extended to 90% of people with TB, and 90% were successfully cured, existing efforts would have failed to avert 800,000 deaths in 2017. Global research investment needs to increase by up to four times (from US$726 million in 2016) to develop treatments and prevention tools that would transform TB outcomes.

Affected countries, donor nations, private sector, and philanthropies must also devise effective financing strategies to end the TB epidemic. The initial global costs to reduce TB deaths by 90% could be in the order of US$10 billion a year, and investments would need to increase by about US$5 billion a year initially. However, this would be followed by reduced costs as the number of new cases reduces.

Accountability

Increased accountability for TB at the local, national and global level is needed. Heads of government must be held accountable for their TB outcomes and report these biannually at the United Nations; donors must be accountable for drug-resistant TB and for research and development. To meet this need, the authors launch The Lancet TB Observatory – an independent annual report evaluating progress towards the 2022 UNHLM targets, and monitoring domestic and global financing. The authors also created individual report cards monitoring progress on TB, political will and TB financing for the ten highest burden countries.

WHO announces major reforms to modernise the organisation

WHO has announced the most wide-ranging reforms in the organization's history to modernize and strengthen the institution.

The reforms, announced in a statement issued in March, will enable the organisation to play its role more effectively and efficiently as the world's leading authority on public health.

The changes are designed to support countries in achieving the ambitious "triple billion" targets that are at the heart of WHO's strategic plan for the next five years: one billion more people benefitting from universal health coverage (UHC); one billion more people better protected from health emergencies; and one billion more people enjoying better health and well-being.

These changes include:

- Aligning WHO's processes and structures with the "triple billion" targets and the Sustainable Development Goals by adopting a new structure and operating model to align the work of headquarters, regional offices and country offices, and eliminate duplication and fragmentation.
- Reinforcing WHO's normative, standard-setting work, supported by a new Division of the Chief Scientist and improved career opportunities for scientists.
- Harnessing the power of digital health and innovation by supporting countries to assess, integrate, regulate and maximize the opportunities of digital technologies and artificial intelligence, supported by a new Department of Digital Health.
- Making WHO relevant in all countries by overhauling the Organization's capabilities to engage in strategic policy dialogue. This work will be supported by a new Division of Data, Analytics and Delivery to significantly enhance the collection, storage, analysis and usage of data to drive policy change in countries. This division will also track and strengthen the delivery of WHO's work by monitoring progress towards the "triple billion targets" and identifying roadblocks and solutions.
- Investing in a dynamic and diverse workforce through new initiatives including the WHO Academy, a proposed state-of-the-art school to provide new learning opportunities for staff and public health professionals globally. Other measures include a streamlined recruitment process to cut hiring time in half, management trainings, new opportunities for national professional officers, and previously-announced improvements in conditions for interns.
- Strengthening WHO's work to support countries in preventing and mitigating the impact of outbreaks and other health crises by creating a new Division of Emergency Preparedness, as a complement to WHO's existing work on emergency response.
- Reinforcing a corporate approach to resource mobilization aligned with strategic objectives and driving new fundraising initiatives to diversify WHO's funding base, reduce its reliance on a small number of large donors and strengthen its long-term financial stability.

"The changes are about so much more than new structures, they're about changing the DNA of the organization to deliver a measurable impact in the lives of the people we serve," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General. "Our vision remains the same as it was when we were founded in 1948: the highest attainable standard of health for all people. But the world has changed, which is why we have articulated a new mission statement for what the world needs us to do now: to promote health, keep the world safe and serve the vulnerable."

The new measures were developed following an extensive period of consultation with staff, and were developed jointly by WHO's Global Policy Group, which consists of the Director-General and each of the organization's six regional directors: Dr Matshidiso Moeti (Regional Director for Africa), Dr Carissa Etienne (Regional Director for the Americas), Dr Poonam Khetrapal Singh (Regional Director for South-East Asia), Dr Zsuzsanna Jakab (Regional Director for Europe), Dr Ahmed Al-Mandhari (Regional Director for the Eastern Mediterranean) and Dr Takeshi Kasai (Regional Director for the Western Pacific).

WHO's new corporate structure is based on four pillars which will be mirrored throughout the organization.

- The Programmes pillar will support WHO's work on universal health coverage and healthier populations.
- The Emergencies pillar will be responsible for WHO's critical health security responsibilities, both in responding to health crises and helping countries prepare for them.
- The External Relations and Governance pillar will centralize and harmonize WHO's work on resource mobilization, communications.
- The Business Operations pillar will likewise ensure more professionalized delivery of key corporate functions such as budgeting, finance, human resources and supply chain.

The four pillars will be supplemented by the Division of the Chief Scientist at WHO Headquarters in Geneva to strengthen WHO's core scientific work and ensure the quality and consistency of WHO's norms and standards.

Underpinning the new structure, 11 business processes have been redesigned, including planning, resource mobilization, external and internal communications, recruitment, supply chain, performance management, norms and standards, research, data and technical cooperation.

The Global Policy Group stressed the role of working with partners. Dr Tedros said WHO must develop a new mindset to seek out and build partnerships that harness the combined strength of the global health community – both in the public and private sectors. One example of this is a new Global Action Plan for Healthy Lives and Well-Being for All, under which 12 partner organizations are working together to achieve health-related Sustainable Development Goals.

Organizations unite on critical recommendations to combat drug-resistant infections

UN, international agencies and experts have released a groundbreaking report demanding immediate, coordinated and ambitious action to avert a potentially disastrous drug-resistance crisis.

If no action is taken - warns the UN Ad hoc Interagency Coordinating Group on Antimicrobial Resistance who released the report – drug-resistant diseases could cause 10 million deaths each year by 2050 and damage to the economy as catastrophic as the 2008-2009 global financial crisis. By 2030, antimicrobial resistance could force up to 24 million people into extreme poverty.

Currently, at least 700,000 people die each year due to drug-resistant diseases, including 230,000 people who die from multidrug-resistant tuberculosis. More and more common diseases, including respiratory tract infections, sexually transmitted infections and urinary tract infections, are untreatable; lifesaving medical procedures are becoming much riskier, and our food systems are increasingly precarious.

The world is already feeling the economic and health consequences as crucial medicines become ineffective. Without investment from countries in all income brackets, future generations will face the disastrous impacts of uncontrolled antimicrobial resistance.

Recognizing that human, animal, food and environmental health are closely interconnected, the report calls for a coordinated, multisectoral "One Health" approach.

It recommends countries:

- prioritize national action plans to scale-up financing and capacity-building efforts;
- put in place stronger regulatory systems and support awareness programs for responsible and prudent use of antimicrobials by professionals in human, animal and plant health;
- invest in ambitious research and development for new technologies to combat antimicrobial resistance;
- urgently phase out the use of critically important antimicrobials as growth promoters in agriculture.

"Antimicrobial resistance is one of the greatest threats we face as a global community. This report reflects the depth and scope of the response needed to curb its rise and protect a century of progress in health," said Amina Mohammed, UN Deputy Secretary-General and Co-Chair of the IACG. "It rightly emphasizes that there is no time to wait and I urge all stakeholders to act on its recommendations and work urgently to protect our people and planet and secure a sustainable future for all."

The recommendations require immediate engagement across sectors, from governments and the private sector, to civil society and academia.

This report reflects a renewed commitment to collaborative action at the global level by the World Food and Agriculture Organization of the UN (FAO), the World Organisation for Animal Health (OIE) and the World Health Organization (WHO).

"We are at a critical point in the fight to protect some of our most essential medicines," said Dr Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization and Co-Chair of the IACG. "This report makes concrete recommendations that could save thousands of lives every year."

- Read: No Time to Wait: Securing the future from drug-resistant infections
www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/ MEH

US biomedical research makes headlines around the world

The large amount of funding that is poured into healthcare research by the National Institutes of Health (NIH) regularly leads to major breakthroughs that in many cases result in significant improvements to patients' quality of living and, in some cases, results in the saving of the lives of patients who would have ultimately died from their disease.

There is an astounding volume of healthcare research published in the United States every year and it continues to proliferate at a seemingly exponential rate. This is a big deal, not only for Americans, but for mankind as a whole, who all benefit in some way from this accelerating advance in biomedical knowledge.

To give you a taste of this, *Middle East Health* looks at only the past few months and reviews a small selection of this research that is making waves not only in the scientific world, but the world's mainstream media as well. This goes to show that the US remains one the world leaders in advancing our knowledge in healthcare.

The NIH deserves massive applause. According to 2019 data from the medical research agency, it invests nearly $39.2 billion annually in medical research. More than 80% of the NIH's funding is awarded through almost 50,000 competitive grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every US state and around the world. About 10% of the NIH's budget supports projects conducted by nearly 6,000 scientists in its own laboratories, most of which are on the NIH campus in Bethesda, Maryland.

For example, the NIH recently announced that it was significantly increasing investment in the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative

by funding more than 200 new awards, totalling over $220 million to advance cutting-edge brain research.

The BRAIN Initiative is a trans-agency effort to arm researchers with revolutionary tools to fundamentally understand the neural circuits that underlie the healthy and diseased brain.

Supported by the US Congress through both the regular appropriations process and the 21st Century Cures Act, this brings the total support to date for the program to more than $400 million, which is 50% more than the amount spent in 2017.

Many of the new awards explore the human brain directly. Furthermore, the NIH is trying to leverage some BRAIN Initiative advances to help tackle the pain and opioid crisis that is sadly afflicting many Americans.

Commenting on the new research awards, Francis S. Collins, M.D., Ph.D., NIH Director, said: "Brain diseases are some of the greatest mysteries in modern medicine. These projects will provide new tools and knowledge needed to discover answers for some of the most difficult neurological and neuropsychiatric disorders."

Examples of these new awards include the creation of a wireless optical tomography cap for scanning human brain activity; the development of a noninvasive brain-computer interface system for improving the lives of paralysis patients; and the testing of noninvasive brain stimulation devices for treating schizophrenia, attention deficit disorders, and other brain diseases. All these awards can be found on the new NIH BRAIN Initiative website <www.braininitiative.nih.gov >.

Through this expanded program, more than 100 research institutions received awards to support the projects of upwards of 500 investigators representing fields as diverse as engineering and psychology, says the NIH. Many of the awards fund the development of new tools and technologies to capture a dynamic view of brain circuits in action, including the development of self-growing biological electrodes for recording brain activity and the creation of an indestructible hydrogel system to help map neural circuits.

"New tools to map the brain deepen our understanding of how circuit activity relates to behaviour," commented Joshua A. Gordon, M.D., Ph.D., director of NIH's National Institute of Mental Health. "The BRAIN Initiative is laying the foundation for improved ways to target brain circuits disrupted in brain disorders."

In response to the opioid crisis, NIH is trying to take advantage of BRAIN Initiative-funded advances to help find new treatments for pain.

Walter J. Koroshetz, M.D., director of NIH's National Institute of Neurological Disorders and Stroke, explained: "Our country is in the midst of a serious public health challenge from drug use. We hope the advances made by BRAIN Initiative researchers will help us rapidly solve the problems we face in treating pain and opioid addiction." MEH

The BRAIN Initiative

Launched in 2013, the BRAIN Initiative is a large-scale effort to accelerate neuroscience research by equipping researchers with the tools and insights necessary for treating a wide variety of brain disorders, including Alzheimer's disease, schizophrenia, autism, epilepsy, and traumatic brain injury. Since then, BRAIN Initiative-funded researchers have discovered a new type of human brain cell; mapped out the neural circuit activity that controls thirst and drinking and reactions to threats; tested theories about how a songbird brain uses feedback from sound while learning how to sing; engineered a sensor to monitor the neurotransmitter dopamine in real time; created a self-tuning deep brain stimulation device for treating Parkinson's disease; watched human brains make decisions; and located the neurons in the brain that control the pitch of our speech. In addition, researchers used a tool developed through the BRAIN Initiative, called Drop-seq, to investigate the effects of concussions on individual brain cells, which pointed to novel treatments. These are just a few of many examples of how the BRAIN Initiative is catalyzing rapid advances in neuroscience.

The NIH BRAIN Initiative is managed by 10 institutes whose missions and current research portfolios complement the goals of the BRAIN Initiative: National Center for Complementary and Integrative Health, National Eye Institute, National Institute on Aging, National Institute on Alcohol Abuse and Alcoholism, National Institute of Biomedical Imaging and Bioengineering, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institute on Drug Abuse, National Institute on Deafness and other Communication Disorders, National Institute of Mental Health, and National Institute of Neurological Disorders and Stroke.

The National Institutes of Health

The NIH, the United States of America's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. The NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and investigates the causes, treatments, and cures for both common and rare diseases.

Scientists translate brain signals into speech sounds

It's been recently reported that scientists used brain signals recorded from epilepsy patients to program a computer to mimic natural speech – an advancement that could one day have a profound effect on the ability of certain patients to communicate. The study was supported by the National Institutes of Health's Brain Research through Advancing Innovative Technologies (BRAIN) Initiative.

"Speech is an amazing form of communication that has evolved over thousands of years to be very efficient," said Edward F. Chang, M.D., professor of neurological surgery at the University of California, San Francisco (UCSF) and senior author of this study published in *Nature*. "Many of us take for granted how easy it is to speak, which is why losing that ability can be so devastating. It is our hope that this approach will be helpful to people whose muscles enabling audible speech are paralyzed."

In this study, speech scientists and neurologists from UCSF recreated many vocal sounds with varying accuracy using brain signals recorded from epilepsy patients with normal speaking abilities. The patients were asked to speak full sentences, and the data obtained from brain scans was then used to drive computer-generated speech. Furthermore, simply miming the act of speaking provided sufficient information to the computer for it to recreate several of the same sounds.

The loss of the ability to speak can have devastating effects on patients whose facial, tongue, and larynx muscles have been paralyzed due to stroke or other neurological conditions. Technology has helped these patients to communicate through devices that translate head or eye movements into speech. Because these systems involve the selection of individual letters or whole words to build sentences, the speed at which they can operate is very limited. Instead of recreating sounds based on individual letters or words, the goal of this project was to synthesize the specific sounds used in natural speech.

"Current technology limits users to, at best, 10 words per minute, while natural human speech occurs at roughly 150 words/minute," said Gopala K. Anumanchipalli, Ph.D., speech scientist, UCSF and first author of the study. "This discrepancy is what motivated us to test whether we could record speech directly from the human brain."

The researchers took a two-step approach to solving this problem. First, by recording signals from patients' brains while they were asked to speak or mime sentences, they built maps of how the brain directs the vocal tract, including the lips, tongue, jaw, and vocal cords, to make different sounds. Second, the researchers applied those maps to a computer program that produces synthetic speech.

Volunteers were then asked to listen to the synthesized sentences and to transcribe what they heard. More than half the time, the listeners were able to correctly determine the sentences being spoken by the computer.

By breaking down the problem of speech synthesis into two parts, the researchers appear to have made it easier to apply their findings to multiple individuals. The second step specifically, which translates vocal tract maps into synthetic sounds, appears to be generalizable across patients.

"It is much more challenging to gather data from paralyzed patients, so being able to train part of our system using data from non-paralyzed individuals would be a significant advantage," said Dr. Chang.

"This study combines state-of-the-art technologies and knowledge about how the brain produces speech to tackle an important challenge facing many patients," said Jim Gnadt, Ph.D., program director at the NIH's National Institute of Neurological Disorders and Stroke. "This is precisely the type of problem that the NIH BRAIN Initiative is set up to address: to use investigative human neuroscience to impact care and treatment in the clinic."

The researchers are currently experimenting with higher-density electrode arrays and more advanced machine learning algorithms that they hope will improve the synthesized speech even further. The next major test for the technology is to determine whether someone who can't speak could learn to use the system without being able to train it on their own voice and to make it generalize to anything they wish to say.

Gopala Anumanchipalli, PhD, holds an example array of intracranial electrodes of the type used to record brain activity in the current study.

Preliminary results from one of the team's research participants suggest that the researchers' anatomically based system can decode and synthesize novel sentences from participants' brain activity nearly as well as the sentences the algorithm was trained on. Even when the researchers provided the algorithm with brain activity data recorded while one participant merely mouthed sentences without sound, the system was still able to produce intelligible synthetic versions of the mimed sentences in the speaker's voice. MEH

on the WEB YouTube: Speech synthesized from brain activity
www.youtube.com/watch?v=kbX9FLJ6WKw

New synthesis strategy speeds identification of simpler versions of a natural product

Baylor University professor and chemist Daniel Romo, Ph.D., discusses research with doctoral candidate Christian M. Chaheine, co-author on new synthesis strategy. The study is published in *Nature Chemistry*.

A new chemical synthesis strategy to harvest the rich information found in natural products – organic compounds isolated from natural sources – has led to the identification of novel, simpler derivatives with potential to selectively protect neurons, important for neurodegenerative diseases like Alzheimer's disease, or to prevent the immune system from rejecting organ transplants, according to a Baylor University-led study.

The study is published in the journal *Nature Chemistry*.

Researchers caution that their research has led only to potential drug leads rather than drug discovery, and that possible applications likely would be many years away and would require extensive development by pharmaceutical companies. But the research is significant because the strategy to reach these drug leads has the potential to profoundly reduce the time it takes to go from an initial complex natural product to simplified versions ripe for further development.

The pilot study for this new approach began with gracilin A, a natural product derived from a sea sponge, which other researchers had found to have medicinal potential but lacked detailed structure and bioactivity relationships, said lead author Daniel Romo, Ph.D., The Schotts Professor of Chemistry in Baylor's College of Arts & Sciences.

The streamlined synthetic method – called "pharmacophore-directed retrosynthesis" – is "like the difference between constructing an eight-story building when all you need may be a six- or seven-floor building," Romo said. A pharmacophore is the minimal structure required for activity of a bioactive molecule.

The long-term goal is quicker identification of simpler versions of the natural product that retain the bioactivity of interest. This can be done en route to synthesizing the more complex natural product target "by stopping and looking at what is on the fifth, sixth and seventh floors on your way up to the top floor," Romo said.

This could greatly reduce the time to identify useful compounds derived from natural products, which also could ultimately impact the cost of drugs. MEH

Breaking open the gates of antibiotic resistance

Antibiotic resistance is a major health threat, with about two million people in the US getting an antibiotic-resistant infection per year, according to the Centers for Disease Control and Prevention (CDC). Gram negative bacteria, including types like *E.coli* and *Salmonella*, are often more difficult to kill because of their two-pronged defenses – they have two membranes rather than one, and also have numerous toxin pumps embedded in the membranes to expel any antibiotic that may have made it through. Now researchers from Thomas Jefferson University have uncovered how to target both of these defenses with one hit, which could help make antibiotics more effective.

"We showed that interfering with a transfer RNA (tRNA) molecule, in a way that is unique to bacteria, cripples the bacterial cell's ability to make membrane proteins required for the drug barrier and efflux activity," says senior author Ya-Ming Hou, PhD, Professor of Biochemistry at the Sidney Kimmel Medical College at Jefferson (Philadelphia University + Thomas Jefferson University). The work was published in the journal *Cell Systems*.

tRNA molecules are not a typical antibiotic target. These molecules are part of the protein-building machinery that is essential for the daily function of cells in every living being. However, Dr. Hou's team examined a kind of chemical "decoration" process in bacterial tRNAs that is absent from human cells. This difference between bacteria and humans makes this process a better drug target, since it's less likely affect human cells.

tRNAs are decorated with chemical groups that are added on after tRNAs are synthesized in a cell. Dr. Hou's group examined one such decoration, the addition of a methyl group to one particular location on the spine of several tRNAs. In earlier work, Dr. Hou's lab showed that when these tRNAs were deficient in this one methylation, they were more likely to create errors in protein building. But not just any protein, the deficient tRNAs were particularly prone to mistakes at building proteins that sit within cell membrane.

This result made Dr. Hou think that perhaps a defect in the tRNA methylation might affect not only the bacteria's toxin-pump, but a host of other types of proteins that help keep the membrane stable and cohesive.

In this paper, together with first author postdoctoral fellow Isao Masuda and others, Dr. Hou tested whether these defective tRNAs could make ▶

bacteria more susceptible to antibiotics, by creating bacteria that are genetically deficient in making the methyl-group decoration.

Through an elegant series of experiments, Dr. Hou's team showed that these bacteria had membranes that were less cohesive and more permeable than normal. The bacteria with defective tRNAs were less effective at pumping out chemicals relative to the normal bacteria, suggesting that their toxin pumps were affected. Finally the team showed that when the bacteria with defective tRNAs were exposed to various antibiotics, they died faster and were also less capable of developing drug resistance.

"Speed of killing is important in antibiotics," says Dr. Hou. "The longer it takes for bacteria to die from antibiotics, the more likely they are to develop resistance."

While pharmaceutical companies such as AstraZeneca and GSK have discovered compounds that can inhibit the enzyme from making the critical methylation on tRNAs, progress has stalled. The primary reason is that the inhibitors are unable to permeate through the bacterial membrane structure, which resonates with the major challenge confronting the entire field of antibiotic discovery.

Dr. Hou acknowledges the challenge. "First, we need to formulate the inhibitors in such a way as to be able to enter the cell more effectively," says Dr. Hou. "Then, combining these inhibitors with traditional antibiotics to kill bacteria faster and reduce the likelihood of antibiotic resistance."

At the moment, there are no drugs that can effectively attack this pathway. Dr. Hou's lab is currently working on developing better inhibitors. MEH

Autism diagnoses prove highly stable as early as 14 months

Scientists at University of California San Diego School of Medicine report that diagnoses of autism spectrum disorder (ASD) by trained professionals in children as young as 14 months are remarkably stable, suggesting that accurate screening and earlier treatment is feasible, Their study is published online April 29, 2019 in *JAMA Pediatrics*.

Growing evidence suggests ASD has its origins in prenatal life – most likely during the first or second trimester of pregnancy – and children begin to display symptoms of the condition by their first birthdays, such as failing to respond to their names or positively interact with others.

Early diagnosis of ASD means earlier intervention and improved therapeutic benefit. "The sooner you can address issues of ASD, the better the outcome for the child," said the study's first author, Karen Pierce, PhD, professor of neurosciences and co-director of the UC San Diego Autism Center of Excellence. She led the study with senior author Eric Courchesne, PhD, also a professor of neurosciences.

Multiple studies, including research conducted by Pierce, have found that simple parent checklists performed at the child's first birthday can identify symptoms of ASD. And yet the mean age of ASD diagnoses in the United States, write the researchers, is "often years later, generally between ages three and four".

Pierce said the lag between the first signs of ASD and diagnosis represents a missed opportunity, particularly given the accelerated pace of brain development in the first years of life.

"Synaptic density or connections between neurons in the prefrontal and temporal cortex, brain regions centrally involved in higher order social behavior, doubles between birth and one to two years in age," said Pierce. "It's conceivable that outcomes for children with autism could be improved if treatment occurred during this period of rapid brain growth, rather than after, which is more commonly the case."

To conduct their study, Pierce and colleagues assessed 1,269 toddlers from the general population (441 ASD, 828 non-ASD) who received their first diagnostic evaluation between 12 and 36 months and at least one subsequent evaluation, all by licensed psychologists. Diagnoses ranged from ASD and features of ASD to language and developmental delay or other developmental issues.

The overall diagnostic stability for ASD was 0.84, higher than for any other diagnostic group. Only 2 percent of toddlers initially considered to have ASD transitioned to later diagnoses of typical development. Within the group diagnosed with ASD, the most common transition was from ASD to ASD features at 9 percent.

Diagnostic stability of ASD was weakest at 12 to 13 months, just 0.50, but increased to 0.79 by 14 months and 0.83 by 16 months. Twenty-four percent of toddlers were not designated as ASD at their first evaluations, but later identified. The most common transition in this group was an initial designation of developmental delay (25 percent) or language delay (16 percent), transitioning to later-onset ASD.

"Our findings suggest that an ASD diagnosis becomes stable starting at 14 months, and overall is more stable than other diagnoses, such as language or developmental delay," said Pierce.

"Once a toddler is identified as ASD, there is an extremely low chance that he or she will test within typical levels at age three or four, so it's imperative that we use every effective tool as early as we can to begin treating diagnosed children to the benefit of them and their families over the long-term." MEH

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A new heart enables gospel singer to keep to the beat

A decade ago, gospel singer Otis Wimberly was sidelined from his usual full-throated, energetic performances.

His arms and legs had ballooned. He could barely walk a few steps without stopping and gasping for five or six deep breaths. No matter how much he wanted to lie down, that wasn't an option because "it felt like I was drowning", he said.

The symptoms and a subsequent diagnosis of congestive heart failure meant the Humble, Texas resident couldn't fully participate in The Wimberly Family Gospel Singers, which was founded in 1976 in New Orleans. Over the last four decades, the group has delighted listeners at local churches, concerts and music festivals, including the inimitable New Orleans Jazz & Heritage Festival (Jazz Fest).

"I couldn't sing. I couldn't play," he said, with a timbre of disappointment in his deep, mellifluous voice about an interruption of decades of music.

Approximately 5.7 million American adults suffer from heart failure, with about half of them dying within five years of being diagnosed, according to the U.S. Centers for Disease Control and Prevention.

During his childhood in New Orleans, Otis Wimberly and his brothers would sneak upstairs to play their father's guitar while the patriarch was at work and their mother was cooking downstairs.

"My mom caught us one day. She came upstairs and said, 'I thought I left the radio on. That was y'all playing?'" Wimberly said. "Every day, when my dad left, she had us practicing."

When the elder Wimberly heard them play, he was astonished by his sons' natural musical talent and immediately purchased a trailer full of music equipment.

"We've been singing and playing ever since," Wimberly said.

A new lease on life

Weeks, years and decades of singing came to a halt for Otis Wimberly in 2008, when pain caused him to seek treatment and medication. Still, his condition worsened.

By the time he became a patient at the Texas Heart Institute in the Texas Medical Center, his heart's pumping ability was at just eight percent.

"He was really out of it – just barely fighting to live," said his wife, Shannon Wimberly.

During a July 2011 surgery at Baylor St. Luke's Medical Center, prominent heart surgeon O. H. "Bud" Frazier, M.D., connected Otis Wimberly's failing heart to a left ventricular assist device (LVAD). The implanted pump, which whirls instead

Gospel singer Otis Wimberly and heart surgeon O. H. "Bud" Frazier, M.D (center).

of beats, takes over cardiac circulation for a patient who has end-stage heart failure as a bridge to a transplant.

"I was really in a bad place," Otis Wimberly recalled. "Too weak to have the surgery and too far gone not to."

The pump gave the gospel singer a new lease on life. Everywhere he went, he carried a bag containing two batteries and the controller for the LVAD. It was cumbersome and earned him the nickname "battery man" from his family and friends, but – compared to heart failure – the LVAD was exactly what he needed while he waited on a new heart.

He even rejoined his family group, making a powerful performance at Jazz Fest in the spring of 2018 wearing his gear in a backpack.

A heartbeat returns

Shannon Wimberly had turned in for the night on October 17, 2018, as her husband nestled in his chair in the living room to watch the latest episode of the CW's *The Flash*. Then, his phone rang. Doctors finally had a heart for him.

"We got the call," Otis Wimberly said. "I tell ya, it was exciting."

They grabbed clothes and other necessities they had prepared for this moment. Too excited and nervous to drive, so they called his daughter, who lived nearby, to take them to the hospital.

The next evening, two days before his 53rd birthday, Otis Wimberly went into surgery to receive his new organ.

Over the course of four hours, Frazier and his team opened the gospel singer's chest and carefully removed the mechanical pump with its valves and lines. Then, they took out his weakened heart and replaced it with a healthy one.

After seven years, Otis had a heartbeat again.

"You really can't top that as far as birthday gifts go," his wife said.

Organ donor

Otis Wimberly doesn't know much about his donor – other than that he was a young, male athlete in his 20s – but he's already thinking about what he would say to the donor's family.

"I would first give my condolences on the loss," he said. "Then I would let them know that a part of their son is alive in me."

The demand for organ donations far exceeds the available supply. Today in the U.S., 113,727 patients are waiting to receive a new organ. According to the U.S. Department of Health and Human services, another patient is added to the waiting list every 10 minutes. Each day, 20 people in the United States die waiting for a transplant.

"One of the problems that we've had as the population grows is that we have fewer donors. Of course, that's good because we have fewer deaths from car accidents," Frazier said. "All those are good things, but if you need heart transplant, it's not. … You have to depend on someone else's misfortune to get a heart. I'd like to see that day come to an end."

Being able to "have these pumps that we can just pull off the shelves" to replace the heart, as Frazier puts it, is a goal he is actively working on. For years, Frazier has been collaborating with fellow Houston heart surgeon and medical device inventor William "Billy" Cohn, M.D., and biomedical engineer Daniel Timms, Ph.D., on the BiVACOR, a next-generation, total artificial heart that could replace heart transplants.

It will be a few years before the BiVACOR is available, but in the meantime, patients – like Otis Wimberly – are alive today thanks to the LVAD.

"Seeing him at his weakest moments and watching him progress, become stronger and do better did my heart all the good," Shannon Wimberly said. MEH

Healthy fasting for kids during Ramadan

Keeping kids healthy and hydrated has never been an easy task. With Ramadan coinciding with the summer months, maintaining proper hydration and a healthy diet for your kid can be a challenge. **Joel Steelman**, M.D., an endocrinologist at Cook Children's Medical Center, the leading pediatric health care system in Fort Worth, Texas, provides tips on healthier fasting habits during summer months.

Don P. Wilson, M.D., Medical Director, REACH Program at Cook Children's holds hands with one of his pediatric patients.

Hydrate, hydrate, hydrate...

Make sure your kids stay hydrated and drink plenty of water during non-fasting hours. Organic juices and yogurt-based drinks can be used if your child won't eat fruit. According to Joel Steelman, M.D., "juices deliver a lot of sugar without much else. Whole fruits are better, have fibre and more available nutrients". Water and/or milk and yogurt-based drinks such as buttermilk and Laban are better sources for hydration and much tastier options if you are having trouble with your kids drinking water. If your child is observing fasts during Ramadan, add fruit salads during Suhoor and Iftar meals to keep up their energy levels. Watermelon, or other high water content fruits and vegetables, is also a great way to rehydrate. A fun and healthy way to encourage consumption of fruit is to slice them in small cubes and shapes and serve them as popsicles.

Plan a protein powered start

Ensure that your kids get the right start by planning a protein powered Suhoor. It is essential that kids consume a lot of proteins, such as peanut butter, cheese, yogurt or milk. Dr. Steelman suggests adding nuts, especially almonds, to Suhoor because they have protein and carbs in them. Other protein-based items that can be included are beans, lentils, eggs and other dairy products. If lactose intolerant, there are choices such as almond or soy milks.

Increase intake of fibre

Encourage your child to break their fast with high-fiber items, such as dates and lentil soups. Breaking fast with items rich in fibre, minerals and vitamins helps in retaining hydrating ingredients and fluids and also prevents constipation. Dates are excellent natural power packs and are rich in fibre. Encourage the tradition of breaking fasts with a date.

Avoid serving carbonated and sugary drinks

Dr. Steelman says that high sugar intake, which contributes to childhood obesity, is particularly easy to consume when children drink it in the form of sodas or other sugar-sweetened beverages. "The fructose component in sucrose (table sugar) or in high fructose corn syrup is strongly suspected in impacting how our liver works and increases the risk for diabetes. Also, high sugar intake can create a continued craving for more sugar."

Avoid spicy/fried delicacies

Spicy and fried delicacies might be tempting to your kids, but consuming them while fasting leads to indigestion and acidity. Avoid deep fried items and consuming too much oil, as it could lead to nausea attacks and vomiting. Dr. Steelman suggests sticking to grilled meats instead, especially during Iftar. Using cooking methods such as air frying and steaming can be used as an alternative to deep frying.

Avoid overeating

A common mistake made by parents is to encourage their kids to overeat during Suhoor or Iftar. This is an extremely unhealthy habit which causes indigestion and bloating. Overeating can also lead to extreme cases of vomiting and nausea. To avoid indigestion, Dr. Steelman recommends that you split your child's Iftar into two or three smaller nutrient rich meals. Space the meals between one and a half hours to allow your child to digest. If you are serving a heavy main dish, follow it with fruit or a light salad.

Limit physical activities while fasting

Limit your kids from getting extremely exhausted and decrease their physical activities while fasting. Plan some indoor activities and games to keep them busy and distracted from hunger pangs. While outdoors, plan activities during the evening and around greener areas to avoid direct heat contact. Also, encourage your child to nap during the afternoon to relax a bit.

- For more information, please visit *cookchildrensinternational.org*

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Silva Arslanian, MD, pediatric endocrinologist and diabetologist, scientific director, Center for Pediatric Research in Obesity and Metabolism

UPMC Children's Hospital of Pittsburgh study finds early and aggressive medication treatment does not slow progression of Type 2 diabetes in youth

A study conducted at UPMC Children's Hospital of Pittsburgh shows that early and aggressive medication treatment did not preserve the body's ability to make insulin in high-risk obese youth with type 2 diabetes.

The findings were published online in *Diabetes Care* and the results were presented in June 2018 at the American Diabetes Association Scientific Sessions in Orlando, Florida.

The study included 91 youth participants ages 10 to 19, part of the larger Restoring Insulin Secretion (RISE) study. To determine if early, aggressive treatment would improve outcomes, participants at four study sites were randomly assigned to one of two treatment groups.

The first group received three months of glargine – a long-acting insulin – followed by nine months of metformin. The second group received only metformin for 12 months. Participants were then monitored for three more months after treatment ended.

The RISE pediatric medication study found that beta cell function – key to the body's ability to make and release insulin – declined in both groups during treatment and worsened after treatment ended.

"I am not entirely surprised with the outcome of RISE not only because the disease appears to be more severe in youth, but because its pathogenetic mechanisms also are worse even in the stage of prediabetes," said Silva Arslanian, MD, pediatric endocrinologist and diabetologist, scientific director, Center for Pediatric Research in Obesity and Metabolism, and principal investigator of RISE.

UPMC Children's Hospital was one of four sites that conducted the RISE pediatric medication study; the others were Children's Hospital Colorado, Indiana University, and Yale University.

National Institutes of Health support for RISE comes primarily through National Institute of Diabetes and Digestive and Kidney Diseases grants U01DK94430, U01DK94431, U01DK94406, U01DK94438 and U01DK094467, with additional support from the National Center for Advancing Translational Sciences.

The Department of Veterans Affairs, Kaiser Permanente Southern California, and the American Diabetes Association also support the studies, with additional donations of supplies from Allergan Corporation, Apollo Endosurgery, Abbott Laboratories, and Novo Nordisk A/S.

- For more information about this study, please visit: *www.chp.edu/rise*

About UPMC Children's Hospital of Pittsburgh

Regionally, nationally, and globally, UPMC Children's Hospital of Pittsburgh is a leader in the treatment of childhood conditions and diseases, a pioneer in the development of new and improved therapies, and a top educator of the next generation of pediatricians and pediatric subspecialists. With generous community support, UPMC Children's Hospital has fulfilled this mission since its founding in 1890. UPMC Children's is named consistently to several elite lists of pediatric hospitals, including ranking in nine of the 10 pediatric subspecialties in the prestigious U.S. News & World Report annual Honor Roll of America's Best Children's Hospitals for 2018–2019. MEH

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Interview

Renting medical equipment: An operating model that is gaining traction in the market

Basil Qazmieh, Business Development Manager, Byrne Group

***Middle East Health*: Can you give our readers a bit of background about Byrne?**

Basil Qazmieh: The Byrne Group of today started with the formation of Byrne Equipment Rental in the early 1990s. Subsequent acquisitions of the group by HSBC private equity in 2007 and by Hanco Group in 2014 followed by the most recent acquisition with the combination of Itqan Investments (UAE), V-Power (Hong Kong) and Citic Pacific (China) has allowed the business to grow rapidly over the years. Today, Byrne is one of the largest and most diversified companies in the field of equipment rental solutions as well as the design and manufacturing of modular structures and services.

Byrne Medical was established in 2017, and it is the only rental specialist for medical equipment in the GCC. All members of our management team have a wealth of medical expertise in medical technology, hospital management, and healthcare supply chain.

***MEH*: What types of medical equipment does Byrne rent?**

BQ: A vast range of medical equipment is provided by Byrne Medical, for example, we provide equipment for: Radiology, ophthalmology, dermatology, operating rooms, dental care and physiotherapy. We also cover any modular or mobile requirements our client's have.

***MEH*: Renting medical equipment is generally not the traditional way hospitals fulfil their equipment requirements. What are the benefits of this model of medical equipment acquisition that you are offering to hospitals?**

BQ: Market research shows that in developed countries the medical sector leases equipment and the Middle East region is leaning towards this operating model. In fact, the Kingdom of Saudi Arabia's 2030 vision with regards to the medical field includes leasing in their operating model. We have designed a rental model to include the following which provides a positive outcome for our clients:

- CAPEX to OPEX
- No upfront investment required so our clients can focus on expansion
- Flexible payment plans
- Supplier independence
- Monthly or quarterly invoicing
- Competitive pricing

***MEH*: Besides Byrne's two new contracts which has made headlines recently, to whom is Byrne currently supplying rental equipment?**

BQ: We have supplied medical equipment on a rental basis to several healthcare facilities in the UAE and KSA varying from small clinics to major hospitals.

***MEH*: Byrne has recently won two big contracts to rent medical equipment to two new hospitals in Dubai and Riyadh, which are part of the Beirut-headquartered Clemenceau Medicine Network. What is the value of these contracts? What medical equipment will Byrne be supplying?**

BQ: Valued at approximately AED 150 million (US$40.8 million) Clemenceau Medicine will be receiving medical equipment manufactured by Siemens, Olympus, Karl Storz and Philips, with the first equipment delivery scheduled in May 2019.

***MEH*: What arrangement does Byrne have with these manufacturers with regards installation, servicing and maintenance?**

BQ: A full-service package is provided including planned installation with the client and Byrne is bridging the gap to manage the servicing and maintenance side of the equipment.

***MEH*: How long do these rental contracts run for? Do they include replacement of equipment when it becomes obsolete or when new more technologically advanced equipment becomes available?**

BQ: Typically, these contracts have a tenure of 4 to 7 years structured according to our customer requirements which include service and maintenance. Even though the replacement option is not part of this particular contract, this can be considered based on customer preference.

***MEH*: Are you expecting this model of renting equipment to grow? Why?**

BQ: Yes, we expect this model of equipment renting to grow due to the various benefits it can offer to both healthcare facilities and to suppliers. The key benefit is that healthcare facilities can rely on Byrne Medical for renting their equipment, which would help them tremendously through deployment of their funds for other business priorities.

***MEH*: Does this model also offer benefits for equipment manufacturers? What are these?**

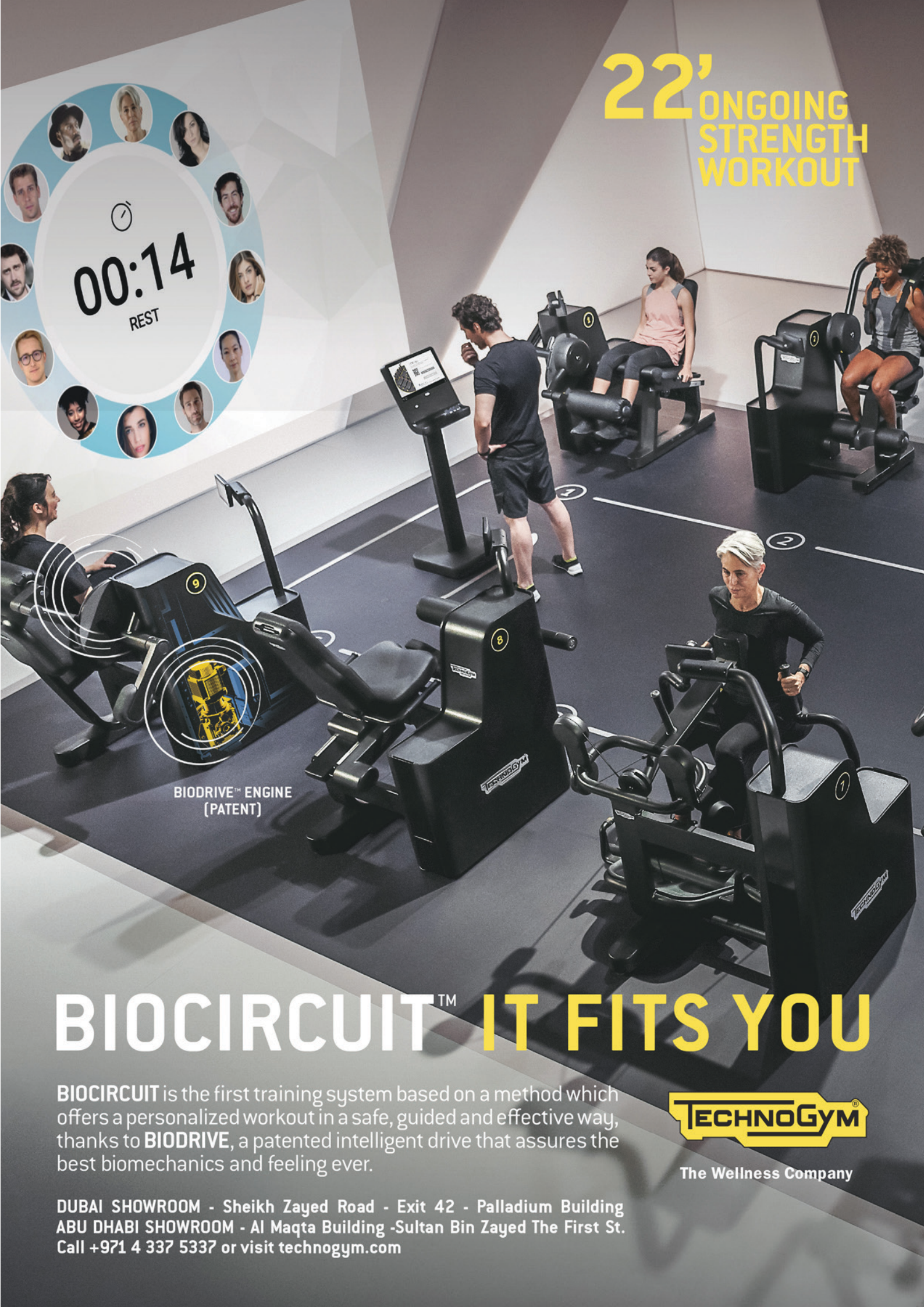
BQ: There is a great advantage for equipment manufacturers/suppliers as this solution allows them to get their payment quicker and this has a positive impact on their cash flow.

MEH: What is in the pipeline for Byrne?

BQ: The pipeline is very promising with many leads from various medical centers and hospitals in both the UAE & KSA.

***MEH*: Is there anything you'd like to add with regards Byrne and medical equipment rental?**

BQ: We know the financial concerns facing healthcare organizations today. Many issues can affect a hospital's budget, yet top-of-the-line equipment is still necessary in order to provide excellent patient care. Byrne Medical offers flexible and customized rental solutions that help overcome these challenges. MEH



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The leading gym circuit for rehabilitation and all fitness needs

We spoke to Technogym at Arab Health 2019 and they introduced us to their new innovative fitness solution – Biocircuit.

Technogym, is one of the world's leading producers of design and technology-driven fitness equipment and solutions. Their new Biocircuit is an innovative solution designed to suit a wide range of fitness needs including rehabilitation, losing weight, building strength, and ageing in good health.

Biocircuit is a circuit-training solution and method offering a personalized workout to help users achieve their goals in a short time.

The guided program delivers an engaging experience that requires no adjustments or wait time, since exercises, workload, work/rest ratio and pace have been defined and integrated into personalized programs.

Biocircuit offers effective training and is always ready for the user. It includes everything end-users need for the best muscle activation. In addition, thanks to the Biodrive patent, Biocircuit is the first training line offering a personalized workout in a safe, guided and effective way. Based on revolutionary aerospace technology, Biodrive is a motor controller that delivers a tailored workout to help users to achieve the best results in a short amount of time. It is the only system in the market connected with the native software of the circuit; it requires only one login and is totally customizable to the users' needs.

Different needs require different programs. Only Biodrive can balance all phases of movement, both concentric and eccentric in order to provide each user a personal program:

- **Resistance profiles** – Biodrive guarantees the possibility to define different intensity profiles in order to meet the needs of people requiring

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Founded in 1983, Technogym is a world leading international supplier of technology and design driven products and services in the Wellness and Fitness industry. Technogym provides a complete range of cardio, strength and functional equipment alongside a digital cloud based platform allowing consumers to connect with their personal wellness experience anywhere, both on the equipment and via mobile when outdoors. With over 2,000 employees and 14 branches globally, Technogym is present in over 100 countries. More than 80,000 Wellness centers and 200,000 private homes in the world are equipped with Technogym. Technogym was the official supplier for the last seven editions of the Olympic Games: Sydney 2000, Athens 2004, Turin 2006, Beijing 2008, London 2012, Rio 2016 and Pyeongchang 2018.

isotonic resistance, needing to reduce inertia, or willing to use viscous resistance

- **Adaptive workload** – Biodrive ensures that the workload is constantly controlled
- **Spotter assistance** – Biodrive activates the spotter function to relieve and provides assistance to the user when he/she can't fully manage his/her workout
- **Pace** – Biodrive selects the proper pace based on user's needs to achieve maximum effectiveness.

The Biocircuit format includes: An automatic setting that is triggered after first use; consoles display the program to users on each machine; Flooring to hide cables and guide users to the next station: Unity Self, a dedicated kiosk, where users start and finish their journey. The kiosk, keeps all the equipment synchronized and an external screen is connected to the kiosk to create a more engaging experience.

BIOCIRCUIT

The BIOCIRCUIT equipment range includes:

- BIOSTRENGTH equipment offers a personalized workout thanks to different resistance profiles, adaptive workload, spotter assistance and pace monitoring provided by Biodrive. In terms of posture, Biostrength offers a motorized seat adjustment system, to ensure a fast and seamless setup
- RUN provides a dynamically adaptive running surface, the best console position and 'fast track' system enabling users to adjust speed and incline on the fly
- BIKE offers 3 different training positions, easy entry pedals, fast track and fully automatic saddle height adjustment.

• Choosing Biocircuit means more than purchasing a turnkey format. It represents a whole system of business support. The Biocircuit Consultants and Business Guides will provide you with profitable business models to maximize ROI. You will also receive practical advice on how to market the product inside the Club, together with site-specific marketing suggestions. MEH

• Visit: *www.technogym.com/ae/biocircuit/*

Arab Health 2019

Advantech showcases its advanced medical computing platforms

At Arab Health in Dubai earlier this year we spoke to Muiayed Kuo, Sales Manager for MEA, Advantech, a hi-tech Taiwan-based company specializing in medical computing platforms. Kuo introduced us to some of their latest products.

The AVAS 60 is an integrated solution for intelligent operating rooms. This mobile medical cart is designed to enhance the capabilities for telemedicine, education and video-streaming applications in the operating room.

Kuo explained that with the increased complexity of surgical procedures, several factors including the use of diverse image sources and external communication difficulties are reducing the efficiency of operating room workflows. He said Advantech's AVAS solutions support real-time image and video streaming, centralized control, remote teaching and consultation, and cloud-based management in order to streamline operating room workflows and improve overall efficiency.

Some key elements of the AVAS solution include its zero latency enabling imaging data to be transmitted at the same frame rate, ensuring uninterrupted real-time communication between collaborating physicians located remotely. It has 4K end-to-end resolution so medical images can be displayed with greater accuracy, clarity, and detail to enable more precise diagnoses. It provides multi-view functionality for the simultaneous display of four image streams on a single monitor. It has integrated switching technology which enables glitch-free transitions between input sources for seamless switching and consistent visual performance.

Advantech provides open APIs and SDKs for the solution to ensure easy integration with existing infrastructure and management systems.

In addition, Kuo added, that all AVAS computers, displays, and tablets are certified to relevant medical standards for infection control and patient safety.

Kuo also showed us their intelligent medical cart, part of their AmiS series of medication distribution solutions.

The AmiS series includes a Decentralized Medication Distribution Solution – AmiS 850 & AMiS 870, and the Advantech Pharmacy Automation Dispensing Cart – AmiS 50E.

Kuo explained that nurses and other healthcare professionals spend nearly 90% of their time moving from place to place as they provide care to patients, moving from nursing stations, to wards, to patient rooms. Many hospitals are still struggling with makeshift carts, strapping desktop computers or laptops on board and rolling them from place to place, which create many inconveniences and potential hazards, such as loose wires and issues with cleaning and hygiene. He said Advantech's mobile Point-of-Care systems are designed to move with busy healthcare professionals. They use wireless infrastructure, mobile devices and specialized applications to meet the needs of caregivers.

The mobile carts provide closed-loop medication administration (CLMA), This is a workflow improvement process that involves electronic medication management for seamless information integration. Kuo explained that the CLMA process provides a traceable information flow from the prescribing doctor, through to the pharmacy, nursing station, and patient wards. It minimizes inpatient medication errors and increases overall patient safety.

In addition, vital sign monitors can be integrated with the mobile workstations, medical carts, and tablets for easy access and management. Patients' real-time vital sign data can then be automatically transmitted to the hospital information system (HIS) or nursing information system (NIS) via a cable or Bluetooth. This allows caregivers to monitor patients' status remotely. Nurses can also use a medical tablet to access and update patient data, and provide superior care and treatment.

With this solution too, Advantech provides the API to enable easy integration with the HIS and NIS.

Advantech also offers a wide range of medical tablets – 5", 8" & 10" – specifically designed for hospital applications. Kuo gave some examples of what they can be used for, such as capturing images on the spot for diagnosis, medical history, or insurance needs; they can also be used to identify, track and trace patients throughout the hospital. The tablets are programmable and flexible so they can be exchanged with ease between a number of hospital information systems.

These solutions are just a small sample of what Advantech has to offer. Other solutions include bedside infotainment systems; real-time location systems; and intelligent ward solutions. Speak to Advantech to find out more about what they can do to make your hospital intelligent.

- For more information, visit: *www.advantech.com/digital-healthcare* MEH

Future Healthcare Exhibition and Conference 2019

Pushing healthcare forward

On 18-19 March, the truly international Future Healthcare Exhibition and Conference 2019 at Olympia London, presented us with cutting-edge technology. These technologies are destined to push healthcare forward with the potential to change the way that healthcare professionals deliver and monitor healthcare. It was a showcase of international innovation in the healthcare space. This year, over 350 brands attended.

The event was opened by the Rt Hon Patricia Hewitt, former UK Secretary of State for Health and the Rt Hon Lord Drayson, former UK Minister of Science, who addressed a crowd drawn from both the UK and globally. This two-day exhibition and conference featured speakers from industry, the clinical setting, as well as a strong showing of start-up companies.

With Brexit nudging closer, considering its impact on your business has never been more important. Future Healthcare 2019 enabled new relationships to be forged at the leading edge of the healthcare market. With visitors and delegates from around the world, this event was a fantastic springboard for suppliers to find new business on the international stage. It provided a prime opportunity to learn about the latest developments in the B2B healthcare market, to collaborate with others; from healthcare providers to start-up companies, and to explore future commercial opportunities.

World-class speakers explored the future of healthcare and how lives will be improved with innovation. Topics covered included; integrating digital healthcare solutions in the NHS and private practice for increased patient benefit and operational efficiency. Contemporary issues also found their way into discussions with the future of blockchain in healthcare and a post-Brexit European health landscape; both understandably hot topics.

In addition, how attractive UK innovation is to healthcare systems in other parts of the world, along with the importance of innovation as a driver for the strong reputation of the NHS were also discussed. Participants went on to debate healthcare tourism; overseas hotspots, foreign patient placements and the global health tourism landscape.

Wearables were a key theme of the event, with some impressive innovations on display. A session was dedicated to the disruptive potential of the technology, while Thrive Wearables gave attendees an insight into the opportunities and challenges that come from the unique data stream that wearables generate.

There were also targeted sessions addressing the path to scaling-up a technology and how to partner directly with the NHS in healthcare delivery. Panel discussions featured a wide range of topics, including; the challenges and benefits of expanding AI into the clinical setting as well as mental health management through patient empowerment.

The futurist and global focus of the event's second day ended with speakers grappling with intelligently and seamlessly integrating healthcare into patients' environment with perspectives drawn from local government, architecture, and city planning.

- The event returns to London next year as Future Healthcare 2020, 17-18 March, Olympia London. MEH

Imaging system helps surgeons remove tiny ovarian tumours

Ovarian cancer is usually diagnosed only after it has reached an advanced stage, with many tumours spread throughout the abdomen. Most patients undergo surgery to remove as many of these tumours as possible, but because some are so small and widespread, it is difficult to eradicate all of them.

Researchers at MIT, working with surgeons and oncologists at Massachusetts General Hospital (MGH), have now developed a way to improve the accuracy of this surgery, called debulking. Using a novel fluorescence imaging system, they were able to find and remove tumours as small as 0.3 millimetres – smaller than a poppy seed – during surgery in mice. Mice that underwent this type of image-guided surgery survived 40% longer than those who had tumours removed without the guided system.

"What's nice about this system is that it allows for real-time information about the size, depth, and distribution of tumours," says Angela Belcher, the James Mason Crafts Professor of Biological Engineering and Materials Science at MIT, a member of the Koch Institute for Integrative Cancer Research, and the recently appointed head of MIT's Department of Biological Engineering.

The researchers are now seeking FDA approval for a phase 1 clinical trial to test the imaging system in human patients. In the future, they hope to adapt the system for monitoring patients at risk for tumour recurrence, and eventually for early diagnosis of ovarian cancer, which is easier to treat if it is caught earlier.

Belcher and Michael Birrer, formerly the director of medical gynaecologic oncology at MGH and now the director of the O'Neal Comprehensive Cancer Center at the University of Alabama at Birmingham, are the senior authors of the study, published online in the journal *ACS Nano*.

Neelkanth Bardhan, a Mazumdar-Shaw International Oncology Fellow at the Koch Institute, and Lorenzo Ceppi, a researcher at MGH, are the lead authors of the paper. Other authors include MGH researcher YoungJeong Na, MIT Lincoln Laboratory technical staff members Andrew Siegel and Nandini Rajan, Robert Fruscio of the University of Milan-Bicocca, and Marcela del Carmen, a gynaecologic oncologist at MGH and chief medical officer of the Massachusetts General Physicians Organization.

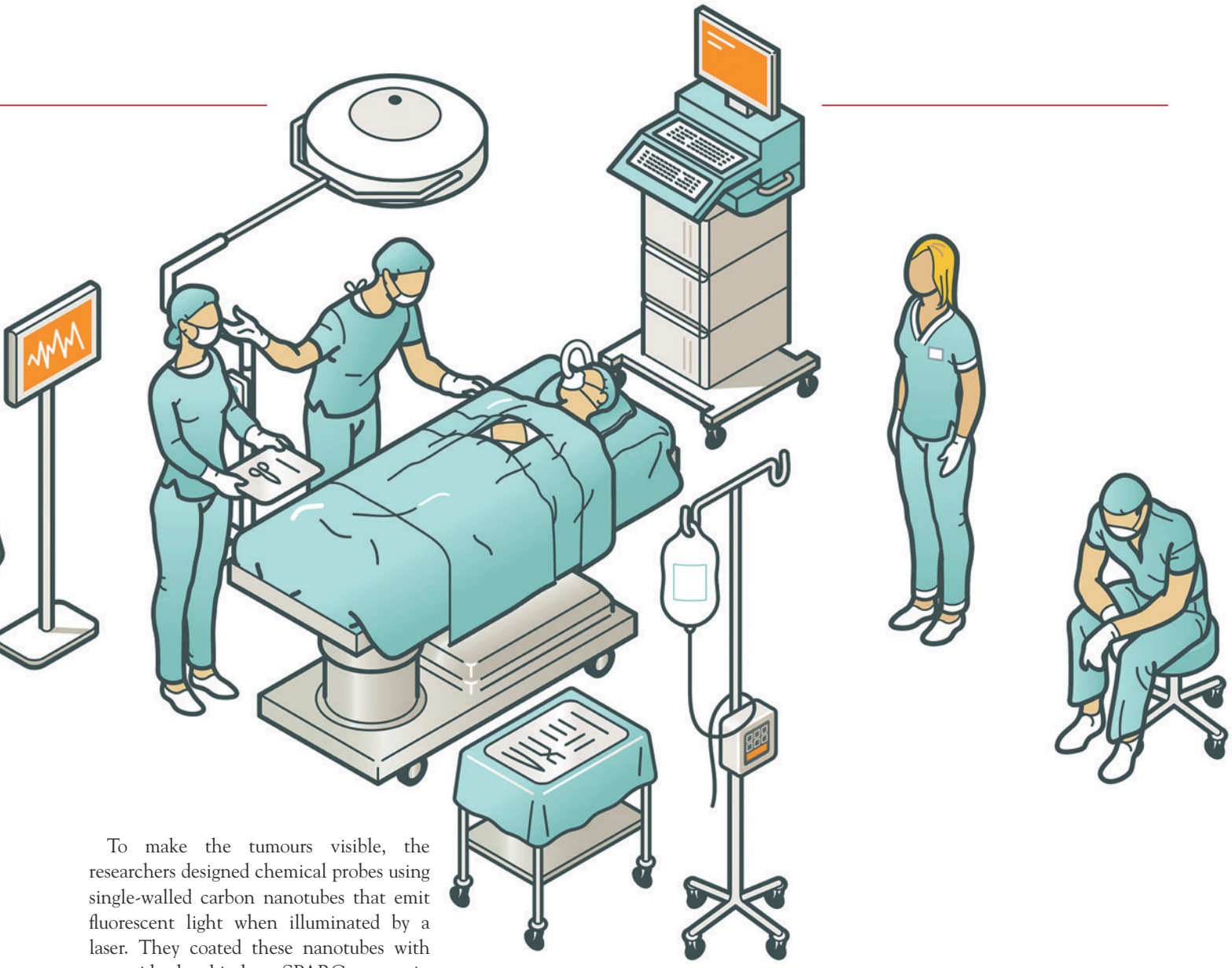
Glowing tumours

Because there is no good way to detect early-stage ovarian cancer, it is one of the most difficult types of cancer to treat. Of 250,000 new cases diagnosed each year worldwide, 75% are in an advanced stage. In the United States, the five-year combined survival rate for all stages of ovarian cancer is 47%, only a slight improvement from 38% three decades ago, despite the advent of chemotherapeutic drugs such as cisplatin, approved by the FDA in 1978 for ovarian cancer treatment. In contrast, the five-year combined survival rate for all stages of breast cancer has steadily improved, from around 75% in the 1970s to over 90% now.

"We desperately need better upfront therapies, including surgery, for these (ovarian cancer) patients," Birrer says.

Belcher and Birrer joined forces to work on this problem through the Bridge Project, a collaboration between the Koch Institute and Dana-Farber/Harvard Cancer Center. Belcher's lab has been developing a novel type of medical imaging based on light in the near-infrared (NIR) spectrum. In a paper published in March, she reported that this imaging system could achieve an unprecedented combination of resolution and penetration-depth in living tissue.

In the new study, Belcher, Birrer, and their colleagues worked with researchers at MIT Lincoln Laboratory to adapt NIR imaging to help surgeons locate tumours during ovarian cancer surgery, by providing continuous, real-time imaging of the abdomen, with tumours highlighted by fluorescence. Previous analyses have shown that survival rates are strongly inversely correlated with the amount of residual tumour mass left behind in the patient during debulking surgery, but many ovarian tumours are so small or hidden that surgeons can't find them.



To make the tumours visible, the researchers designed chemical probes using single-walled carbon nanotubes that emit fluorescent light when illuminated by a laser. They coated these nanotubes with a peptide that binds to SPARC, a protein that is overexpressed by highly invasive ovarian cancer cells. This probe binds to the tumours and makes them fluoresce at NIR wavelengths, allowing surgeons to more easily find them with fluorescence imaging.

The researchers tested the image-guided system in mice that had ovarian tumours implanted in a region of the abdominal cavity known as the intraperitoneal space, and showed that surgeons were able to locate and remove tumours as small as 0.3 millimetres. Ten days after surgery, these mice had no detectable tumours, while mice that had undergone the traditional, non-image-guided surgery, had many residual tumours missed by the surgeon.

By three weeks after the surgery, many of the tumours had grown back in the mice that underwent image-guided surgery, but those mice still had a median survival rate that was 40% longer than that of mice that underwent traditional surgery.

No other imaging system would be able to locate tumours that small during a surgical procedure, the researchers say.

"You can't have a patient in a CT machine or an MRI machine and have the surgeon perform this surgical debulking procedure at the same time, and you can't expose the patient to X-ray radiation for multiple hours of the long surgery. This optics-based imaging system allows us to do that in a safe manner," Bardhan says.

Monitoring patients

For most ovarian cancer patients, tumour debulking surgery is followed by chemotherapy, so the researchers now plan to do another study where they treat the mice with chemotherapy after image-guided surgery, in hopes of preventing the remaining tiny tumours from spreading.

"We know that the amount of tumour removed at the time of surgery for patients with advanced-stage ovarian cancer is directly correlated with their outcome," Birrer says. "This imaging device will now allow the surgeon to go beyond the limits of resecting tumours visible to the naked eye, and should usher in a new age of effective debulking surgery."

Now that they have demonstrated that this concept can be successfully applied to imaging during surgery, the researchers hope to begin adapting the system for use in human patients.

"In principle, it's quite doable," Siegel says. "It's purely the mechanics and the funding at this point, because this mouse experiment serves as the proof of principle and may actually have been more challenging than building a human-scale system."

The researchers also hope to deploy this type of imaging to monitor patients after surgery, and eventually to develop it as a diagnostic tool for screening women at high risk for developing ovarian cancer.

"A major focus for us right now is developing the technology to be able diagnose ovarian cancer early, in stage 1 or stage 2, before the disease becomes disseminated," Belcher says. "That could have a huge impact on survival rates, because survival is related to the stage of detection." MEH

Inappropriate pain management after surgery is a major cause of the opioid crisis

Targets to eliminate pain after surgery have driven increases in the use of opioids, and are a major cause of the opioid crisis in the USA, Canada and other countries. For the first time, a new Series of three papers, published in *The Lancet*, brings together global evidence detailing the role of surgery in the opioids crisis.

Chronic post-surgical pain is a growing problem as the population ages and more surgeries are done. It can occur after any type of surgery. Each year there are 320 million people having surgery, and chronic pain occurs in 10% of cases.

It typically begins as acute postoperative pain that is difficult to control, and develops into a persistent pain condition with features that are unresponsive to opioids. In response to this pain, clinicians often prescribe higher levels of opioids, but this can lead to tolerance and opioid-induced hyperalgesia (a counterintuitive increase in pain in line with increased opioid consumption), creating a cycle of increased pain and increased opioid use where pain remains poorly managed.

"Providing opioids for surgical patients presents a particularly challenging problem requiring clinicians to balance managing acute pain, and minimising the risks of persistent opioid use after surgery," says Series lead Professor Paul Myles, Monash University, Australia. "Over the past decade there has been an increasing reliance on strong opioids to treat acute and chronic pain, which has been associated with a rising epidemic of prescription opioid misuse, abuse, and overdose-related deaths. To reduce the increased risk of opioid misuse for surgery patients, we call for a comprehensive approach to reduce opioid prescriptions, increase use of alternative medications, reduce leftover opioids in the home, and educate patients and clinicians about the risks and benefits of opioids."

Risks associated with prescription opioids

The opioid crisis began in the US during the mid-1990s and early 2000s, when inadequate pain relief was seen as a marker of poor quality healthcare. Opioids are now one of the most commonly prescribed medications in the USA with similar, although less marked, trends in other high-income countries, including the UK. Comparatively, many low-income countries worldwide have little access to opioids and cannot provide appropriate pain relief – as highlighted in The Lancet Commission on Global Access to Palliative Care and Pain Relief.

"From the mid-1990s, clinical guidelines and policies were created that aimed to eliminate pain, and clinicians

were encouraged to increase opioid prescriptions. As a result, the use of prescription opioids more than doubled between 2001-2013 worldwide – from 3 billion to 7.3 billion daily doses per year, and has been linked to increases in misuse and abuse in some countries – like the US, Canada, Australia and the UK," says Series author Dr Brian Bateman, Brigham and Women's Hospital, USA. [1]

Currently, opioids are often the best pain relief available for managing acute pain. In surgery, opioid administration reduces the dose of general anaesthetic needed, and timely and appropriate opioids after surgery improve patient comfort. However, the persistent use of opioids after surgery can predispose patients to long-term opioid use and misuse so ongoing must be carefully considered. In the USA, opioid prescribing for minor surgery has increased (up to 75% of patients are prescribed opioids at hospital discharge), and the risk of misuse increases by 44% for every week and for repeat prescription after discharge.

A US study of more than 155,000 patients having one of four low-risk surgeries (carpal tunnel repair, knee arthroscopy, keyhole surgery for gallbladder removal, or keyhole surgery for inguinal hernia repair) found that opioid prescriptions for each increased from 2004-2012, and that the average daily dose of opioid prescribed for post-surgical pain also increased by 13% (30 milligrams of morphine equivalent [MME]) across all procedures on average, with increases ranging from 8% (17 MMEs) for patients undergoing inguinal hernia repair to 18% (45 MMEs) for patients undergoing knee arthroscopy.

There are also marked international differences in opioid prescribing after surgery. Data comparing one US and one Dutch hospital found that 77% of patients undergoing hip fracture repair in the US hospital received opioids, whereas none did in the Netherlands hospital, and 82% of US patients received opioids after ankle fracture repair compared with 6% of Dutch patients. Despite these differences, patients in each of these countries show similar levels of satisfaction with pain management.

In addition, excessive amounts of opioids are prescribed to US patients after surgery. Studies between 2011-2017 found that 67-92% of US surgery patients reported not using all of their opioid tablets, typically leaving 42-71% of their prescribed pills unused.

As well as often being ineffective at treating chronic pain, opioid prescriptions for pain after surgery have been linked to prescription opioid misuse and diversion, the development of opioid use disorder, and opioid overdose. Storing excess opioid pills in the home is an important source of diversion, and in one study 61% of surgery patients had surplus medication with 91% keeping leftover pills at home.

> To reduce the increased risk of opioid misuse for surgery patients, we call for a comprehensive approach to reduce opioid prescriptions, increase use of alternative medications, reduce leftover opioids in the home, and educate patients and clinicians about the risks and benefits of opioids.

Reducing opioid risks and improving management of chronic post-surgical pain

The authors call for a comprehensive approach to reduce these risks, including specialist transitional pain clinics, opioid disposal options for patients (such as secure medication disposal boxes and drug take-back events) to help reduce home-stored opioids and the risk of diversion, and options for non-opioid and opioid-sparing pain relief. More research is also needed to help effectively manage opioid tolerance and opioid-induced hyperalgesia.

"Ultimately, chronic pain after surgery requires a comprehensive biopsychosocial approach to treatment. Transitional pain clinics are a new approach at bridging the divide, aiming to eliminate overprescribing of opioids after surgery. These clinics could help identify those at risk of chronic pain after surgery, and offer additional clinic visits, review treatment, refer the patient to alternative services, such as rehabilitation, addiction medicine, mental health services, and chronic pain services. Together this could help to reduce opioid use and abuse." says Professor Myles.

Clinical guidelines and policies must also provide consensus for prescribing opioids after surgery, offering clinicians default and maximum prescription levels. For example, there is currently no guide on how long surgical patients should remain on opioids. To counter this, in the USA, a study devised prescribing recommendations for various surgeries (based on patient surveys and prescription refills data) – recommending postoperative opioids for 4-9 days for general surgery procedures, 4-13 days for women's health procedures, and 6-15 days for musculoskeletal procedures. In addition, a study that adapted the default number of opioid pills prescribed from 30 to 12 showed marked decreases in the number of pills given after 10 common surgical procedures.

"Better understanding of the effects of opioids at neurobiological, clinical, and societal levels is required to improve future patient care," says Series author Professor Lesley Colvin, University of Dundee, UK. "There are research gaps that must be addressed to improve the current opioid situation. Firstly, we must better understand opioid tolerance and opioid-induced hyperalgesia to develop pain relief treatments that work in these conditions. We also need large population-based studies to help better understand the link between opioid use during surgery and chronic pain, and we need to understand what predisposes some people to opioid misuse so that we can provide alternative pain relief during surgery for these patients. These recommendations affect many areas of the opioid crisis and could benefit to the wider crisis too." MEH

Open heart surgery outperforms stents in patients with multivessel disease

Coronary artery bypass grafting (CABG) surgery may be the best treatment option for most patients with more than one blocked heart artery, according to research published in *The Annals of Thoracic Surgery*.

"Our data demonstrate a significant mortality benefit with CABG over percutaneous coronary intervention (PCI), and this benefit is consistent across virtually all major patient groups, suggesting that CABG should be considered in broader patient populations, not just in cases of patients with diabetes and left ventricular dysfunction, which is what is commonly practiced," said lead author Suresh R. Mulukutla, MD, from the University of Pittsburgh Medical Center (UPMC) in Pennsylvania, USA.

Dr Mulukutla and colleagues examined data from two major clinical outcomes registries for heart patients – The Society of Thoracic Surgeons (STS) National Database, and the American College of Cardiology Foundation National Cardiovascular Data Registry (NCDR). The researchers identified patients with multivessel coronary artery disease who underwent CABG or PCI between 2010 and 2018 at UPMC. Those who met the eligibility criteria were separated into two groups – CABG and PCI – each including 844 patients. The analyses focused on outcomes for mortality, readmission and revascularization.

The researchers found that the estimated one-year mortality for patients in the CABG group was 7.2%, as compared to 11.5% the PCI group. The CABG group also experienced lower risk of hospital readmission (28.1% vs. 38.4%) and revascularization (1.0% vs. 6.7%) than the PCI group.

"A major point in the study is the focus on the current era of revascularization with the most currently available stents," said Dr Mulukutla. "This research is really a modern, 'real-world' experience. While randomized clinical trials are clearly important, real-world analyses also can be very instructive because they provide insights on how we are making clinical decisions. For instance, the last several years have seen a shift toward more PCI over CABG. While there may be valid reasons for this, our data – which show CABG outperforming PCI in almost every patient group – should push us to further discuss all of the options."

PCI, often referred to as angioplasty, is a nonsurgical procedure that uses a thin, flexible catheter placed into an artery in the groin or arm. A balloon on the end of the catheter is positioned in the narrowed coronary artery and inflated to open-up the blockage. A stent is a metal mesh tube that is left behind to help keep the artery from collapsing. Drugs attached to the stent help prevent the body from reacting to the stent and shutting down the artery again.

CABG, the most commonly performed heart operation in the United States, is designed to bypass the blockages in the coronary arteries in order to create a new path for blood flow to the heart. The surgeon removes a healthy blood vessel, usually from the leg, arm, chest, or abdomen, and connects it to the other arteries (usually the aorta) in the heart. This enables blood flow to "bypass" or go around the diseased or blocked portion of the coronary artery.

The decision between open heart surgery and PCI for treatment of patients with multiple narrowed arteries is not always straightforward, according to Dr Mulukutla. Thus, these more complex treatment decisions should be made with the guidance of a heart care team.

"Both cardiac surgery and stenting have roles among patients with coronary artery disease," said Dr Mulukutla. "Because of this, it is important to deliberate carefully with the help of a heart team. The team can ensure that a multidisciplinary approach is used when offering recommendations to patients and assisting them in making informed decisions."

A heart care team generally includes cardiothoracic surgeons and cardiologists. Other health care providers such as primary care physicians, physician assistants, nurse practitioners, imaging specialists, and anesthesiologists also may be part of the team. This approach leverages the expertise of these advanced practice providers in an effort to improve the efficiency and advance the quality of care for patients.

This research is really a modern, 'real-world' experience. While randomized clinical trials are clearly important, real-world analyses also can be very instructive because they provide insights on how we are making clinical decisions.

With revascularization, heart team input is often limited because PCI can be completed at the time of a patient's diagnostic procedure. When this happens, the physicians do not have the opportunity to discuss the spectrum of possible treatment options. As a result, the practical and consistent use of the heart team for decision-making in the treatment of patients with complex coronary artery diseases is lacking, Dr Mulukutla explained.

"We are working to better facilitate a heart team approach and overcome some of the limitations given the current infrastructure of how these decisions are made," said Dr Mulukutla. "We also are continuing to identify specific patient populations that may benefit from either CABG or PCI so that we can best advocate for our patients." MEH

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Mohammed Abdullah, 4, is vaccinated in Aden, Yemen during a UNICEF-sponsored Measles and Rubella vaccination campaign on 9 February 2019. In Yemen, years of conflict have led to an outbreak of the deadly virus. UNICEF, however, with the backing of the Measles and Rubella Initiative – a private-public partnership of five global partners including the World Health Organization (WHO), Centers for Disease Control (CDC), United Nations Foundation and American Red Cross – has spearheaded a global push towards measles and rubella elimination.

Surge in measles cases globally

UNICEF is warning that global cases of measles are surging to alarmingly high levels, led by ten countries accounting for more than 74% of the total increase, and several others that had previously been declared measles free.

Globally, 98 countries reported more cases of measles in 2018 compared to 2017, eroding progress against this highly preventable, but potentially deadly disease.

Ukraine, the Philippines and Brazil saw the largest increases in measles cases from 2017 to 2018. In Ukraine alone, there were 35,120 cases of measles in 2018. According to the government, another 24,042 people were infected just in the first two months of 2019. In the Philippines so far this year, there have been 12,736 measles cases and 203 deaths, compared to 15,599 cases in the whole of 2018.

Countries with ten highest increases in cases between 2017 and 2018

• Ukraine	30,338
• Philippines	13,192
• Brazil	10,262
• Yemen	6,641
• Venezuela	4,916
• Serbia	4,355
• Madagascar	4,307
• Sudan	3,496
• Thailand	2,758
• France	2,269

"This is a wake-up call. We have a safe, effective and inexpensive vaccine against a highly contagious disease – a vaccine that has saved almost a million lives every year over the last two decades," said Henrietta Fore, UNICEF's Executive Director. "These cases haven't happened overnight. Just as the serious outbreaks we are seeing today took hold in 2018, lack of action today will have disastrous consequences for children tomorrow."

Measles is highly contagious, more so than Ebola, tuberculosis or influenza. The virus can be contracted by someone up to two hours after an infected person has left a room. It spreads through air and infects the respiratory tract, potentially killing malnourished children or babies too young to be vaccinated. Once infected, there is no specific treatment for measles, so vaccination is a life-saving tool for children.

In response to these outbreaks, UNICEF and its partners are supporting governments to urgently reach millions of children in countries around the globe. For example:

- In Ukraine, UNICEF has provided ongoing support to accelerate routine immunization across the country and address vaccine hesitancy, including additional efforts to stop the most recent outbreak that has claimed 30 lives since 2017. In February, the Ministry of Health, with UNICEF's support, launched an immunization drive at schools and clinics in the worst-hit Lviv region in western Ukraine, where negative attitudes toward immunization, and previous shortages in vaccine supply, have resulted in low vaccination rates.
- In the Philippines, the government, with support from UNICEF and partners, will conduct a campaign to vaccinate 9 million children against measles across 17 regions. Using social media, campaigners plan to encourage apprehensive parents, and health workers.
- In Brazil, from August to September 2018, the government carried out a campaign against polio and measles, targeting more than 11 million children under five. UNICEF encouraged people to get vaccinated, and trained health monitors working in migrant shelters for Venezuelans. UNICEF has included the measles vaccine as part of the Municipal Seal programme that covers 1,924 municipalities.
- In Yemen, where years of conflict led to an outbreak, local authorities with support from UNICEF, WHO and GAVI vaccinated more than 11.5 million children in February.
- In Madagascar, from 3 September to 21 February, 76,871 people were infected by

Notable reported measles cases in 2018 in countries with no reported cases in 2017

• Brazil	10,262
• Moldova	312
• Montenegro	203
• Colombia	188
• imor-Leste	59
• Peru	38
• Chile	23
• Uzbekistan	17

measles and 928 died, a majority of which were children. In January, the government, with support of partners including UNICEF, launched an immunization campaign to target all 114 districts. Over 2 million children were immunized in 25 districts. In February, 1.4 million children were vaccinated, with another 3.9 million more to follow in March.

Poor health infrastructure, civil strife, low community awareness, complacency and vaccine hesitancy in some cases have led to these outbreaks in both developed and developing countries. For example, in the United States, the number of measles cases increased six-fold between 2017 and 2018, reaching 372 cases. More recently, the U.S. has seen outbreaks in New York and Washington state.

"Almost all of these cases are preventable, and yet children are getting infected even in places where there is simply no excuse," said Fore. "Measles may be the disease, but, all too often, the real infection is misinformation, mistrust and complacency. We must do more to accurately inform every parent, to help us safely vaccinate every child."

To fight measles, UNICEF is issuing an urgent appeal to governments, healthcare providers, and parents to do more to contain the disease by:

- Understanding that vaccines are safe and effective and can save a child's life
- Vaccinating all children between the ages of six months to five years during outbreaks
- Training and equipping health workers so they can provide quality services
- Strengthening immunization programmes to deliver all life-saving vaccines MEH

Children in Aden, Yemen proudly show off the spots on their arms where they were vaccinated during a mobile Measles and Rubella vaccination campaign backed by UNICEF, 9 February 2019.

Yemen sees 1000 cases of cholera a day

In just two weeks in March nearly 40,000 new cases of cholera were reported in Yemen, including 14,842 children aged under fifteen, according to the World Health Organisation's Emergency Operations Centre (EOC). That's an average of 1,000 cases every day – and marks a dramatic spike of 150% compared to the same period in February. More than a third were children under the age of fifteen.

With heavy rains arriving, the outbreak is now set to spread even faster without urgent action, the Save the Children aid organisation says.

The country's worst outbreak in history infected more than a million people in 2017, but declined significantly at the start of 2018.

Since January this year there have been 124,493 suspected cases of cholera nationwide.

Four years of war have created the perfect conditions for cholera to spread rapidly, with sanitation systems in ruins, water sources contaminated, and displaced families left without access to clean water.

Increasing rates of malnutrition have also left millions of Yemeni children more likely to contract – and die – from the disease.

Two million children under the age of five will need treatment for acute malnutrition this year, according to the United Nations.

Malnourished children have substantially reduced immune systems and are at least three times more likely to die if they contract cholera. Diarrhoeal diseases like cholera are also themselves a major cause of malnutrition.

Save the Children has previously estimated 85,000 children under the age of five may have died from starvation and disease since the conflict escalated on March 26, 2015.

Tamer Kirolos, Save the Children's Yemen Country Director, said: "A massive outbreak will be yet another killer for children left starved and weakened by four years of war. The tragedy is cholera can be easily prevented with access to clean water and basic hygiene. But that's where we are right now. Yemen's sewage system, which was already lacking before the conflict, is now almost non-existent. There's an increasing number of people forced to camp out in unsanitary conditions simply to escape the fighting.

"All parties to this conflict, and those supporting them, must take the only responsible action which is to urgently reach a peaceful resolution. Yemen's children cannot be made to wait while war and deadly disease rage around them." MEH

Globally, one in five deaths are associated with poor diet

People in almost every region of the world could benefit from rebalancing their diets to eat optimal amounts of various foods and nutrients, according to the Global Burden of Disease study tracking trends in consumption of 15 dietary factors from 1990 to 2017 in 195 countries, published in *The Lancet*.

The study estimates that one in five deaths globally – equivalent to 11 million deaths – are associated with poor diet, and diet contributes to a range of chronic diseases in people around the world. In 2017, more deaths were caused by diets with too low amounts of foods such as whole grains, fruit, nuts and seeds than by diets with high levels of foods like trans fats, sugary drinks, and high levels of red and processed meats.

The authors say that their findings highlight the urgent need for coordinated global efforts to improve diet, through collaboration with various sections of the food system and policies that drive balanced diets.

"This study affirms what many have thought for several years – that poor diet is responsible for more deaths than any other risk factor in the world," says study author Dr Christopher Murray, Director of the Institute for Health Metrics and Evaluation, University of Washington, USA. "While sodium, sugar, and fat have been the focus of policy debates over the past two decades, our assessment suggests the leading dietary risk factors are high intake of sodium, or low intake of healthy foods, such as whole grains, fruit, nuts and seeds, and vegetables. The paper also highlights the need for comprehensive interventions to promote the production, distribution, and consumption of healthy foods across all nations."

Impact of diet on non-communicable diseases and mortality

The study evaluated the consumption of major foods and nutrients across 195 countries and quantified the impact of poor diets on death and disease from non-communicable diseases (specifically cancers, cardiovascular diseases, and diabetes). It tracked trends between 1990 and 2017.

Previously, population level assessment of the health effects of suboptimal diet has not been possible because of the complexities of characterising dietary consumption across different nations. The new study combines and analyses data from epidemiological studies – in the absence of long-term randomised trials which are not always feasible in nutrition – to identify associations between dietary factors and non-communicable diseases.

The study looked at 15 dietary elements – diets low in fruits, vegetables, legumes, whole grains, nuts and seeds, milk, fibre, calcium, seafood omega-3 fatty acids, polyunsaturated fats, and diets high in red meat, processed meat, sugar-sweetened beverages, trans fatty acids, and sodium. The authors note that there were varying levels of data available for each dietary factor, which increases the statistical uncertainty of these estimates – for example, while data on how many people ate most dietary factors was available for almost all countries (95%), data for the sodium estimates was only available for around one in four countries.

Overall in 2017, an estimated 11 million deaths were attributable to poor diet. Diets high in sodium, low in whole grains, and low in fruit together accounted for more than half of all diet-related deaths globally in 2017.

The causes of these deaths included 10 million deaths from cardiovascular disease, 913,000 cancer deaths, and almost 339,000 deaths from type 2 diabetes. Deaths related to diet have increased from 8 million in 1990, largely due to increases in the population and population ageing.

Global trends in consumption

The authors found that intakes of all 15 dietary elements were suboptimal for almost every region of the world – no region ate the optimal amount of all 15 dietary factors, and not one dietary factor

was eaten in the right amounts by all 21 regions of the world.

Some regions did manage to eat some dietary elements in the right amounts. For example, intake of vegetables was optimal in central Asia, as was seafood omega-3 fatty acids intake in high-income Asia Pacific, and legume intake in the Caribbean, tropical Latin America, south Asia, western sub-Saharan Africa, and eastern sub-Saharan Africa.

The largest shortfalls in optimal intake were seen for nuts and seeds, milk, whole grains, and the largest excesses were seen for sugar sweetened beverages, processed meat and sodium. On average, the world only ate 12% of the recommended amount of nuts and seeds (around 3g average intake per day, compared with 21g recommended per day), and drank around ten times the recommended amount of sugar sweetened beverages (49g average intake, compared with 3g recommended).

In addition, the global diet included 16% of the recommended amount of milk (71g average intake per day, compared with 435g recommended per day), about a quarter (23%) of the recommended amount of whole grains (29g average intake per day, compared with 125g recommended per day), almost double (90% more) the recommended range of processed meat (around 4g average intake per day, compared with 2g recommended per day), and 86% more sodium (around 6g average intake per day, compared with 24 h urinary sodium 3g per day).

Regional variations

Regionally, high sodium intake (above 3g per day) was the leading dietary risk for death and disease in China, Japan, and Thailand. Low intake of whole grains (below 125g per day) was the leading dietary risk factor for death and disease in the USA, India, Brazil, Pakistan, Nigeria, Russia, Egypt, Germany, Iran, and Turkey. In Bangladesh, low intake of fruits (below 250g per day) was the leading dietary risk, and, in Mexico, low intake of nuts and seeds (below 21g per day) ranked first. High consumption of red meat (above 23g per day), processed meat (above 2g per day), trans fat (above 0.5% total daily energy), and sugar-sweetened beverages (above 3g per day) were towards the bottom in ranking of dietary risks for death and disease for highly populated countries [3].

In 2017, there was a ten-fold difference between the country with the highest rate of diet-related deaths (Uzbekistan) and the country with the lowest (Israel). The countries with the lowest rates of diet-related deaths were Israel (89 deaths per 100,000 people), France, Spain, Japan, and Andorra. The UK ranked 23rd (127 deaths per 100,000) above Ireland (24th) and Sweden (25th), and the United States ranked 43rd (171 deaths per 100,000) after Rwanda and Nigeria (41st and 42nd), China ranked 140th (350 deaths per 100,000 people), and India 118th (310 deaths per 100,000 people). The countries with the highest rates of diet-related deaths were Uzbekistan (892 deaths per 100,000 people), Afghanistan, Marshall Islands, Papua New Guinea, and Vanuatu.

The magnitude of diet-related disease highlights that many existing campaigns have not been effective and the authors call for new food system interventions to rebalance diets around the world. Importantly, they note that changes must be sensitive to the environmental effects of the global food system to avoid adverse effects on climate change, biodiversity loss, land degradation, depleting freshwater, and soil degradation.

In January 2019, *The Lancet* published the EAT-Lancet Commission, which provides the first scientific targets for a healthy diet from a sustainable food production system that operates within planetary boundaries for food. This report used 2016 data from the Global Burden of Disease study to estimate how far the world is from the healthy diet proposed.

The authors note some limitations of the current study, including that while it uses the best available data, there are gaps in nationally representative individual-level data for intake of key foods and nutrients around the world. Therefore, generalising the results may not be appropriate as most of the studies of diet and disease outcomes are largely based on populations of European descent, and additional research in other populations is desirable. The strength of epidemiological evidence linking dietary factors and death and disease is mostly from observational studies and is not as strong as the evidence linking other major risk factors (such as tobacco and high blood pressure) to ill health. However, most of the diet and health associations are supported by short term randomized studies with risk factors for disease as the outcomes.

For sodium, estimates were based on 24-hour urinary sodium measurements, rather than spot urine samples, which was only available for around a quarter of the countries in the study. Accurate estimation of some nutrients (such as fibre, calcium, and polyunsaturated fatty acids) is complex. As a result, the authors call for increased national surveillance and monitoring systems for key dietary risk factors, and for collaborative efforts to collect and harmonise dietary data from cohort studies.

In addition, the authors only looked at food and nutrient intake and did not evaluate whether people were over- or underweight. Lastly, some deaths could have been attributed to more than one dietary factor, which may have resulted in an overestimation of the burden of diseases attributable to diet.

Writing in a linked Comment, Professor Nita G Forouhi, Medical Research Council Epidemiology Unit, University of Cambridge School of Clinical Medicine, UK, says: "Limitations notwithstanding, the current GBD findings provide evidence to shift the focus, as the authors argue, from an emphasis on dietary restriction to promoting healthy food components in a global context. This evidence largely endorses a case for moving from nutrient-based to food based guidelines… There are of course considerable challenges in shifting populations' diets in this direction, illustrated by the cost of fruits and vegetables being disproportionately prohibitive: two servings of fruits and three servings of vegetables per day per individual accounted for 52% of household income in low-income countries, 18% in low to middle-income countries, 16% in middle to upper-income countries, and 2% in high-income countries. A menu of integrated policy interventions across whole food systems, internationally and within countries, is essential to support the radical shift in diets needed to optimise human, and protect planetary health." MEH

Alex Gindin

Traffic-related air pollution associated with 4 million new cases of childhood asthma every year

Kuwait, UAE top the list of number of cases

The first global estimates of their kind suggest that more than one in ten childhood asthma cases could be linked to traffic-related air pollution every year, according to a health impact assessment of children in 194 countries and 125 major cities worldwide, published in *The Lancet Planetary Health* journal.

With 92% of cases developing in areas that have traffic pollution levels below the WHO guideline level, the authors suggest that this limit may need to be reviewed.

"Nitrogen dioxide pollution appears to be a substantial risk factor for childhood asthma incidence in both developed and developing countries, especially in urban areas," says senior author Dr Susan Anenberg, George Washington University, USA. "Our findings suggest that the World Health Organization guideline for annual average nitrogen dioxide concentrations might need to be revisited, and that traffic emissions should be a target to mitigate exposure."

Lead author Ploy Achakulwisut, George Washington University, USA, adds: "Our study indicates that policy initiatives to alleviate traffic-related air pollution can lead to improvements in children's health and also reduce greenhouse gas emissions. Recent examples include Shenzhen's electrification of its entire bus fleet and London's Ultra-Low Emission Zone congestion charges."

Globally, asthma is the most common non-communicable disease among children, and, according to the WHO, prevalence has increased dramatically since the 1950s. The reasons for this are multiple.

Traffic-related air pollution may result in asthma development as pollutants may cause damage to the airways, leading to inflammation that triggers asthma in genetically predisposed children. Although it is not yet clear which specific pollutant within the traffic-related air pollution mixture is the source of asthma development, reviews by the US Environmental Protection Agency and Health Canada suggest that a causal relationship is likely to exist between long-term nitrogen dioxide (NO2) exposure and childhood asthma development.

In the new study, the authors used NO2 as a surrogate for the traffic pollution mixture to focus specifically on the effects of traffic pollution on childhood asthma development. NO2 is a pollutant formed mainly from fossil fuel combustion, and traffic emissions can contribute up to 80% of ambient NO2 in cities. NO2 is just one component of air pollution, which is made up of many pollutants (including particulate matter, ozone, carbon monoxide), which are known to have numerous adverse effects on health.

The authors combined a global dataset of ambient NO2 (modelled from ground-level monitors, satellite data, and land use variables such as road networks) with data on population distribution and asthma incidence to estimate the number of new traffic pollution-related asthma cases in children aged 1-18 years.

Globally, the estimates suggest that there are 170 new cases of traffic pollution-related asthma per 100,000 children every year, and 13% of childhood asthma cases diagnosed each year are linked to traffic pollution.

Kuwait, UAE top the list

The country with the highest rate of traffic pollution-related childhood asthma was Kuwait (550 cases per 100,000 children each year), followed by the United Arab Emirates (460 per 100,000), and Canada (450 per 100,000). Of the 125 cities studied, there was a large variation in the estimated rate of traffic pollution-related childhood asthma – from 83 cases per 100,000 children every year in Orlu, Nigeria, to 690 cases per 100,000 children in Lima, Peru. These rates of traffic pollution-related asthma are influenced by asthma rates overall, as well as pollution levels, and may underestimate true

> Our study indicates that policy initiatives to alleviate traffic-related air pollution can lead to improvements in children's health and also reduce greenhouse gas emissions.

levels in many low- and middle-income countries. This is because asthma cases often go undiagnosed in these regions.

The largest number of cases of traffic pollution-related asthma were estimated for China (760,000 cases), which is likely a result of China having the second largest population of children and the third highest concentrations of NO2. Although less than half the size of China's burden, India had the next largest number of cases (350,000) due to its large population of children. The USA (240,000), Indonesia (160,000) and Brazil (140,000) had the next largest burdens, with the USA having the highest pollution levels of these three countries, while Indonesia had the highest underlying asthma rates.

The country with the highest percentage of traffic pollution-attributable childhood asthma incidence was South Korea (31%), followed by Kuwait (30%), Qatar (30%), United Arab Emirates (30%), and Bahrain (26%). The UK ranked 24th out of 194 countries, the US 25th, China 19th, and India 58th. The authors explain that India ranks below other countries for this metric because, although levels of other pollutants (particularly PM2.5) in India are among the highest in the world, NO2 levels from 2010-2012 in Indian cities appear to be lower than or comparable to levels in European and US cities.

Two-thirds of traffic pollution-related asthma cases occurred in urban centres globally, and when suburbs were included this proportion increased to 90% of cases.

The percentage of new asthma cases attributable to traffic pollution by city ranged from 6% in Orlu, Nigeria, to 48% in Shanghai, China, and largely reflected the variations in NO2 exposures within each region. Of the ten cities with the highest proportion of traffic pollution-related asthma cases, eight were in China (Shanghai, Tianjin, Beijing, Shenyang, Xi'an, Taiyuan, Zhengzhou, and Harbin) alongside Moscow, Russia, and Seoul, South Korea – all of which had high urban NO2 concentrations. Paris ranked 21st (33%), New York ranked 29th (32%), London 35th (29%), and New Delhi 38th (28%).

The authors note some limitations, including that studies linking traffic pollution and asthma, and NO2 monitoring data are largely from North America, Europe and east Asia, and NO2 ground-level monitors are mostly in urban areas, so could overestimate pollution levels in rural areas.

Due to limited data availability, the NO2 levels used in this study are for 2010-2012, whereas the population and asthma incidence rates are for 2015. Given recent global changes in NO2 levels (decreases in US and European cities, and increases in Asia), the estimates may not be exact and further research with the latest NO2 levels is needed.

Writing in a linked Comment, Professor Rajen N Naidoo, University of KwaZulu-Natal, South Africa, says: "An important outcome from this study is the further evidence that the existing WHO standards are not protective against childhood asthma. Achakulwisut and colleagues estimated that approximately 92% of the childhood asthma incidence attributable to NO2 exposure was in areas with NO2 concentrations below the values of the WHO annual average guidelines. This strengthens the case for the downward revision of these global standards and for stronger national policy initiatives in countries without air quality standards. Furthermore, these findings not only support the association of NO2 exposure with childhood asthma incidence, but also, because this pollutant serves as an important proxy for broader traffic related air pollutants, highlight that urgent intervention is necessary to protect the health of those most vulnerable in society: children, particularly those with pre-existing respiratory disease." MEH

- Reference:

www.thelancet.comjournals/lanpla/article/PIIS2542-5196(19)30046-4/fulltext

Siemens Healthineers introduces functions to standardize imaging in the hybrid OR

At the 2019 Charing Cross Symposium in London, an international congress for the management of vascular diseases, Siemens Healthineers introduced software and hardware functions for imaging that will simplify surgical workflows in the hybrid OR and standardize treatments for a wide range of cases. This could mean shorter procedure time in the OR and a lower complication rate for the patients.

The number of cases requiring endovascular repair in hybrid OR is on the rise, since improvements in medical technology are making more and more patient groups eligible for minimally invasive treatment. But imaging in the hybrid OR often necessitates time-consuming, manual settings of the imaging system. The functions offered by Siemens Healthineers for "Procedural Intelligence" will now help automate complex workflows in the hybrid OR and standardize endovascular procedures. As a result, the medical team can devote more attention to the patient during the operation, and also cut down the length of time the patient needs to spend in the OR.

The functions for "Procedural Intelligence" are a combination of new hardware design and new software functionalities. They will be available for both the Artis pheno, a robot-assisted angiography system, and the Artis icono floor, the new floor-mounted angiography system from Siemens Healthineers.

"As the number and complexity of image-guided minimally invasive treatments continue to grow, automation and standardization will become the keys to efficient and effective patient care," says Peter Seitz, General Manager Surgery at Siemens Healthineers. "Our imaging systems with Procedural Intelligence enable us to optimize clinical operations in the hybrid OR and achieve consistent results for the patient, no matter how complex the procedures."

The Artis icono and Artis pheno offer "Case Flows" as a means of reducing the number of manual steps on the angiography system. These are standardized presets covering many procedures, which let operators set the device in accordance with the requirements of the current stage and the operators' own preferences at the push of a button.

Applications like Syngo EVAR Guidance can speed up the work of preparing for surgery. The pre-procedural CT image is prepared automatically for subsequent overlaying with the 2D x-ray image, a process known as fusion imaging. The applications recognize the vessel walls in the aorta, mark the main vessels branching away from it, and calculate the ideal angulation (the setting angle for the C-arm) for each landing zone. At this point the anatomical markings on the pre-procedural CT image can be displayed on the x-ray image to serve as a guide for the surgeon, enabling the stent to be precisely positioned.

Using the new OPTIQ image chain, image processing has been fundamentally redesigned, from image acquisition to post-processing and visualization of the images on the display of the angiography systems from Siemens Healthineers. For example, the OPTIQ software uses algorithms to select the right image parameters. As a result, image quality remains consistently high across a wide range of angulations and patient weights, which permits significant savings in radiation dose.

The requirements health care providers place on their hybrid OR can vary greatly, for example, depending on whether a modality requiring less space is needed for routine cardiovascular procedures, or whether they want to prepare for complex cases and multidisciplinary use. Siemens Healthineers has the appropriate hybrid OR imaging system for every scenario. The fixed C-arms with the functionality "Procedural Intelligence" support the surgeons' individual needs by automating workflows and providing optimized imaging. The floor-mounted angiography systems also provide sterile air circulation above the operating area. In addition, the antimicrobial surfaces ensure infection control in the OR. MEH

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Scientists restore some functions in a pig's brain hours after death

Circulation and cellular activity were restored in a pig's brain four hours after its death, a finding that challenges long-held assumptions about the timing and irreversible nature of the cessation of some brain functions after death, Yale scientists report in the April 18 issue of the journal *Nature*.

The brain of a postmortem pig was isolated and circulated with a specially designed chemical solution. Many basic cellular functions, once thought to cease seconds or minutes after oxygen and blood flow cease, were observed, the scientists report.

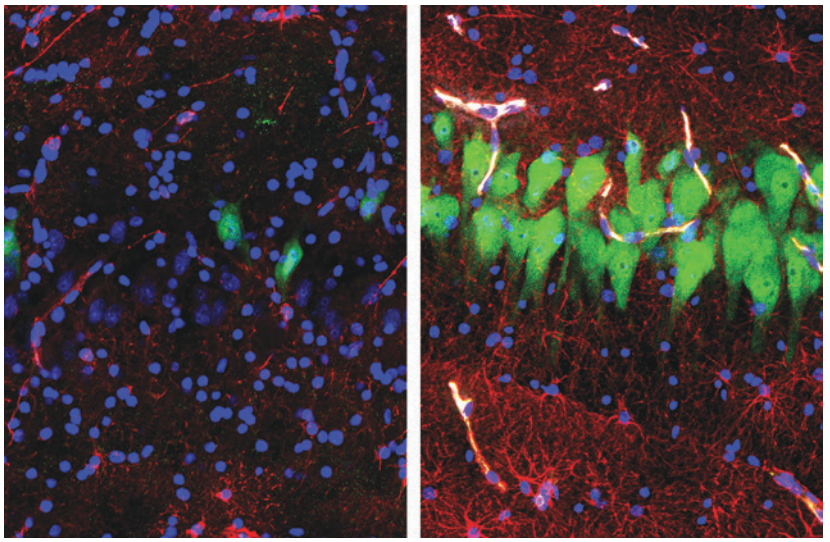
"The intact brain of a large mammal retains a previously underappreciated capacity for restoration of circulation and certain molecular and cellular activities multiple hours after circulatory arrest," said senior author Nenad Sestan, professor of neuroscience, comparative medicine, genetics, and psychiatry.

However, researchers also stressed that the treated brain lacked any recognizable global electrical signals associated with normal brain function.

"At no point did we observe the kind of organized electrical activity associated with perception, awareness, or consciousness," said co-first author Zvonimir Vrselja, associate research scientist in neuroscience. "Clinically defined, this is not a living brain, but it is a cellularly active brain."

Cellular death within the brain is usually considered to be a swift and irreversible process. Cut off from oxygen and a blood supply, the brain's electrical activity and signs of awareness disappear within seconds, while energy stores are depleted within minutes. Current understanding maintains that a cascade of injury and death molecules are then activated leading to widespread, irreversible degeneration.

However, researchers in Sestan's lab, whose research focuses on brain development and evolution, observed that the small tissue samples they worked with routinely showed signs of cellular viability, even when the tissue was harvested multiple hours postmortem. Intrigued, they obtained the brains of pigs processed for food production to study how widespread this postmortem viability might be in the intact brain. Four hours after the pig's death, they connected the vasculature of the brain to circulate a uniquely formulated solution they developed to preserve brain tissue, utilizing a system they call BrainEx. They found neural cell integrity was preserved, and certain neuronal, glial, and vascular cell functionality was restored.



Immunofluorescent stains for neurons (green), astrocytes (red), and cell nuclei (blue) in a region of the hippocampus of a pig's brain left untreated 10 hours after death (left) or subjected to perfusion with the BrainEx technology. Ten hours postmortem, neurons and astrocytes undergo cellular disintegration unless salvaged by the BrainEx system.

The new system can help solve a vexing problem – the inability to apply certain techniques to study the structure and function of the intact large mammalian brain – which hinders rigorous investigations into topics like the roots of brain disorders, as well as neuronal connectivity in both healthy and abnormal conditions.

"Previously, we have only been able to study cells in the large mammalian brain under static or largely two-dimensional conditions utilizing small tissue samples outside of their native environment," said co-first author Stefano G. Daniele, an M.D./Ph.D. candidate. "For the first time, we are able to investigate the large brain in three dimensions, which increases our ability to study complex cellular interactions and connectivity."

While the advance has no immediate clinical application, the new research platform may one day be able to help doctors find ways to help salvage brain function in stroke patients, or test the efficacy of novel therapies targeting cellular recovery after injury, the authors say.

The research was primarily funded by the National Institutes of Health's (NIH) BRAIN Initiative.

"It's quite a surprising result," Andrea Beckel-Mitchener, PhD, BRAIN Initiative Team Lead said in an NIH press briefing. "We did not know that brain cells were this resilient, and under the right conditions – such as what's been shown here with BrainEx – that the cells could maintain some healthy function hours after loss of blood flow."

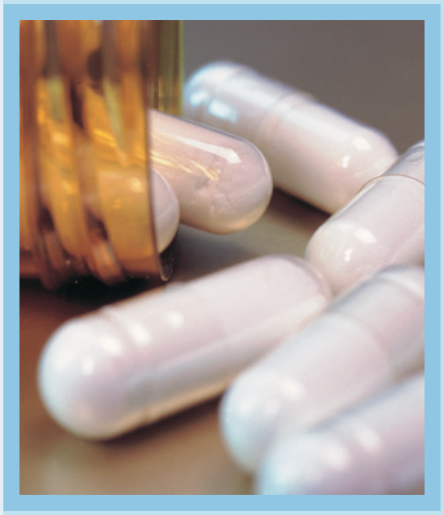
"This line of research holds hope for advancing understanding and treatment of brain disorders and could lead to a whole new way of studying the postmortem human brain," said Beckel-Mitchener.

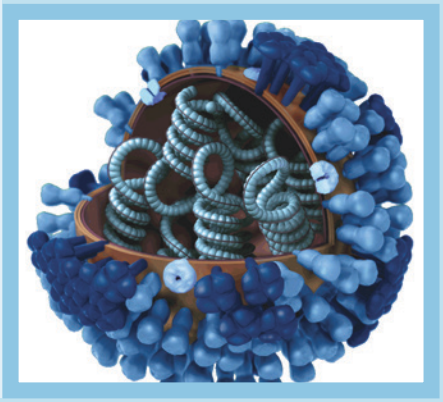
The researchers said that it is unclear whether this approach can be applied to a recently deceased human brain. MEH

Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

Event	Date / City	Contact
June 2019		
6th International Conference on Rare Diseases and Orphan Drugs	17-18 June 2019 Dubai, UAE	*rare-diseases@memeetings.net*
International Conference on Vaccines and Immune Response	17-18 June 2019 Dubai, UAE	*immuneresponse@me healthevents.org*
Middle East Health Revolution Summit	18-19 June 2019, Abu Dhabi, UAE	*https://go.evvnt.com/372515-0*
The 4th Middle East International Nursing & Midwifery Congress	21-22 June 2019, Dubai, UAE	*https://go.evvnt.com/372515-0*
Advanced Diabetes Conference	21-22 June 2019, Abu Dhabi, UAE	*https://orthopaedics. healthconferences.org/*
July 2019		
14th World Congress on Healthcare and Medical Tourism	18-19 July 2019 Abu Dhabi, UAE	*https://healthcare.global-summit. com/middleeast/*
September 2019		
5th Abu Dhabi International Conference in Dermatology and Aesthetics (AIDA)	19-21 September 2019 Abu Dhabi, UAE	*https://go.evvnt.com/407453-0*
The 5th Annual MENA International Orthopaedic Congress	19-21 September 2019 Dubai, UAE	*https://go.evvnt.com/349042-0*





Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

Event	Date / City	Contact

October 2019

The Abu Dhabi ID Week	16-20 October 2019 Abu Dhabi, UAE	*https://go.evvnt.com/378477-0*
XXIV World Congress of Neurology - WCN 2019	27-31 October 2019 Dubai, UAE	*https://go.evvnt.com/323182-5*
The MENA Physical Medicine & Rehabilitation Congress	31 Oct – 2 Nov 2019 Dubai, UAE	*https://go.evvnt.com/372515-0*

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*

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Giving new hope to children with 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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Source: Internal data, Hillman Center for Pediatric Transplantation