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May - June 2018

Pregnant with anaemia

Risk of maternal death doubles

Reversing type 2 diabetes

Researchers show it can be done with primary care-led weight management

Interview

Aladin Niazmand, Director of TAHPI

- on modular hospital design and development

- 90% of people worldwide breathe polluted air, says WHO
- WHO, UNICEF issue new guidance to promote breastfeeding in health facilities
- McAfee report warns of cybersecurity threat to health care
- 2.7 million children in Yemen targeted for diphtheria vaccination





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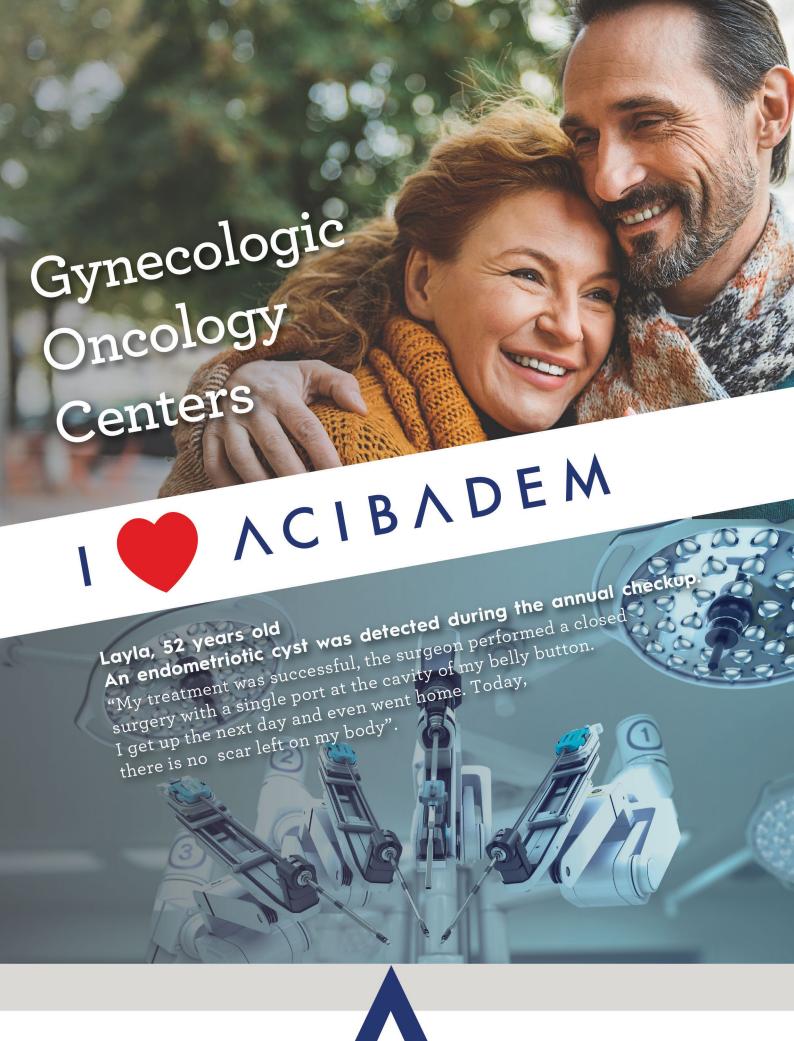
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Research is key

In this issue, as we do regularly, we have curated some interesting reviews of recently published research in a variety of medical specialties. Of particular interest is a study that was published in The Lancet Global Health in March, which is set to have important implications for pregnant women. In the largest study of its kind, researchers show that, when all known contributing factors are controlled for, the odds of maternal death are doubled in mothers with severe anaemia. The study covered more than 300,000 women in 29 countries, including several in the Middle East. The study authors say that clinicians, policy makers and healthcare professionals should now focus their attention on preventing anaemia, using a multifaceted approach, not just hoping that iron tablets will solve

In another study reviewed in this issue that has particular relevance to the diabetes epidemic in the Middle East, researchers show that remission from type 2 diabetes can be achieved through a primary care-led intensive weight management programme. Their findings show that, at 12 months, almost half of participants achieved remission to a non-diabetic state and off antidiabetic drugs.

In our United States report we look at the importance of government funding for basic research and how a new Omnibus Bill approved in March has provided much sought after funding for several important research organisations, such as the National Institutes of Health. This renewed funding is set to enable the United States to maintain its status as the world leader in healthcare discovery.

Also in this issue, we publish an interesting interview we held with the Director of TAHPI, a company that is making waves in the Middle East with their modular hospital design and construction.

As in each issue, this one is full of relevant healthcare news and research reviews. We trust you will find some knowledge-enhancing articles pertinent to your interests.

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middle east monitor

Update from around the region

2.7 million children in Yemen targeted for diphtheria vaccination

The World Health Organization (WHO), UNICEF and national health authorities have completed a large-scale vaccination campaign in March this year to control the spread of diphtheria in Yemen.

The campaign targeted nearly 2.7 million children aged 6 weeks to 15 years in 11 governorates. It focused on locations reporting suspected cases of diphtheria and areas at high risk of spread of the infectious respiratory disease. More than 6000 health workers were mobilized during the campaign, including for community engagement and the administration of the vaccine.

First reported in October 2017, the outbreak has spread rapidly across the country, infecting more than 1300 people and killing over 70. Almost 80% of the caseload is children and young adults below 25 years of age.

"We are in a race against time to control this outbreak and save lives," said Dr Nevio Zagaria, WHO Representative to Yemen. "The almost collapsed health system and the conflict has severely hampered the response, but we have managed to deliver urgently needed antibiotics and diphtheria anti-toxins (DAT) to support treatment, and are now scaling up vaccination efforts to stop the outbreak from spreading even further."

The rapid spread of diphtheria in Yemen highlights major gaps in routine vaccination coverage in recent years and signifies a collapsing health system. Only 50% of all health facilities are partially or fully functioning.

In November and December 2017, WHO and UNICEF vaccinated almost 450,000 children under 7 years of age against diphtheria in Ibb – the worst affected governorate accounting for nearly 35% of all cases reported.

The vaccination campaign is part of a larger response plan to control diphtheria implemented by national health authorities, UNICEF and WHO. Parallel activities include strengthening surveillance and case detection, enhancing laboratory testing capacity, procuring and distribut-

ing the DAT to the Diphtheria Isolation Units in health facilities, and training and deploying Rapid Response Teams to trace contacts and provide preventative antibiotics in the community. Health education and awareness campaigns are also being conducted to inform communities on how to protect themselves against diphtheria and other infectious diseases.

Diphtheria is an infectious respiratory disease caused by a potent toxin produced by certain strains of the bacterium *Corynebacterium diphtheriae*. It spreads through air droplets by coughing or sneezing. According to the WHO, vaccination against diphtheria is safe and effective for prevention of the disease.

WHO DG calls for urgent action to improve health in Gaza

World Health Organization (WHO) Director-General Dr Tedros Adhanom Ghebreyesus on 19 March this year called for urgent action to improve health conditions in Gaza after concluding his first visit to the occupied Palestinian territory.

During his visit to Gaza, Dr Tedros witnessed the challenges that many people face in accessing quality health services. Chronic electricity shortages in Gaza are hindering the provision of life-saving medical services, and emergency fuel supplies are only enough to keep generators running for another few months. More than 40% of essential drugs are completely depleted in Gaza's Central Drug Store, including drugs used in emergency departments and other critical units.

Access for patients requiring health care outside the Gaza Strip has also been declining: only 54% of patient applications to access services outside Gaza were accepted by Israeli authorities in 2017 compared to more than 90% of applications accepted in 2012. Approximately one third of these are for access to cancer treatment and diagnostic services lacking in Gaza. WHO and its partners are working with the Palestinian health ministry to address these issues.

Dr Tedros visited Shifa hospital, Gaza's largest, to deliver essential lifesaving medi-

cal equipment procured as part of WHO's emergencies programme. He also met with UNRWA, the United Nations Relief and Works Agency for Palestine Refugees in the Near East, which is playing an essential role in providing primary care services for Palestinian refugees. Despite new funding of \$100 million pledged at a ministerial conference in Rome on 15 March, UNRWA faces a critical funding shortage which may result in social services including primary health care being curtailed as soon as July.

"Despite the best efforts of health workers, many of whom have not been paid in months, Gaza's health services are at breaking point," Dr Tedros said. "Shortages of electricity, fuel and essential medicines are putting lives at risk. I call on all parties and partners to alleviate the suffering of many people."

In separate meetings with Palestinian President Mahmoud Abbas and representatives from the Government of Israel, Dr Tedros emphasised the need to use health as a bridge to peace, and to respect, protect and fulfil the right to health for all, including for Palestinians living in the occupied Palestinian territory. Israeli representatives agreed to work with WHO to address the issues raised.

He raised concerns over access restrictions for vulnerable patients to exit Gaza for health care not available within the Gaza Strip and highlighted the need to address the humanitarian health needs in Gaza and to develop the capacities of the local health system, including, for example, by ensuring reliable energy infrastructure for hospitals and clinics.

In addition to addressing Gaza's health challenges, Dr Tedros discussed how to strengthen the Palestinian health system and achieve universal health coverage. He visited the Palestinian National Institute of Public Health, which aims to strengthen the Palestinian health system, with technical support from WHO and funding from the Government of Norway.

WHO, the World Bank and the Palestinian Ministry of Health also agreed recently to establish a partnership to make progress towards universal health coverage

by supporting work on health financing reform, health workforce planning, and to expand the family practice model of primary care. Work has already started to address critical gaps in cancer treatment.

Merck opens regional scientific office in Dubai

Merck, the science and technology company, inaugurated its scientific office in the United Arab Emirates on 9 April this year, in the presence of Dr Amin Hussein Al Amiri, Assistant Undersecretary for Public Health Policy and Licensing Sector in the Ministry of Health and Prevention, and Dr Frank Stangenberg-Haverkamp, chairman of the Executive Board and the Family Board of E. Merck KG. The company's regional hub is located in Central Park Towers, Dubai International Financial Centre (DIFC), and covers the Middle East, Africa and Turkey region.

Coinciding with the company's 350th anniversary in the science and technology field, where it started with a pharmacy in Darmstadt in the year 1668, the inauguration was celebrated in the presence of representatives from the UAE Ministry of Health and Prevention and Merck employees.

Speaking at the inauguration, Dr Al Amiri said: "The United Arab Emirates continues to attract leading global pharmaceutical companies to run their operations for the region as a result of the country's strong business infrastructure. Merck was the first global company to start the manufacturing of innovative drugs in the UAE and we are pleased with Merck's continuous commitment towards investing in the UAE and the wider region to cover countries that go beyond the Middle East region. The UAE places a high priority on the continuous advancement of its standards of care. As we march towards a healthier nation, our community's health and happiness remains at the forefront of all our efforts. It is of utmost importance for us to make sure our people have access to the newest treatments which can greatly improve their quality of life."



Dr Frank Stangenberg-Haverkamp, chairman of the Executive Board and the Family Board of Merck, (second from left) stands with His Excellency Dr Amin Hussein Al Amiri, Assistant Undersecretary for Public Health Policy and Licensing Sector in the UAE Ministry of Health and Prevention (centre) at the inauguration of Merck's scientific office in the United Arab Emirates.

Paolo Carli, the Head of Merck Middle East, Africa & Turkey, said: "We consider the UAE as a prime market for us given its robust infrastructure and healthcare system. Patients are at the heart of our endeavors and we look forward to working closely with the UAE leadership in the ministry of health and prevention to make sure the community has access to the latest treatments."

The Ministry of Health and Prevention also announced the approval of Merck's breakthrough medicine MAVENCLAD, the first oral short-course treatment to help patients suffering from Multiple Sclerosis. MAVENCLAD is used to treat multiple sclerosis (MS) in adults. The new treatment is characterized by 20 days of treatment over two years with sustained efficacy of up to four years. The UAE is the first country in the MENA region and the fifth globally to approve the registration of this new therapy, which is a direct outcome of the successful implementation of the Ministerial Decree (28) of year 2018 concerning the registration of breakthrough medicines and orphan drugs by the Ministry of Health and Prevention that aims to make the latest advances and best quality of healthcare services and medications available within the country.

82,000 deaths from TB in the EMR in 2016

In an effort to raise awareness about tuberculosis (TB), World TB Day is marked each year on 24 March. TB remains one of the top 10 causes of death worldwide claiming as many as 5000 lives each day. The estimated number of TB cases globally in 2016 was 10.4 million with 1.8 million deaths. In the same year in the Eastern Mediterranean Region there were an estimated 766,000 cases and 82,000 deaths.

The theme of this year's Day "Wanted: leaders for a TB-free world" focused on the role of leaders in building commitment to end TB, not only at the political level but at all levels. From community leaders, to people affected with TB, civil society advocates, health workers, doctors or nurses, nongovernmental organizations and other partners, all can be leaders of efforts to end TB in their own area of work.

World TB Day aims to raise the public's awareness about the devastating health, social and economic consequences of TB and to step up efforts to end the global TB epidemic. The heaviest burden is still carried by low-income countries and vulnerable groups such as women, children, older people, migrants, refugees, prisoners, eth-



nic minorities, miners and others working and living in risk-prone settings.

Factors such as malnutrition, poor housing and sanitation, compounded by other risk factors such as tobacco and alcohol use, and diabetes, affect vulnerability to TB and access to care. Furthermore, this access is often hindered by catastrophic costs associated with illness, seeking and staying in care, and lack of social protection, resulting in a vicious cycle of poverty and ill-health. The transmission of multidrug-resistant TB (MDR-TB) adds great urgency to these concerns.

Dr Jaouad Mahjour, acting WHO Regional Director for the Eastern Mediterranean, noted that TB continued to represent a grave threat to public health and much more needed to be done to achieve the End TB Strategy and targets of the Sustainable Development Goals. He highlighted regional progress in the fight against TB saying: "Our Region is one of four WHO regions that met the target to halve the tuberculosis mortality rate by 2015 compared with 1990 estimates".

"The TB situation in the Eastern Mediterranean Region varies, some countries have already made significant progress towards TB control but others are still carrying a heavy burden of the disease. National control programmes, health workers, donors, activists and communities have persistently struggled to provide TB care services amid the instability and uncertainty posed by conflicts and disasters in countries of the Region in recent years," said Dr Mohamed Abdel Aziz, WHO's Regional Advisor for the Stop TB programme. "The progress against all odds in the Region's fight against TB is significant. However, there are also major obstacles still to overcome. Despite the availability of rapid diagnosis and low cost treatment, one third of the estimated TB cases in 2016 in our Region were missed or not reported. This is a major challenge for ending the TB epidemic, as it sustains transmission and constitutes a major risk for individual patients," Dr Aziz added.

World TB Day provides an opportunity to shine a spotlight on the disease and mobilize political and social commitment for accelerating progress to end TB and to control MDR-TB that poses a major threat to health security and the gains made in the fight against TB.

• Meanwhile, the UN announced that

Heads of State will gather in New York on 26 September this year at the United Nations General Assembly for the first-ever high-level meeting on tuberculosis (TB). The meeting will aim to accelerate efforts in ending TB and reach all affected people with prevention and care.

The high-level meeting should result in an ambitious Political Declaration on TB endorsed by Heads of State that will strengthen action and investments for the end TB response, saving millions of lives.

World Malaria Day 2018: Call for more investment as number of cases increase in the region

On World Malaria Day 2018 was marked on 25 April with the World Health Organization (WHO) and its partners calling on all concerned parties to be ready to end malaria – a disease which affects millions of people and claims many lives annually.

"Ready to beat malaria" is the theme of this year's day. The theme underscores the collective energy and commitment of the global malaria community in uniting around the common goal of achieving a malaria-free world.

Malaria is a preventable and curable disease and yet the global burden of this disease is very high. According to the latest "World Malaria Report", released in November 2017, there were 216 million cases of malaria in 2016, up from 211 million cases in 2015. The estimated number of malaria deaths stood at 445,000 in 2016, a similar number to the previous year (446,000).

In areas with high transmission of malaria, children under 5 are particularly susceptible to infection, illness and death; more than two thirds (70%) of all malaria deaths occur in this age group. The number of under-5 malaria deaths has declined from 440,000 in 2010 to 285,000 in 2016. However, malaria remains a major killer of children under 5, taking the life of a child every 2 minutes on average.

In the Eastern Mediterranean Region, the number of malaria cases increased from 3.9 million in 2015 to 4.3 million in 2016 with 8200 deaths.

Ninety-five percent of confirmed ma-







laria cases are reported from four countries in the Region and six countries are at high risk of malaria but are at the stage of burden reduction.

Commenting on the malaria burden in the Region, Jaouad Mahjour, acting WHO Regional Director for the Eastern Mediterranean, said: "Although coverage of main interventions in endemic countries is increasing it falls short of universal health coverage targets. Humanitarian emergencies taking place in some countries are decreasing the capacity of malaria programmes and insufficient resources in high-burden countries are among the main challenges."

Over the past few years, the Region has made some achievements towards eliminating malaria. The Islamic Republic of Iran and Saudi Arabia are at the stage of malaria elimination.

Fourteen countries in the Region are free from indigenous malaria transmission and are at the stage of prevention of establishment of local malaria transmission.

Increasing insecticide resistance in many malaria-endemic countries of the Region is a threat for vector control as the main preventive measure for malaria.

Together with diagnosis and treatment, WHO recommends a package of proven prevention approaches, including insecticide treated nets, spraying indoor walls with insecticides, and preventive medicines for the most vulnerable groups: pregnant women, under 5s and infants.

Without urgent action, the major gains in the fight against malaria are under threat, WHO said and issued a call for greater investment from national resources and donors from the Region as well as expanded coverage of proven tools to prevent, diagnose and treat malaria.

World Malaria Report 2017
www.who.int/malaria/publications/
world-malaria-report-2017

Seven years of health tragedy in Syria must end: WHO

After seven years of conflict in Syria, WHO has renewed its call for the protection of health workers and for immediate access to besieged populations.

"The suffering of the people of Syria must stop. We urge all parties to the conflict to end attacks on health, to provide access to all those in Syria who need health assistance, and, above all, to end this devastating conflict," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General.

Attacks on the health sector have continued at an alarming level in the past year.

The 67 verified attacks on health facilities, workers, and infrastructure recorded during the first two months of 2018 amount to more than 50% of verified attacks in all of 2017.

"This health tragedy must come to an end," said Dr Tedros "Every attack shatters communities and ripples through health systems, damaging infrastructure and reducing access to health for vulnerable people. WHO calls on all parties to the conflict in Syria to immediately halt attacks on health workers, their means of transport and equipment, hospitals and other medical facilities."

Health systems are being attacked in the very places where they are needed most. An estimated 2.9 million Syrians live in UN-declared hard-to-reach and besieged locations. WHO is providing health assistance to many of these areas but lacks consistent access.

In East Ghouta, nearly 400,000 people have lived under siege for half a decade. Basic health supplies have all but run out, and there are now more than 1,000 people in need of immediate medical evacuation.

"It is unacceptable that children, women, and men are dying from injuries and illnesses that are easily treatable and preventable," said Dr Tedros.

Critical medical supplies are also routinely removed from inter-agency convoys to hard-to-reach and besieged locations. Earlier this month, more than 70% of the health supplies intended to reach East Ghouta were removed by authorities and sent back to the WHO warehouse. The items removed are desperately needed to save lives and reduce suffering.

Seven years of conflict have devastated Syria's healthcare system. More than half of the country's public hospitals and healthcare centres are closed or only partially functioning and more than 11.3 million people need health assistance, including 3 million living with injuries and disabilities.

WHO says it is committed to ensuring that people across Syria have access to essential, life-saving healthcare. Last year, WHO delivered over 14 million treatments across the country, including through cross-border and cross-line services.





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- · Participate in Medicall to appoint dealers, distributors in India







9 out of 10 people worldwide breathe polluted air

Air pollution levels remain dangerously high in many parts of the world, according to a recently released report by the World Health Organization (WHO). New data from WHO shows that 9 out of 10 people breathe air containing high levels of pollutants. Updated estimations reveal an alarming death toll of 7 million people every year caused by ambient (outdoor) and household air pollution.

"Air pollution threatens us all, but the poorest and most marginalized people bear the brunt of the burden," said Dr Tedros Adhanom Ghebreyesus, Director-General of WHO. "It is unacceptable that over 3 billion people – most of them women and children – are still breathing deadly smoke every day from using polluting stoves and fuels in their homes. If we don't take urgent action on air pollution, we will never come close to achieving sustainable development."

WHO estimates that around 7 million people die every year from exposure to fine particles in polluted air that penetrate deep into the lungs and cardiovascular system, causing diseases including stroke, heart disease, lung cancer, chronic obstructive pulmonary diseases and respiratory infections, including pneumonia.

Ambient air pollution alone caused some 4.2 million deaths in 2016, while household air pollution from cooking

with polluting fuels and technologies caused an estimated 3.8 million deaths in the same period.

More than 90% of air pollution-related deaths occur in low- and middle-income countries, mainly in Asia and Africa, followed by low- and middle-income countries of the Eastern Mediterranean region, Europe and the Americas.

Around 3 billion people – more than 40% of the world's population – still do not have access to clean cooking fuels and technologies in their homes, the main source of household air pollution. WHO has been monitoring household air pollution for more than a decade and, while the rate of access to clean fuels and technologies is increasing everywhere, improvements are not even keeping pace with population growth in many parts of the world, particularly in sub-Saharan Africa.

WHO recognizes that air pollution is a critical risk factor for noncommunicable diseases (NCDs), causing an estimated one-quarter (24%) of all adult deaths from heart disease, 25% from stroke, 43% from chronic obstructive pulmonary disease and 29% from lung cancer.

More than 4300 cities in 108 countries are now included in WHO's ambient air quality database, making this the world's most comprehensive database on ambient air pollution. Since 2016, more than 1000 additional cities have been added to

WHO's database which shows that more countries are measuring and taking action to reduce air pollution than ever before.

The database collects annual mean concentrations of fine particulate matter (PM10 and PM2.5). PM2.5 includes pollutants, such as sulfate, nitrates and black carbon, which pose the greatest risks to human health. WHO air quality recommendations call for countries to reduce their air pollution to annual mean values of 20 μ g/m3 (for PM₁₀) and 10 μ g/m³ (for PM_{2.5}).

"Many of the world's megacities exceed WHO's guideline levels for air quality by more than 5 times, representing a major risk to people's health," says Dr Maria Neira, Director of the Department of Public Health, Social and Environmental Determinants of Health, at WHO. "We are seeing an acceleration of political interest in this global public health challenge. The increase in cities recording air pollution data reflects a commitment to air quality assessment and monitoring. Most of this increase has occurred in high-income countries, but we hope to see a similar scale-up of monitoring efforts worldwide."

While the latest data show ambient air pollution levels are still dangerously high in most parts of the world, they also show some positive progress. Countries are taking measures to tackle and reduce air pollution from particulate matter. For example, in just two years, India's Prad-

worldwide monitor

Update from around the globe

han Mantri Ujjwala Yojana Scheme has provided some 37 million women living below the poverty line with free LPG connections to support them to switch to clean household energy use. Mexico City has committed to cleaner vehicle standards, including a move to soot-free buses and a ban on private diesel cars by 2025.

Major sources of air pollution from particulate matter include the inefficient use of energy by households, industry, the agriculture and transport sectors, and coalfired power plants. In some regions, sand and desert dust, waste burning and deforestation are additional sources of air pollution. Air quality can also be influenced by natural elements such as geographic, meteorological and seasonal factors.

Air pollution does not recognize borders. Improving air quality demands sustained and coordinated government action at all levels. Countries need to work together on solutions for sustainable transport, more efficient and renewable energy production and use and waste management. WHO works with many sectors including transport and energy, urban planning and rural development to support countries to tackle this problem.

Key findings:

- WHO estimates that around 90% of people worldwide breathe polluted air. Over the past 6 years, ambient air pollution levels have remained high and approximatively stable, with declining concentrations in some part of Europe and in the Americas.
- The highest ambient air pollution levels are in the Eastern Mediterranean Region and in South-East Asia, with annual mean levels often exceeding more than 5 times WHO limits, followed by low and middle-income cities in Africa and the Western Pacific.
- Africa and some of the Western Pacific have a serious lack of air pollution data. For Africa, the database now contains PM measurements for more than twice as many cities as previous versions, however data was identified for only 8 of 47 countries in the region.

- Europe has the highest number of places reporting data.
- In general, ambient air pollution levels are lowest in high-income countries, particularly in Europe, the Americas and the Western Pacific. In cities of high-income countries in Europe, air pollution has been shown to lower average life expectancy by anywhere between 2 and 24 months, depending on pollution levels.

"Political leaders at all levels of government, including city mayors, are now starting to pay attention and take action," adds Dr Tedros. "The good news is that we are seeing more and more governments increasing commitments to monitor and reduce air pollution as well as more global action from the health sector and other sectors like transport, housing and energy."

This year WHO will convene the first Global Conference on Air Pollution and Health (30 October – 1 November 2018) to bring governments and partners together in a global effort to improve air quality and combat climate change.

on the WEB

WHO Global Urban Ambient

Air Pollution Database

https://tinyurl.com/lm7l87c

BreatheLife air pollution campaign

In conjunction with the data launch, global communications campaign BreatheLife has launched a challenge to encourage citizens to take action to reduce air pollution. The first in the series is "Marathon a month" which calls on people to pledge to leave their car behind and use alternative forms of transport for at least the distance of a marathon (42km/26 miles) for one month.

BreatheLife is a partnership of WHO, UN Environment and the Climate and Clean Air Coalition to Reduce Short-lived Climate Pollutants that aims to increase awareness and action on air pollution by governments and individuals. www.breathelife2030.org

WHO, UNICEF issue new guidance to promote breastfeeding in health facilities

WHO and UNICEF on 11 April issued new ten-step guidance to increase support for breastfeeding in health facilities that provide maternity and newborn services. Breastfeeding all babies for the first two years would save the lives of more than 820,000 children under age 5 annually.

The Ten Steps to Successful Breastfeeding underpin the Baby-friendly Hospital Initiative, which both organizations launched in 1991. The practical guidance encourages new mothers to breastfeed and informs health workers how best to support breastfeeding.

Breastfeeding is vital to a child's lifelong health, and reduces costs for health facilities, families, and governments. Breastfeeding within the first hour of birth protects newborn babies from infections and saves lives. Infants are at greater risk of death due to diarrhoea and other infections when they are only partially breastfed or not breastfed at all. Breastfeeding also improves IQ, school readiness and attendance, and is associated with higher income in adult life. It also reduces the risk of breast cancer in the mother.

"Breastfeeding saves lives. Its benefits help keep babies healthy in their first days and last will into adulthood," says UNICEF Executive Director Henrietta H. Fore. "But breastfeeding requires support, encouragement and guidance. With these basic steps, implemented properly, we can significantly improve breastfeeding rates around the world and give children the best possible start in life."

WHO Director-General Dr Tedros Adhanom Ghebreyesus says that in many hospitals and communities around the world, whether a child can be breastfed or not can make the difference between life and death, and whether a child will develop to reach his or her full potential.

"Hospitals are not there just to cure the ill. They are there to promote life and ensure people can thrive and live their lives to their full potential," says



Dr Tedros. "As part of every country's drive to achieve universal health coverage, there is no better or more crucial place to start than by ensuring the *Ten Steps to Successful Breastfeeding* are the standard for care of mothers and their babies."

The new guidance describes practical steps countries should take to protect, promote and support breastfeeding in facilities providing maternity and newborn services. They provide the immediate health system platform to help mothers initiate breastfeeding within the first hour and breastfeed exclusively for six months.

It describes how hospitals should have a written breastfeeding policy in place, staff competencies, and antenatal and post-birth care, including breastfeeding support for mothers. It also recommends limited use of breastmilk substitutes, rooming-in, responsive feeding, educating parents on the use of bottles and pacifiers, and support when mothers and babies are discharged from hospital.

Ten Steps to Successful
Breastfeeding
www.who.int/nutrition/bfhi/ten-steps

One billion people to be vaccinated against yellow fever in Africa

Nearly one billion people will be vaccinated against yellow fever in 27 highrisk African countries by 2026 with support from the World Health Organization (WHO), Gavi – the Vaccine Alliance, UNICEF and more than 50 health partners.

The commitment is part of the Eliminate Yellow fever Epidemics (EYE) in Africa strategy, which was launched by Dr Tedros Adhanom Ghebreyesus, WHO Director-General, Professor Isaac Folorunso Adewole, Nigeria's Minister of Health and partners at a regional meeting in Abuja, Nigeria on 10 April.

"The world is facing an increased risk of Yellow fever outbreaks and Africa is particularly vulnerable," said Dr Tedros. "With one injection we can protect a person for life against this dangerous pathogen. This unprecedented commitment by countries will ensure that by 2026 Africa is free of Yellow fever epidemics."

During the three-day EYE strategy regional launch meeting representatives from key African countries, WHO, UNICEF, Gavi, and other partners are developing a roadmap on how to rollout the EYE strategy at national level. This implementation effort follows the endorsement of the strategy by African Ministers of Health at the 67th WHO regional committee in September 2017.

"This comprehensive, global strategy offers an unprecedented opportunity to end the devastating Yellow fever epidemics that periodically impact Africa," said Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance. "Ensuring that the most vulnerable communities have access to the vaccine through routine systems plays a central role in making this happen. Vaccine manufacturers and Gavi partners have worked hard to improve the global vaccine supply situation in recent years to make sure there is enough vaccine to respond to outbreaks, allow preventive campaigns and that routine immunization functions at full capacity."

The three objectives of the strategy include protecting at-risk populations through preventive mass vaccination campaigns and routine immunization programmes, preventing international spread, and containing outbreaks rapidly. Developing strong surveillance with robust laboratory networks is key to these efforts.

UNICEF will make vaccines available, advocate for greater political commitment and provide support in vaccinating children through routine immunization as well as during outbreaks of the disease.

"Today, the threat of yellow fever looms larger than ever before, especially for thousands of children across Africa," said Stefan Peterson, UNICEF's Chief of Health. "Given that almost half of the people to be vaccinated are children under 15 years of age, this campaign is critical to saving children's lives, and would go a long way toward stamping out this disease."

McAfee report warns of cybersecurity threat to health care

McAfee, the device-to-cloud cybersecurity company, released its McAfee Labs Threats Report: March 2018, examining the growth and trends of new malware, ransomware, and other threats in Q4 2017. Part of this detailed report refers to the cybersecurity threat to health care.

McAfee says that although publicly disclosed security incidents targeting health care decreased by 78% in the fourth quarter of 2017, the sector experienced a dramatic 210% overall increase in incidents in 2017.

Through their investigations, McAfee Advanced Threat Research analysts conclude many incidents were caused by organizational failure to comply with security best practices or address known vulnerabilities in medical software.

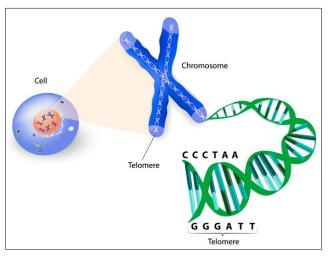
The analysts looked into possible attack vectors related to health care data, finding exposed sensitive images and vulnerable software. Combining these attack vectors, analysts were able to reconstruct patient body parts, and print three-dimensional models.

"Health care is a valuable target for cybercriminals who have set aside ethics in favour of profits," said Christiaan Beek, McAfee Lead Scientist and Senior Principal Engineer. "Our research uncovered classic software failures and security issues such as hardcoded embedded passwords, remote code execution, unsigned firmware, and more. Both healthcare organizations and developers creating software for their use must be more vigilant in ensuring they are up to date on security best practices.

McAfee Labs Threat Report
www.mcafee.com/us/mcafee-labs/
reports.aspx

the laboratory

Medical research news from around the world



Accurate telomere length test influences treatment decisions for certain diseases

In a report published in the 20 February issue of *Proceedings of the National Academy of Sciences*, the researchers found that telomere length testing results also could help identify people who are at increased risk for developing diseases associated with short telomeres.

A group of heritable diseases, which commonly manifest as lung scarring called pulmonary fibrosis or bone marrow failure, are marked by very short telomeres, according to Mary Armanios, M.D., professor of oncology at the Johns Hopkins Kimmel Cancer Center and clinical director of the Telomere Center at Johns Hopkins.

"These diseases affect as many people as certain types of leukaemia, and we think the prevalence may be higher than current estimates," Dr Armanios said.

"Our goal was to establish a clinically reliable tool for telomere length measurement in a hospital setting and make it available to physicians and their patients for precise diagnosis and treatment recommendations," said Armanios.

Telomeres protect the ends of DNA like the plastic tubes on the ends of shoelaces, and they normally shorten with aging. Made up of repetitive sequences of DNA, normal telomeres have enough length to withstand the erosion that occurs over the normal lifespan of a cell. Cells with very short telomeres may blow through these endcaps more quickly and this can lead to

specific diseases. In addition to pulmonary fibrosis and bone marrow failure, people with short telomeres are prone to developing emphysema, liver disease, myelodysplastic syndrome and other cancers.

"Typical clinical findings and current tests are not likely to identify most patients with very short telomeres," said Armanios, "so, there is a need for molecular tests

to diagnose this condition, especially since these patients in hospital or clinical settings are more susceptible to side effects of routine medications and procedures."

The "flow-FISH" test, which stands for flow cytometry and fluorescence in situ hybridization, specifically measures the telomere length in each cell within a patient's blood sample. The test was developed in 2006 by Canadian researcher Peter Lansdorp, M.D., Ph.D. In flowFISH, scientists poke very tiny holes in the nucleus of each cell and slip in fluorescently labelled DNA that attach to telomeres. Then, scientists use a method called flow cytometry to identify the types of cells in each blood sample and quantify the fluorescent signal in cells one at a time.

For the current study, Armanios worked with Jonathan Alder, Ph.D., formerly of Johns Hopkins and now at the University of Pittsburgh, and other colleagues at Johns Hopkins to use the flowFISH test to determine a range for normal telomere length among 192 healthy people. All subjects were recruited from The Johns Hopkins Hospital. This control group included blood samples taken from newborns up to people aged 82.

The Johns Hopkins team compared the Baltimore-based data with values published by researchers in Vancouver, Canada, who also used the flowFISH test to measure telomere lengths in 444 healthy people.

Both the Baltimore and Vancouver groups had similar values, within 5% of each other. Moreover, the ranges of normal telomere length, which is between 8

and 13 kilobases of DNA at birth, were also similar.

"We think this rate of reproducibility and accuracy for a telomere length measurement tool is ideal for a clinical setting," Armanios noted.

Then the researchers measured telomere length in 100 people from 60 families who are known to carry mutations in genes linked to telomeres and their associated enzyme, telomerase. Among them, 73 had symptoms of diseases associated with short telomeres, and 27 had no symptoms. Of the 73, the 21 with bone marrow failure were, on average, three decades younger than the 41 who had pulmonary fibrosis or emphysema. Among this group of patients, those with the shortest telomeres tended to develop disease symptoms at a younger age – in their childhood and teens – than those with milder telomere defects.

In addition, among 38 children and adult patients with bone marrow failure due to an unknown cause who were seen at The Johns Hopkins Hospital between 2012 and 2014, Armanios' team used flow-FISH to find that 10 of them had very short telomeres. In nine of those patients, physicians decided to change their treatment to less harsh therapies, including bone marrow transplants with reduced doses of chemotherapy, less use of immunosuppressant drugs or transplant donor screening for defects in telomere-related genes.

"Telomere measurement needs to be precise and reproducible, but even more important is how this information can be used to guide treatment decisions," says Carol Greider, Ph.D., the Daniel Nathans Professor and director of the Department of Molecular Biology and Genetics at Johns Hopkins. Dr Greider discovered telomerase, the enzyme that controls telomere lengthening, in 1984 and shared the 2009 Nobel Prize for Physiology or Medicine with Elizabeth Blackburn and Jack W. Szostak for the finding.

Armanios believes that patients with certain forms of unexplained low blood counts should have a flowFISH test to help their physicians decide the best course of treatment.

• doi: 10.1073/pnas.1720427115



International team confirms genetic mutation link to ALS

Kinesin family member 5A (KIF5A), a gene previously linked to two rare neurodegenerative disorders, has been definitively connected to amyotrophic lateral sclerosis (ALS) by an international team from several of the world's top ALS research labs. The findings identify how mutations in KIF5A disrupt transport of key proteins up and down long, thread-like axons that connect nerve cells between the brain and the spine, eventually leading to the neuromuscular symptoms of ALS.

The discovery, published in the 21 March 2018, issue of *Neuron*, was led by Bryan Traynor, M.D., Ph.D. of the Intramural Research Program of the National Institute on Aging (NIA) at the National Institutes of Health and John Landers, Ph.D. of the University of Massachusetts Medical School, Worcester, with key funding support from the NIA, the National Institute of Neurological Disorders and Stroke (NINDS) at NIH, and several public and private sector organizations. Genetic data collected by teams of scientists worldwide contributed to the project.

It took a comprehensive, collaborative effort to analyse a massive amount of genetic data to pin down KIF5A as a suspect for ALS, also known as Lou Gehrig's disease. To zero in on KIF5A, the NIH team performed a large-scale genome-wide association study, while the University of Massachusetts team concentrated on analysing rare variants in next generation sequence data. Over 125,000 samples were used in this study, making it by far the largest such study of ALS performed to date.

"The extraordinary teamwork that went into this study underlines the value of global, collaborative science as we seek to better understand devastating diseases like ALS," said Richard J. Hodes, M.D., director of NIA. "These types of collaborative data collection and analysis are important in identifying the pathways underlying disease and in developing approaches to treatment and prevention."

KIF5A regulates part of the kinesin

family of proteins that serve as tiny intracellular motors. Problems with these proteins are connected to ALS, Parkinson's disease and Alzheimer's disease. KIF5A mutations were previously known to be connected to two other rare neurodegenerative diseases with muscle weakening, stiffening and spasticity symptoms similar to ALS: hereditary spastic paraplegia type 10 (SPG10) and Charcot-Marie-Tooth Type 2 (CMT2.) Scientists suspected KIF5A might be associated with ALS but lacked definite proof until now.

"Axons extend from the brain to the bottom of the spine, forming some of the longest single cellular pathways in the body," said Traynor. "KIF5A helps to move key proteins and organelles up and down that axonal transport system, controlling the engines for the nervous system's long-range cargo trucks. This mutation disrupts that system, causing the symptoms we see with ALS."

Traynor cautioned that the discovery, while exciting, still leaves much more work to be done "While this is unlikely to be a very common genetic cause for ALS, it identifies important new directions to explore possible future gene therapies," he said.

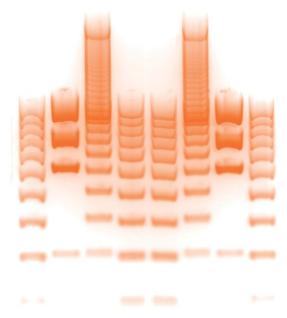
According to Traynor, next steps for the project include further study of the frequency and location of mutations within KIF5A and determining what cargos are being disrupted. He and his team hope this will help reveal what aspect of axonal transport is essential to maintain the cell.

• doi: 10.1016/j.neuron.2018.02.027

US researchers complete in-depth genomic analysis of 33 cancer types

Researchers funded by the US National Institutes of Health have completed a detailed genomic analysis, known as the PanCancer Atlas, on a data set of molecular and clinical information from over 10,000 tumours representing 33 types of cancer.

"This project is the culmination of more than a decade of ground-breaking work," said NIH Director Francis S. Collins, M.D., Ph.D. "This analysis provides



cancer researchers with unprecedented understanding of how, where and why tumours arise in humans, enabling better informed clinical trials and future treatments."

The PanCancer Atlas, published as a collection of 27 papers across a suite of Cell journals, sums up the work accomplished by The Cancer Genome Atlas (TCGA) – a multi-institution collaboration initiated and supported by the National Human Genome Research Institute (NHGRI) and the National Cancer Institute (NCI), both part of NIH. The program, with over \$300 million in total funding, involved upwards of 150 researchers at more than two dozen institutions across North America.

"TCGA was the first project of its scale to characterize – at the molecular level – cancer across a breadth of cancer types," said Carolyn Hutter, Ph.D., director of NHGRI's Division of Genome Sciences and the NHGRI team lead for TCGA. "At the project's infancy 10 years ago, it wasn't even possible, much less on such a scale, to do the types of characterization and analysis that were being proposed. It was a hugely ambitious project."

"The PanCancer Atlas effort complements the over 30 tumor-specific papers <that have been published by TCGA in the last decade and expands upon earlier pan-cancer work that was published in 2013 https://www.nature.com/tcga/,"



said Jean Claude Zenklusen, Ph.D., director of the TCGA Program Office at NCI.

The project focused not only on cancer genome sequencing, but also on different types of data analyses, such as investigating gene and protein expression profiles, and associating them with clinical and imaging data.

The PanCancer Atlas is divided into three main categories, each anchored by a summary paper that recaps the core findings for the topic. The main topics include cell of origin, oncogenic processes and oncogenic pathways. Multiple companion papers report in-depth explorations of individual topics within these categories.

In the first summary paper, the authors summarize the findings from a set of analyses that used a technique called molecular clustering, which groups tumours by parameters such as genes being expressed, abnormality of chromosome numbers in tumour cells and DNA modifications. The paper's findings suggest that tumour types cluster by their possible cells of origin, a result that adds to our understanding of how tumour tissue of origin influences a cancer's features and could lead to more specific treatments for various cancer types.

The second summary paper, presents a broad view of the TCGA findings on the processes that lead to cancer development and progression. Specifically, the authors noted that the findings identified three critical oncogenic processes: mutations, both germline (inherited) and somatic (acquired); the influence of the tumour's underlying genome and epigenome on gene and protein expression; and the interplay of tumour and immune cells. These findings will help prioritize the development of new treatments and immunotherapies for a wide range of cancers.

The final summary paper, details TCGA investigations on the genomic alterations in the signalling pathways that control cell cycle progression, cell death and cell growth, revealing the similarities and differences in these processes across a range of cancers. Their findings reveal new patterns of cancer's potential vulnerabilities that will aid in the development

of combination therapies and personalized medicine.



PanCancer Atlas

www.cell.com/consortium/pancanceratlas

Symposium

Additionally, as the decade-long TCGA effort wraps up, there will be a three-day symposium, TCGA Legacy: Multi-Omic Studies in Cancer http://www.cell-symposia.com/tcga-2018/, in Washington, D.C., September 27-29, 2018, that will discuss the future of large-scale cancer studies, with a session focusing on the PanCancer Atlas. The meeting will feature the latest advances on the genomic architecture of cancer and showcase recent progress toward therapeutic targeting.

Microglia in retina can spontaneously regenerate

Immune cells called microglia can completely repopulate themselves in the retina after being nearly eliminated, according to a new study in mice from scientists at the US National Eye Institute (NEI). The cells also re-establish their normal organization and function. The findings point to potential therapies for controlling inflammation and slowing progression of rare retinal diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). A report on the study was published online in *Science Advances*. The NEI is part of the US National Institutes of Health.

"Neuroinflammation is an important driver of the death of neurons in retinal diseases," said Wai T. Wong M.D., Ph.D., chief of the NEI Section on Neuron-Glia Interactions in Retinal Disease, and the study's lead investigator. "Our study is foundational for understanding ways to control the immune system in the retina." Control of the immune system is important for developing new treatments for a variety of eye conditions, including AMD, RP, or for certain types of retinal injury.

The retina is a thin layer of cells in the back of the eye that includes light-sensing photoreceptor cells and other neurons involved in transmitting visual information to the brain. Mixed in with these cells are microglia, specialized immune cells that help maintain the health of the retina and the function of retinal neurons. Microglia are also present in other parts of the central nervous system, including the brain. In a healthy retina, communication between neurons and microglia is important for maintaining the neuron's ability to send signals to the brain. When the retina is injured, however, microglia have an additional role: They migrate quickly to the injury site to remove unhealthy or dying cells. However, they can also remove healthy cells, contributing to vision loss. Studies show that in degenerative retinal disorders like AMD and RP, inhibiting or removing microglia can help retain photoreceptors, and thus slow vision loss. But return of microglia is still important to support the retina's neurons.

Dr Wong and colleagues were interested in understanding what happens in the retina after microglia have been eliminated, particularly whether the cells could return to their normal arrangement and fulfil their normal functions. To test this, they depleted the microglia in the retinas of mice using the drug PLX5622 (Plexxikon), which blocks the microglial CSF-1 receptor. Microglia depend on continuous signals through this receptor for survival. Interruption of this signalling for several days caused the microglia to nearly disappear, leaving just a few cells clustered around the optic nerve - the cable-like bundle of nerve fibres that carries signals from the retina to the brain - in the mouse retinas. Since loss of microglia for a short time doesn't affect the function of neurons, removing microglia temporarily – in order to reduce inflammation for example - could potentially be useful as a therapeutic intervention for degenerative or inflammatory disorders of the retina.

"If we were to get rid of the microglia while a large, inappropriate immune response was happening," said Dr Wong, "we might be able to miss the worst of the inflammation, but still come back into balance at a later point in time. We could hit pause on the immune system in the retina in a directed way."



Within 30 days after stopping the drug, Dr Wong and colleagues found that the microglia had repopulated the retina, returning to normal density after 150 days. Using a novel method for visually tracking microglial movements in the retina, they determined that the returning microglia initially grew in clusters near where the optic nerve leaves the eye. Gradually, new microglia expanded outwards towards the edges of the retina. Over time, the cells reestablished an even distribution across and through the various layers of the retina.

"The organization of these immune cells is quite elaborate, and all the organization comes right back," Dr Wong said. "We can actually image the eye and watch these cells divide and split and migrate as part of the repopulation response."

To test whether the new microglia were fully functional, the researchers used an injury model where photoreceptor cells are damaged by bright light. The new microglia were able to activate and migrate to the injury site normally. In addition, using electroretinography (ERG), a technique that measures the electrical signals generated by retinal neurons after being stimulated with light, the researchers tested the health of different groups of neurons. They found that the microglia were able to communicate with and fully maintain the function of neurons in the retina, especially when the depletion was short-lived.

Drugs that remove microglia are now administered systemically, affecting the brain and other parts of the central nervous system. More research is needed to find ways to administer these drugs directly to the retina, sparing off-target tissues.

• doi: 10.1126/sciadv.aap8492

Lack of sleep leads to obesity in children and adolescents

Children who get less than the recommended amount of sleep for their age are at a higher risk of developing obesity.

Research at the University of Warwick has found that children and adolescents who regularly sleep less than others of the same age gain more weight when they grow older and are more likely to become overweight or obese.



One of the co-authors, Dr Michelle Miller, Reader of Biochemical Medicine, Health Sciences, Warwick Medical School said: "Being overweight can lead to cardio-vascular disease and type-2-diabetes which is also on the increase in children. The findings of the study indicate that sleep may be an important potentially modifiable risk factor (or marker) of future obesity."

The paper is published in the April 2018 issue of the journal Sleep. The paper's authors reviewed the results of 42 population studies of infants, children and adolescents aged 0 to 18 years which included a total of 75,499 participants. Their average sleep duration was assessed through a variety of methods, from questionnaires to wearable technology.

The participants were grouped into two classifications: short sleeper and regular sleepers. Short sleepers were defined as having less sleep than the reference category for their age. This was based on the most recent National Sleep Foundation guidelines in the U.S. which recommends that infants (4 to 11 months) get between 12-15 hours of nightly sleep, that toddlers (1-2 years) get 11-14 hours of sleep, children in pre-school (3-5 years) get 10-13 hours and school aged children (6-13 years) between 9 and 11 hours. Teenagers (14-17 years) are advised to get 8-10 hours.

Participants were followed up for a median period of three years and changes in BMI and incidences of overweight and/or obesity were recorded over time. At all ages short sleepers gained more weight and overall were 58% more likely to become overweight or obese.

Dr Miller said: "The results showed a consistent relationship across all ages indicating that the increased risk is present in both younger and older children. The study also reinforces the concept that sleep deprivation is an important risk factor for obesity, detectable very early on in life."

Co-author Professor Francesco Cappuccio added: "By appraising world literature we were able to demonstrate that, despite some variation between studies, there is a strikingly consistent overall prospective association between short sleep and obesity."

• doi: 10.1093/sleep/zsy018

Higher waist to hip measurement associated with greater risk of heart attack in women

Higher waist and hip size are more strongly associated with heart attack risk than overall obesity, especially among women, according to research in Journal of the American Heart Association, the Open Access Journal of the American Heart Association/American Stroke Association.

In a study of nearly 500,000 adults (aged 40-69) from the United Kingdom, researchers found that while general obesity and obesity specifically around the abdomen each have profound harmful effects on heart attack risk in both sexes, women were more negatively impacted by higher waist circumference and waist-to-hip ratio than men.

This study suggests that the differences in the quantity and distribution of fat tissue not only results in differences in body shape between women and men, but may also have differential implications for the risk of heart attack in later life, researchers noted.

"Our findings support the notion that having proportionally more fat around the abdomen (a characteristic of the apple shape) appears to be more hazardous than more visceral fat which is generally stored around the hips (i.e., the pear shape)," said lead author Sanne Peters, Ph.D., Research Fellow in Epidemiology at the George Institute for Global Health at the University of Oxford in the United Kingdom.

Additional research on sex differences in obesity may yield insights into the biological mechanisms and could inform sex-specific interventions to treat and halt the obesity epidemic.

• doi: 10.1161/JAHA.117.008507 MEH

Weight management programme can put type 2 diabetes into remission

Type 2 diabetes can be reversed following an intensive weight management programme, according a randomised trial in adults who have had the condition for up to 6 years, published in *The Lancet*.

The study showed that after 1 year, participants had lost an average of 10kg, and nearly half had reverted to a non-diabetic state without using any diabetes treatment. The findings lend support to the widespread use of this type of intervention in the routine care of type 2 diabetes across health services.

"Our findings suggest that even if you have had type 2 diabetes for 6 years, putting the disease into remission is feasible," says Professor Michael Lean from the University of Glasgow who co-led the study. "In contrast to other approaches, we focus on the need for long-term maintenance of weight loss through diet and exercise and encourage flexibility to optimise individual results."

Worldwide, the number of people with type 2 diabetes has quadrupled over 35 years, rising from 108 million in 1980 to 422 million in 2014. This is expected to climb to 642 million by 2040. This increase has been linked to rising levels of obesity and the accumulation of intra-abdominal fat.

"Rather than addressing the root cause, management guidelines for type 2 diabetes focus on reducing blood sugar levels through drug treatments. Diet and lifestyle are touched upon but diabetes remission by cutting calories is rarely discussed", explains Professor Roy Taylor from Newcastle University, UK, who co-led the study.

"A major difference from other studies is that we advised a period of dietary weight loss with no increase in physical activity, but during the long-term follow up increased daily activity is important. Bariatric surgery can achieve remission of diabetes in about three-quarters of people, but it is more expensive and risky, and is only available to a small number of patients."

Previous research by the same team confirmed the Twin Cycle Hypothesis-

that type 2 diabetes is caused by excess fat within the liver and pancreas-and established that people with the disease can be returned to normal glucose control by consuming a very low calorie diet. But whether this type of intensive weight management is practicable and can achieve remission of type 2 diabetes in routine primary care was not known until now.

Diabetes Remission Clinical Trial

The Diabetes Remission Clinical Trial (Di-RECT), included 298 adults aged 20-65 years who had been diagnosed with type 2 diabetes in the past 6 years from 49 primary care practices across Scotland and the Tyneside region of England between July 2014 and August 2016. Practices were randomly assigned to provide either the Counterweight-plus weight management programme delivered by practice dieticians or nurses (149 individuals) or best practice care under current guidelines (control; 149 individuals).

The weight management programme began with a diet replacement phase, consisting of a low calorie formula diet (825-853 calories/day for 3 to 5 months), followed by stepped food reintroduction (2-8 weeks), and ongoing support for weight loss maintenance including cognitive behavioural therapy combined with strategies to increase physical activity. Antidiabetic and blood pressure-lowering drugs were all stopped at the start of the programme.

The primary outcomes were weight loss of 15 kg or more (sufficient to achieve remission of diabetes in most cases), and remission of diabetes. Remission was defined as achievement of a glycated haemoglobin A1c (HbA1c) level of less than 6.5% at 12 months, off all medications.

The weight loss programme was acceptable to most participants, with a dropout rate of 21%, mainly for social reasons (e.g., bereavement, change or loss of job, moving house). 128 (86%) participants in the weight management group and 147 (99%) participants in the control group attended the 12 month assessment. For those whose measurements of weight and HbA1c level were not available it was assumed that no remission had occurred.

Our findings suggest that even if you have had type 2 diabetes for 6 years, putting the disease into remission is feasible.

Almost a quarter (36/149) of the weight management group achieved weight loss of 15 kg or more at 12 months, compared with none in the control group. Additionally, nearly half of the weight management group (68/149) achieved diabetes remission at 1 year, compared with six (4%) in the control group.

On average, participants in the weight management group shed 10kg of bodyweight compared to 1kg in the control group. Importantly, the results showed that remission was closely linked with the degree of weight loss and occurred in around 9 out of 10 people who lost 15 kg or more, and nearly three quarters (47/64) of those who lost 10kg or more.

The researchers also noted an improvement in average triglyceride (blood lipid) concentrations in the weight management group, and almost half remained off all antihypertensive drugs with no rise in blood pressure. Furthermore, the weight management group reported substantially improved quality of life at 12 months, with a slight decrease reported in the control group.

According to Professor Taylor: "Our findings suggest that the very large weight losses targeted by bariatric surgery are not essential to reverse the underlying processes which cause type 2 diabetes. The weight loss goals provided by this programme are achievable for many people. The big challenge is long-term avoidance of weight re-gain. Follow-up of DiRECT will continue for 4 years and reveal whether weight loss and remission is achievable in the long-term."

• doi: 10.1016/S0140-6736(17)33102-1

Universal Health Coverage: everyone, everywhere

World Health Day was celebrated on 7 April this year with the focus is on Universal Health Coverage – one of the founding principles of the World Health Organization, that everyone, everywhere, should be able to enjoy the highest attainable standard of health.

The organisation emphasises that that principle is as valid today as it was in 1948 when the WHO was founded. In addition, it lies at the heart of the Sustainable Development Agenda.

"We know that Universal Health Coverage is feasible. Evidence and experience show that all countries, at all income levels, can make progress with the resources they have," WHO states.

In this 70th anniversary year, the World Health Organization is calling on world leaders to live up to the pledges they made when they agreed the Sustainable Development Goals (SDGs) in 2015, and commit to concrete steps to advance universal health coverage (UHC). This means ensuring that everyone, everywhere can access essential quality health services without facing financial hardship by 2030.

"The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition," says Dr Tedros Adhanom Ghebreyesus, WHO Director-General.

"Good health is the most precious thing anyone can have," he added. "When people are healthy, they can learn, work, and support themselves and their families. When they are sick, nothing else matters. Families and communities fall behind.



By 2023, the midpoint towards 2030, the world needs to extend essential health coverage to 1 billion more people. For this to happen, political leadership is critical. Robust financing structures are key.

That's why WHO is so committed to ensuring good health for all."

WHO universal health coverage data portal (by country): http://apps.who.int/gho/cabinet/uhc.jsp

Current status of Universal Health Coverage

- At least half the world's people don't receive the essential health services they need.
- About 100 million people are being pushed into extreme poverty (<\$1.90 a day) because of payments for health services.
- Over 800 million people (almost 12% of the world's population) spend at least 10% of their household budgets on health expenses for themselves, a sick child or other family member.
- Without UHC, billions of people are at risk of losing the opportunity to live full and productive lives.
- Without UHC, there is a greater risk that outbreaks develop into epidemics, undermining global health security.
- Nobody should get sick or die just because they are poor, or because the services they need are too far away.

- Looking forward
- By 2023, the midpoint towards 2030, the world needs to extend essential health coverage to 1 billion more people. For this to happen, political leadership is critical. Robust financing structures are key.
- UHC encompasses all components of the health system. It requires strong health service delivery systems; a robust and motivated health workforce; good health facilities and communications networks; access to effective medicines and technologies; reliable information systems; quality assurance mechanisms, and good governance and legislation.
- But UHC is not a luxury that only rich countries can afford.
- Valuable lessons can be learnt from countries ranging from Botswana to Brazil; India to Iran; Kenya to

Kyrgyzstan; and Sri Lanka to the Solomon Islands. Evidence and experience show that all countries, at all income levels, can make progress with the resources they have.

- Countries are approaching UHC in different ways. There's no single path to UHC. All countries must find their own way, in the context of their own social, political and economic circumstances. But every country can do something to advance UHC.
- Making health services truly universal requires a shift from designing health systems around diseases and institutions towards health services designed around and for people.
- On World Health Day, WHO is encouraging everyone to play a part in the path to UHC, by taking part in a UHC conversations and policy dialogue.

Cancer immunotherapy: From a dream to reality



By Professor Salem Chouaib Director of Thumbay Research Institute of Precision Medicine, Gulf Medical University, Ajman

Clinical and experimental evidence has been provided to indicate that our very own immune system may help to fight cancer. Scientists first conceived the idea of manipulating the body's immune system to attack cancer more than a century ago. However, it has become clear that cancer can weaken, paralyze and neutralize the immune system of the host.

The immunotherapy concept is simple: unleash the body's immune system to detect and destroy cancer cells. More experiments, out of the box and bold ideas, investments, enthusiasm and persistence is required to prove immunotherapy's worth as a cancer treatment modality. Thanks to the fundamental achievements during the past three decades, non-specific passive immunotherapy of cancer based on the use of cytokines, has shifted to active specific immunotherapy and the development of cancer vaccines. In the last five years, the development of immunotherapies continued to progress rapidly. The Food and Drug Administration approved the first immune checkpoint blocker to treat advanced melanoma in 2011. In 2018, seventeen different type of cancers have FDA approved immunotherapies as a treatment option. At present, we are living a new time and age with tremendous advancements being made to the tumor

immune-biology aiming at making the word "cure" a reality for cancer patients.

Checkpoint inhibitors: The leading and impressive immunotherapy drugs

Cancer immunotherapy (the therapy based on mobilizing the immune system to kill cancer cells) has been revolutionized by the concept of breaking tolerance and represents a major paradigm shift that marks the beginning of a new era. The checkpoint pathways play a key role in the interaction between tumor cells and cells responsible for immune response. Inhibitors to these checkpoints are antibodies that bind to, and inhibit the function of proteins expressed by cancer cells. In fact, immunotherapy drugs, such as antibodies, make cancer cells more vulnerable to destruction by the immune system. Typical immunotherapy drugs are the checkpoint inhibitors targeting the programmed death-1 (PD-1) and programmed deathligand 1 (PD-L1) proteins that provided the foundation of immune checkpoint therapy. When PD1 on the surface of immune T cells binds to its receptor protein PDL1, which is found on the surface of some cancer cells, the T cell becomes inactivated and the cancer cells avoids assault. Thanks to immunotherapy drugs that block PD-1 or PD-L1 proteins, Immune checkpoint therapy has joined the ranks of surgery, radiation and chemotherapy as a pillar of cancer treatment. At present, the impact of anti-PD1 is surpassing all expectations because of its transversal impact across tumor types and immune checkpoint modulation is emerging as a highly effective therapeutic strategy in an increasing number of cancer entities. It is also offering potential new options in particular for patients with advanced disease, especially those who had exhausted all standard therapy options.

The high expectations for these immunotherapies are tempered by the current reality that only a subset of treated patients (20-40%) show sustained responses, while the majority either do not respond or develop resistance. It remains unclear why only a subset of individuals respond to treatment and how to better achieve sustained remissions, driving the need

for a better understanding of the intrinsic and adaptive tumor resistance. Unraveling the cellular and molecular basis of treatment resistance should facilitate rational design of new mechanism-based studies including those of combination therapies. It has become clear that the future of immunotherapy lies in an integrative approach to simultaneously boosting the immune system and target the tumor microenvironment or combine immunotherapy with conventional treatments.

The recent advent of next generation sequencing technologies has enabled rapid and comprehensive discovery of cancer specific mutations in individual cancer patients and provides the opportunity to develop novel potentially achievable personalized immunotherapy based on individual genetic, molecular and immune profiling.

CAR T cells: The next promising cancer treatment

Besides the checkpoint inhibitors, Chimeric antigen receptor (CAR) T cells (synthetic molecules allowing T cells to specifically recognize and kill cancer cells) have proven that engineered immune cells can serve as a powerful new class of cancer therapeutics. The most successful CARs used to date are those targeting the Blymphocyte antigen, also known as CD19 molecule on acute lymphoblastic leukemia, which offer the prospect of complete remission in patients with chemo-refratory or relapsed B-cell malignancies. Much optimism is linked to the further development of CAR T-cells that could be used to design the next generation of smart T cell precision therapeutics as well as their efficient implementation in a broader range of tumors in the near future.

Despite the significant progress in the field of cancer immunotherapy, we are currently facing a wide range of challenges including the severity of immune-related adverse events and their management. Clearly, there is still a need for more effective treatments to maximize cancer patient survival rates.



Risk of maternal death doubles in pregnant women with anaemia

In the largest study of its kind, researchers show that, when all known contributing factors are controlled for, the odds of maternal death are doubled in mothers with severe anaemia. They call on clinicians, policy makers and healthcare professionals to now focus their attention on preventing anaemia.

Pregnant women with anaemia are twice as likely to die during or shortly after pregnancy compared to those without the condition, according to a major international study led by Queen Mary University of London of over 300,000 women across 29 countries, including Jordan, Lebanon, Palestine and Qatar.

The research, published 20 March 2018 in the journal *The Lancet Global Health* and funded by Barts Charity and the Human Reproduction Programme, suggests that prevention and treatment of maternal anaemia must remain a global public health and research priority.

Anaemia, which is characterised by a lack of healthy red blood cells, affects 32 million pregnant women worldwide, and up to half of all pregnant women in low and middle-income countries (LMICs). Women

in LMICs are at increased risk of anaemia due to higher rates of dietary iron deficiency, inherited blood disorders, nutrient deficiencies and infections such as malaria, HIV and hookworm.

Lead author Dr Jahnavi Daru from Queen Mary University of London said: "Anaemia in pregnancy is one of the most common medical problems pregnant women encounter both in low and high income countries. We've now shown that if a woman develops severe anaemia at any point in her pregnancy or in the seven days after delivery, she is at a higher risk of dying, making urgent treatment even more important.

"Anaemia is a readily treatable condition but the existing approaches so far have not been able to tackle the problem. Clinicians, policy makers and healthcare professionals should now focus their attention on preventing anaemia, using a multifaceted approach, not just hoping that iron tablets will solve the problem."

The study, which is the largest of its kind, looked at World Health Organization data on 312,281 pregnancies in 29 countries* across Latin America, Africa, Western Pacific, Eastern Mediterranean and South East Asia. Of these, 4,189 women had severe anaemia (a blood count of less than 70 grams per litre of blood) and were matched with 8,218 women without severe anaemia.

Previous studies had suggested that anaemia was strongly associated with death, but that this was due to other clinical reasons, and not anaemia directly. This analysis is the first to take into account factors that influence the development of anaemia in



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1. Data on file and from public sources, 2017. 2. Results from Friedewald, SM, et al. "Breast cancer screening using tomosynthesis in combination with digital mammography." JAMA 311.24 (2014): 2499-2507; a multi-site (13), non-randomized, historical control study of 454,000 screening mammograms investigating the initial impact of the introduction of the Hologic Selenia® Dimensions® on screening outcomes. Individual results may vary. The study found an average 41% increase and that 1.2 (95% CI: 0.8-1.6) additional invasive breast cancers per 1000 screening exams were found in women receiving combined 2D FFDM and 3D" mammograms acquired with the Hologic 3D" Mammography System versus women receiving 2D FFDM mammograms only. 3. In an internal study comparing Hologic's standard compression technology to the SmartCurve® system (18 x 24cm).

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Only 25% of women receive appropriate advice on pregnancy weight gain

A new study of the role of healthcare provider recommendations on weight gain during pregnancy showed that while provider advice did influence gestational weight gain, only about one in four women received appropriate advice and another 25% received no advice. The impact of provider recommendations for pregnancy weight gain that are consistent with current Institute of Medicine (IOM) guidelines is reported in an article published 10 January 2018 in *Journal of Women's Health*.

In the article entitled "Achieving Appropriate Gestational Weight Gain:

The Role of Healthcare Provider Advice", the researchers examine associations between healthcare provider advice – whether it was received or not, and whether it was consistent with IOM recommendations, above, or below – and likelihood of inadequate or excessive weight gain during pregnancy. The authors also consider the pre-pregnancy body mass index (BMI) of the study participants.

"This study by Deputy et al. highlights the importance of healthcare providers as a crucial source of guidance on appropriate weight gain during pregnancy, which is of utmost importance to maternal and fetal health," says Susan G. Kornstein, MD, Editor-in-Chief of *Journal of Women's Health*, Executive Director of the Virginia Commonwealth University Institute for Women's Health, Richmond, VA, and President of the Academy of Women's Health. "It is essential that provider advice be consistent with the most up-to-date recommendations and best practices. These findings can be extrapolated beyond weight gain to other aspects of a healthy lifestyle that can impact pregnancy."

• doi: 10.1089/jwh.2017.6514

pregnancy (e.g. blood loss or malaria infection) which may have been skewing the results of previous studies.

The study results showed that, when all known contributing factors are controlled for, the odds of maternal death are doubled in mothers with severe anaemia.

Different geographical areas

The relationship was seen in different geographical areas and using different statistical approaches, which suggests an independent relationship between severe anaemia and maternal death does exist.

Francesca Gliubich, Director of Grants at Barts Charity, said: "Barts Charity are proud of having contributed to this work. The research will help to shape health policies worldwide by providing scientific evidence of the importance of prevention and treatment of maternal anaemia, ultimately saving lives and avoiding preventable deaths."

Strategies for the prevention and treatment of maternal anaemia include providing oral iron tablets for pregnant women, food fortification with iron, improving access to antenatal care in remote areas, hookworm treatment and access to transfusion services.

The study has limitations including its observational nature meaning that a direct causal relationship between severe anaemia and maternal death cannot be proven, because other factors may come into play.

The study included authors from CIBER Epidemiology and Public Health (Spain), World Health Organization, National Center for Child Health and Development (Japan), Sao Paulo Federal University (Brazil), Fortis Memorial Research Institute (India), Ministry of Health (Sri Lanka), Khon Kaen University (Thailand) and University of Tsukuba (Japan).

* The countries included in the study were Afghanistan, Angola, Argentina, Brazil, Cambodia, China, Democratic Republic of the Congo, Ecuador, India, Japan, Jordan, Kenya, Lebanon, Mexico, Mongolia, Nepal, Nicaragua, Niger, Nigeria, Pakistan, Palestine, Paraguay, Peru, Philippines, Qatar, Sri Lanka, Thailand, Uganda, Vietnam.

• doi: 10.1016/S2214-109X(18)30078-0

Warm showers and ball exercises may help women during childbirth

A new International *Journal of Nursing Practice* study published 7 March 2018 demonstrates that during childbirth, women may benefit from warm showers, perineal exercises with a ball, or the combination of both strategies. The study found positive effects of these strategies in terms of lessening pain, anxiety, and stress

The study was a randomized controlled trial conducted with 128 women during childbirth who were admitted for hospital birth in São Paulo, Brazil from June 2013 to February 2014.

"When we evaluated pain and anxiety using a visual analogue scale, and also evaluated the salivary release of stress hormones before and after interventions of warm showers and perineal exercises with a ball, we found greater tolerance regarding pain, reduction of anxiety, a decrease in the release stress hormones, and an increase in well-being hormones," said lead author Dr Angelita José Henrique, of the Federal University of São Paulo. "Our results indicate that these interventions should be encouraged because they are safe practices, low-cost, and are directly related to comfort, and they should be used as an adjuvant to medications and anaesthesia during childbirth."

• doi: 10.1111/ijn.12642

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

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

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

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

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

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

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

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

directly integrated into their work.

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

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

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

There are direct flights to Hamburg from Dubai twice a day.



Endometriosis



By Dr. Regina Sider
 Specialist Obstetrics & Gynaecology
 Emirates Specialty Hospital

Does your menstrual bleeding turn you down every month?

Are you suffering from severe pelvic pain around the time of your menstrual bleeding?

Are you unable to leave the house or go to work at the beginning of your menstrual bleeding? Then it's most likely that you are suffering from endometriosis.

So, what is endometriosis all about?

Endometriosis is a disease in which small islets of endometrial cells, which normally form the lining of the uterus, grow abnormally in a location outside of the uterus commonly on other organs of the pelvis.

How do the cells grow outside of the uterus?

The exact mechanism is still unknown. Most specialists believe that there is some kind of migration of the cells through the tubes.

What are the symptoms of endometriosis?

Depending on the location of these cells, it can be responsible for nausea and vomiting, diarrhea and, most of the time, severe pain in the lower abdomen, which makes the person unable to move or walk around.

The timing of the symptoms is generally correlated with the woman's menstrual bleeding, which means that the most



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painful days are typically around the beginning of their menstrual period.

Why are symptoms correlated with the menstrual cycle?

This is caused by the alteration of the small islets of cells due to the course of the woman's hormone cycle. Usually, those cells are situated in the uterus and due to hormonal changes the cells are repelled which causes the menstrual bleeding. But when these cells are not in the uterus, like in the case of endometriosis, their alteration due to the hormonal cycle causes severe pain among other symptoms.

So what can be done?

First of all the woman should see their gynecologist and explain their symptoms. Depending on the severity of the symptoms the gynecologist will most probably start with good pain management medication.

If the medication brings no pain relief, then it is time for the second step. The second step of the therapy depends on the patient's circumstances. If the patient is not married and is not planning for a pregnancy in the upcoming year then it is advisable to start with a gestagen pill or any other gestagen device.

The patient can choose either a continuous course of pills which, means no menstrual bleeding and no break, or a 3-week oral intake with one-week break. This therapy usually gives the patient immediate relief.

If the condition of the patient is severe and the patient plans to become pregnant during the upcoming year then it is advisable to opt for a surgical procedure.

Surgery can be performed with a laparoscopic procedure to detect the endometriosis lesions and to remove them all.

Afterwards, the symptoms of the patient are relieved and it's also easier for the patient to become pregnant.

If this article reflects your symptoms and you feel it is time to take advice we can assure you that you will find a suitable solution for your problems with the obs and gyne team at Emirates Specialty Hospital.

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Lymph node surgery can be avoided for women with aggressive types of breast cancer that respond well to chemotherapy

Sentinel lymph node biopsies, where lymph nodes are surgically removed to check for signs of breast cancer spread, could be safely avoided for some women, according to research presented at the 11th European Breast Cancer Conference in Barcelona in March this year

Breast cancer becomes most dangerous when it begins to spread to other parts of the body and one of the first places it spreads to is nearby lymph nodes, known as sentinel lymph nodes. To check for signs of spread, surgeons remove sentinel lymph nodes from under the arm. This procedure can leave women with long-standing side effects such as swelling, numbness and reduced movement of the arm.

Two new studies show that women with either 'triple negative' or HER2 positive types of breast cancer, whose cancers respond well to chemotherapy given before surgery, have a very low risk of having any cancer cells in these lymph nodes.

The first study was by a team at University Hospital Vall Hebron, Barcelona, Spain, led by breast surgeon Christian Sisó MD.

They studied a group of 90 patients treated at the hospital between January 2011 and December 2016. All had either HER2 positive cancer (where the cancer cells have a high level of human epidermal growth factor receptor 2, which stimulates them to grow), or triple negative breast cancer (where the tumour is HER2 negative, and does not respond to the hormones oestrogen and progesterone). Both are known to be aggressive forms of breast cancer.

All patients were given chemotherapy treatment to shrink their tumours before surgery. They were also given ultrasound scans to check for signs of cancer in the lymph nodes and this was confirmed with pathology tests.

Fifty-four of the patients (60%) had no obvious signs of cancer in their lymph nodes before treatment. Following chemotherapy, all but two (96.3%) had no cancer cells growing

in their lymph nodes. Twenty-three of these women (42.5%) also had no cancer cells growing in the breast and none of those had cancerous cells in their lymph nodes.

Of the remaining 36 (40%) patients who did have signs of cancer in their lymph nodes before treatment, 17 (47.2%) had no cancer cells growing in the breast after treatment and, of these, 13 (76.5%) were also free of cancer cells growing in their lymph nodes.

Dr Sisó explained: "Our results suggest that giving chemotherapy to patients with these types of breast cancer before considering surgery offers the possibility of reducing or even avoiding surgery. By giving drug treatment first we are able to see how well the drugs work against an individual tumour. If they are working well, they can clear cancer cells from the lymph nodes and in the breast.

"In women who had no signs of cancer in their lymph nodes and where treatment seems to have cleared the cancer in the breast, lymph node surgery might be avoided. On the other hand, in women who had signs of cancer in their lymph nodes before treatment, there is still a risk that the disease will remain there, even when it has been successfully treated in the breast itself."

The second study

The second study was presented by Marieke van der Noordaa MD. This study was performed by the breast cancer team of at the Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital.

They studied a group of 294 patients with breast cancer treated at the institute between January 2013 and September 2017. All had no signs of cancer in their lymph nodes according to ultrasound, PET/CT or cytology taken with a needle. All patients were treated with upfront chemotherapy.

Following chemotherapy, none of the

patients with HER2 positive breast cancer had tumour cells in their sentinel lymph nodes and almost none (1%) of patients with triple negative tumours had cancer cells in their lymph nodes. Only 2% of patients with a poor grade tumour, had cancer cells in their lymph nodes. All patients whose breast tumours responded completely to the chemotherapy were also cancer-free in their lymph nodes.

Dr van der Noordaa explained: "These results suggest that sentinel lymph node biopsies are most likely not needed in many women who undergo upfront chemotherapy and who have no sign of cancer in their lymph nodes before the start of chemotherapy. This could mean the side-effects sentinel lymph node biopsies could be prevented in these women."

Following this work, Dr van der Noordaa, together with Dr Vrancken Peeters and colleagues, will start a trial (the ASICS trial) for patients with HER2 positive or triple negative breast cancer, and patients with a poor grade tumour, who are treated with upfront chemotherapy to evaluate whether avoiding sentinel lymph node biopsies results in recurrences in the lymph nodes, and to examine overall survival and quality of life.

Professor Robert Mansel is chair of the 11th European Breast Cancer Conference and Emeritus Professor of Surgery at Cardiff University School of Medicine, UK, and was not involved in the research. He said: "Whether or not a breast cancer has spread to nearby lymph nodes is a key indicator of a patient's prognosis. That's why sentinel lymph node biopsy has been an important part of treating breast cancer.

"These two studies give us clues on which patients have a very low risk of cancer in their lymph nodes after chemotherapy. This could enable us to reduce unnecessary surgery when it's safe to do so, helping us tailor treatments towards individual patients."

What is inflammation?



By Dr Polyvios Pavlidi, MD, PHD, MSC Consultant - Vascular Surgeon, Emirates Specialty Hospital

Think of inflammation as the body's response to protect itself against harm. Your immune system dispatches an army of white blood cells to surround and protect the area. The inflammation can also occur in response to other unwanted substances in the body, such as toxins, cigarette smoke or an excess of fat cells (especially fat in the belly area).

Inside arteries, inflammation helps kick off atherosclerosis – the build-up of fatty, cholesterol-rich plaque. Your arteries perceive this plaque as abnormal and foreign, it attempts to wall off the plaque from the flowing blood. But if that wall breaks down, the plaque may rupture. The contents then mingle with blood, forming a clot that blocks blood flow. These clots are responsible for the majority of heart attacks and most strokes.

A simple blood test called hsCRP test can measure C-reactive protein (CRP), which is marked for inflammation, including arterial inflammation. Nearly 20 years ago, Harvard researchers found that men with higher CRP levels – approximately 2

mg/liter or greater — had three times the risk of heart attack and twice the risk of stroke as men with little or no chronic inflammation. They also found that people with a high level of arterial inflammation benefited from aspirin, medication a drug that helps prevent blood clots and also reduces inflammation.

We recommend the hsCRP test. If you have heart disease, you should already be taking medications that lower your heartattack risk, such as cholesterol-lowering statins. Aspirin and statins also appear to work particularly well in people with arterial inflammation. Statins reduce the risk of death in people with average cholesterol levels. So, if you are a middleaged or older and have signs of looming heart trouble, like high blood pressure, high cholesterol, or a family history of heart disease, knowing that you have a high CRP level may nudge you toward more aggressive actions to protect your heart. These include doing regular aerobic exercise and (if needed) losing weight and quitting smoking.

Arterial inflammation

The mechanism of arterial inflammation is pretty clear. A coronary artery is gradually narrowed by a buildup of plaque, as in a corroded pipe. When it is around 80% closed, small clot gets stuck in it and stops the blood flow to the heart, resulting in a heart attack.

About 70% of attacks are caused by much smaller obstructions which can narrow the artery by perhaps only a third, which is too small to cause symptoms detected by an X-ray angiogram. However, it can cause small arterial deposits to suddenly rupture like popcorn kernels, choking off the blood supply to the heart.

This has propelled research into the biology of atherosclerosis to find out what makes plaques rupture and how to identify and treat them before they rupture. It is known that there is an inflammatory response which alters the biology of the artery wall and can make the plaque susceptible to rupture.

The new research does not detract from well-known risk factors for heart disease including high blood pressure, high cholesterol and smoking.

Bypass surgery and artery opening technology, such as angioplasty balloons and stents, are very effective in relieving its chief symptom – severe chest pain, called angina.

Statins are a powerful weapon with proven ability to prevent heart attack as well as reduce the need for heart bypass surgery and angioplasty. But statins do not save everyone. Half of the people who suffer heart attacks have normal cholesterol levels.

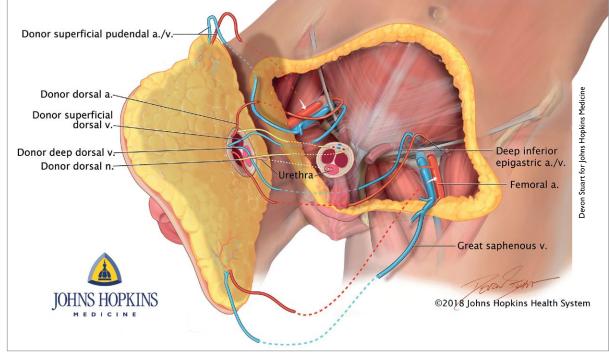
One function of the body's repair system is to clear cholesterol from the cells lining the artery wall, a role that falls to cellular macrophages.

However, particularly with fatty plaque, the immune system macrophages can become engorged with so much cholesterol that they cannot do their job. They turn into foam cells and die because they become so laden with fat that they are squishy and unable to perform their duties. As they die, they add their contents to the plaque and release toxic substances that lay the groundwork for the plaque to rupture.

One of the toxic culprits they release, is a group of enzymes that attack the fibrous cap covering the plaque thereby destabilizing it. It was found that macrophages can do more damage. The case for inflammation is not fully proven. However, there is nothing more promising and exciting as the next frontier in vascular surgery.

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US surgeons perform first total penis and scrotum transplant

Many soldiers returning from combat bear visible scars, or even lost limbs, caused by blasts from explosive devices. However, some soldiers also return with debilitating hidden injuries – the loss of all or part of their genitals. Surgeons in the United States have now treated this injury for the first time with a total penis and scrotum transplant.

The reconstructive surgery team at Johns Hopkins University School of Medicine that performed the United States' first bilateral arm transplant in a wounded soldier has successfully performed the first total penis and scrotum transplant in the world.

This US penis and scrotum (without testicles) transplant surgery follows a successful penis transplant in 2014 by a team from Stellenbosch University and the Tygerberg Academic Hospital in South Africa. This team also performed a second successful penis transplant last year.

"We are hopeful that this transplant will help restore near-normal urinary and sexual functions for this young man," said W.P. Andrew Lee, M.D., professor and director of plastic and reconstructive surgery at the Johns Hopkins University School of Medicine.

A team of nine plastic surgeons and two urological surgeons was involved in the 14-hour surgery on 26 March this year. They transplanted from a deceased donor the entire penis, scrotum (without testicles) and partial abdominal wall.

The recipient who is a war veteran who sustained injuries in Afghanistan and wishes to remain anonymous, said: "It's a

real mind-boggling injury to suffer, it is not an easy one to accept. When I first woke up, I felt finally more normal... [with] a level of confidence as well. Confidence... like finally I'm okay now."

While it's possible to reconstruct a penis using tissue from other parts of the body, says Dr Lee, a prosthesis implant would be necessary to achieve an erection, and that comes with a much higher rate of infection. Additionally, due to other injuries, servicemen often don't have enough viable tissue from other parts of their bodies to work with.

This type of transplant, where a body part or tissue is transferred from one individual to another, is called vascularized composite allotransplantation. The surgery involves transplanting skin, muscles and tendons, nerves, bone and blood vessels. As with any transplant surgery, tissue rejection is a concern. The patient is put on a regimen of immunosuppressive drugs to prevent rejection. Lee's team has developed an immune modulation protocol aimed at minimizing the number of these drugs needed to prevent rejection.

Speaking about the transplant in a telebriefing, Dr Lee said: "In a 2014 symposium co-sponsored by Johns Hopkins titled "Intimacy After Injury", we heard from the spouses, families, and caregivers of these wounded warriors about the devasting impact of genitourinary injuries on their identity, self-esteem, and intimate relationships.

"We believed that genitourinary transplantation can help those warriors with missing genitalia just as hand and arm transplants transformed the lives of amputees. In 2013, we assembled a team of plastic surgeons, urologists, transplant specialists, psychologists, and bioethicists and began the preparation for genitourinary transplantation. We carried out anatomic dissections to understand the blood supply to different parts of penis and scrotum. We performed multiple surgical rehearsals of transplant in cadavers. We took notes of what we learned, refined our techniques, and devised a plan for both graft procurement and transplantation."

Dr Lee said the recipient sustained a severe blast injury to his pelvis, lower abdominal wall, and lower extremities. He added: "Two weeks after transplant, he received donor bone marrow infusion according to our immune modulation protocol in order to reduce his anti-rejection regimen to a single medication."

Commenting on the transplant surgery, Rick Redett, the clinical director of the Johns Hopkins genitourinary transplant program, said: "This procedure represents the culmination of more than 5 years of research and collaboration across multiple disciplines within Johns Hopkins to address logistical, procedural, and ethical considerations. During the time leading up to the transplant our team developed the surgical approach through rigorous preparation to define the blood supply to the transplanted tissues and coordinate all aspects of this complex surgery. Our anatomic studies



The reconstructive surgery team at Johns Hopkins University School of Medicine that carried out the world's first total penis and scrotum transplant.

demonstrated the importance of utilizing multiple blood vessels to provide optimal graft perfusion and maximize the potential benefits afforded by the procedure.

"To perform the transplant, we procured the necessary tissue from the donor to restore normal anatomy in the recipient. The donor testicles were not transplanted. The damaged and scarred tissues were removed from our patient and the necessary blood vessels and nerves were identified. For the transplant, 3 arteries, 4 veins, and 2 nerves were connected under the microscope to provide complete blood perfusion and sensation to the transplanted tissue."

Dr Redett added that the 14-hour procedure was successfully completed by a team of surgeons, anaesthesiologists, nurses and

surgical technicians and said it would not have been possible without the help of countless individuals who worked as a team to provide the finest care possible for their patient. "In addition, many nurses, physical and occupational therapists and support staff have provided outstanding care for our patient in the postoperative period."

Bariatric surgery for severely obese teens may help prevent premature heart disease

Bariatric surgery is predicted to cut in half the risk of premature heart disease and stroke in teens with severe obesity, according to preliminary research presented at the American Heart Association's Epidemiology and Prevention | Lifestyle and Cardiometabolic Health Scientific Sessions 2018, a leading global exchange of the latest advances in population-based cardiovascular science for researchers and clinicians.

The researchers used a model based on research from the Framingham Heart Study that predicts the likelihood of heart disease events over a 30-year period. They found that prior to bariatric surgery the overall risk of a severely obese teen having a fatal or non-fatal heart attack, stroke, heart failure or other heart disease event over a 30-year period was 8 percent on average. One year after surgery, the model predicted that the risk of a heart disease event would be cut in half – to 4 percent overall – and was sustained every year for the five years following surgery.

"This study clearly shows that the benefits of bariatric surgery to treat severe obesity, at least from a cardiovascular event perspective, outweighs the risk of having the surgery. Teens with severe obesity are at high risk for having a premature cardiovascular event, such as a heart attack, stroke, heart failure and others by the time they are 50, which has significant implications in terms of their healthcare costs and their quality of life," said Justin Ryder, Ph.D., study author and assistant professor of pediatrics at the University of Minnesota Medical Center in Minneapolis.

The prediction model was applied to 215 participants of the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS), a study designed to assess the short and longer-term safety and usefulness of bariatric surgery in teens. The teens in the study had average BMI's - body mass index, a weight-to-height measurement - of 53. In adults, that translates to a 5'5" woman who weighs 120kg (320 pounds) and a 6' man who weighs 145kg (390 pounds). Participants were average age 17 before surgery. Data on gender, age, blood pressure, treatment for high blood pressure, smoking, diabetes, total cholesterol, high-density lipoprotein cholesterol and weight was collected and analyzed before surgery and annually for five years after surgery.

Bariatric surgery helps obese people lose weight by surgically altering the digestive system. In some cases that means making the stomach smaller, so a sense of fullness is more easily achieved, or shortening the intestines so that less food is absorbed. Previous studies have shown that bariatric surgery results in substantial weight loss and the reduction of risk factors for heart disease in adults, but little is known about how the reduction in risk factors translates into a reduction of heart disease events, later in life for teens who undergo this procedure.

"These findings add another piece to the mountain of evidence suggesting that bariatric surgery is the most effective treatment for sustained reduction of weight and risk factors for chronic diseases such as cardiovascular disease and diabetes in teens with severe obesity," Ryder said.

The researchers note that the study is limited because it uses a prediction model that estimates the likelihood of having a heart disease event but does not measure true events.



Single-port laparoscopy ensures scar free gynecologic surgeries

Robotic laparoscopic surgeries can be performed through a small single incision instead of three, four or five incisions used in traditional laparoscopy. When the belly button is used as an entry point this procedure does not leave a scar and the patient recovers faster. Using a robot is important to overcome the technical difficulties of single-incision surgeries.

In laparoscopic surgery – the so-called closed surgery method – smaller incisions are used for rapid healing, less pain, less scarring and more convenient treatment for the patients. Laparoscopic surgeries, which used to be performed through three, four or five ports of sizes ranging from 5mm to 10mm, can now be performed through a single-entry point, also known as a single-port laparoscopy. Since the cavity of the belly button is used as an entry point; there is no scar left on the body of women who undergo this procedure for gynecological surgery.

Professor Dr Mete Güngör, Gynecologic Oncology Specialist at Acibadem Maslak Hospital, Istanbul, Turkey, describes the single-port surgery: "We can perform the surgery just using the belly button as an entry point and making an incision of only 15-20mm. We do not touch any other part of the body. After the patient's belly button heals, there is no scar left behind and the patient is much more satisfied aesthetically and cosmetically. In addition, a single incision accelerates healing, so in many cases the patient can get up the next day and go home."

Robotic surgery and 3D imaging

Prof Dr Güngör emphasizes that closed

surgery can be performed just like open surgery, thanks to three-dimensional imaging that provides a clear depth of field for the surgeon operating the robotic surgery device. The imaging is so clear that it does not skip even the finest details. There are many benefits of robotic laparoscopic surgery as the instruments used in robotic surgery can precisely cut and remove tissues and have a higher rotational ability compared to those used in traditional laparoscopic surgery.

In cases where the uterus is to be removed, if the uterus is of acceptable size, it can be removed through a single incision. Problems such as ovarian cysts, uterine prolapse, adhesions, women with miscarriage problems due to tubal reconnection or cervical incompetence can be treated with robotic surgery. Prof Dr Güngör says that not all of these surgeries can be applied through a single port, but thanks to robotics, as new single-port applications are developed, the scope for this type of surgery will increase. He also remarked that it is compelling to use a single port surgery for some cancers such as the removal of cysts and the uterus if they are not very large.

In single-port robotic surgery an instrument with four holes is pushed through a



Professor Dr Mete Güngör, Gynecologic Oncology Specialist at Acibadem Maslak Hospital, Istanbul, Turkey

single 20mm incision. One of these holes is for the camera, two of them are for the arms of the robot, and the fourth hole is used by the assistant at the surgery.

Prof Dr Güngör says: "Most gynecological cancer patients require chemotherapy or radiotherapy after surgery. However, when open surgery is performed, a 20-25 cm incision can take a month to heal, delaying the progress of treatment. In addition, the fact that these patients are generally older, have weight problems and systemic diseases complicates both open surgery and post-operative recovery. In robotic surgery, the recovery is much quicker. The patient is discharged within a few days and chemotherapy or radiotherapy treatment can be initiated quickly."









Baylor St. Luke's Medical Center first in Texas to perform Breathing Lung Transplant



Dr. Gabriel Loor, surgical director of the lung transplant program at Baylor St. Luke's Medical Center and director of lung transplantation in the Michael E. DeBakey Department of Surgery at Baylor College of Medicine.

Baylor St. Luke's Medical Center (Baylor St. Luke's) is the first hospital in Texas to perform a breathing lung transplant using the Ex Vivo Lung Perfusion (EVLP) procedure with Organ Care System Lung (OCS Lung) technology. This technology is designed to keep donor lungs functioning and "breathing" in human-like conditions from the time of the donor procedure all the way to the transplant surgery.

"This transplant is significant for Baylor St. Luke's. The groundbreaking research and hard work behind this surgery shows our dedication to offering the highest levels of care and delivering the most effective treatment options for our patients," said Gay Nord, market president, Baylor St. Luke's.

Led by Dr. Gabriel Loor, surgical director of the lung transplant program at Baylor St. Luke's Medical Center and director of lung transplantation in the Michael E. DeBakey Department of Surgery at Baylor College of Medicine, the transplant was performed using the newest generation of EVLP platforms, Transmedics Organ Care System (OCS), a portable device that



maintains the organ in its own physiologic state with warm blood perfusion, ventilation and a sophisticated monitoring system to continually assess the organ in flight. In this case, the donated lungs were flown in to Houston from the Midwest. The device is the only portable EVLP system in the world and the only one that has undergone a positive FDA panel review in the United States as well as two rigorous international clinical trials. The OCS Lung System was officially approved by the FDA on 23 March 2018.

The surgery was performed as part of the EXPAND II OCS trial, for which Baylor St. Luke's is a study site, testing the outcomes of transplanted donor lungs that are transported, preserved, optimized and monitored on a portable OCS device.

"The surgery was a success and the transplanted lungs will vastly improve this patient's quality of life," said Dr. Loor. "There are over 100,000 people waiting for lifesaving organ donations at any given time in the U.S. Advances in this technology are incredibly exciting for the future of

organ transplantation at Baylor St. Luke's and the Texas Medical Center."

Dr. Loor is the International Principal Investigator for the largest study in the US evaluating the ability to increase the number of useable donor lungs using the OCS technology. He is exploring ways to significantly expand the amount of time an organ can be out of the body prior to transplant, which expands the available donor pool and opens more opportunities for patients waiting for life-saving organ donations, as time and location are no longer limiting factors.

The lung transplant program at Baylor St. Luke's in Houston's renowned Texas Medical Center continually strives to meet the needs of patients through innovative breakthrough research and cutting-edge technology, and is committed to compassionate quality healthcare that improves and saves lives.

• For more information contact International Services at Baylor St Luke's Medical Center

Via email at international@stlukeshealth.org or call +1 832 355 3350 or visit

StLukesInternational.org Texas Medical Center, Houston, Texas - USA.



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Government funding: The key to discovery

Several sectors in the US healthcare industry have been expressing concern that declining government funding of basic research was having a negative effect on the country's leading role in medical discovery, but this changed with the government's approval a new Omnibus Bill in March this year.

For many years the United States has been a world leader in biomedical research innovation. This is in large part enabled by federal government funding for biomedical research through the National Institutes of Health.

Recently there has been growing concern in certain quarters that the US was losing its edge in medical discovery to other countries due to declining levels of federal funding. According to a STAT report in January, this not only "threatened the creation of new therapies but also imperiled an industry that supports more

than 300,000 jobs". The report notes that declining levels of federal funding for biomedical research, along with inefficient allocation of funds by the National Institutes of Health, are jeopardizing innovation.

The authors state: "At the same time, universities and nonprofit research institutes are experiencing funding cuts at the state level. In some instances, private philanthropy and disease-specific foundations have increased funding for biomedical research, but this is but a small piece of the pie that does not make up for the federal funding shortfall."

Research spending increase

So it comes with great relief for this sector that the US Congress on 21 March revealed a \$1.3 trillion Omnibus Appropriations Bill for Fiscal Year 2018 (albeit six months late) which covers federal spending for the current fiscal year – through September 2018. The budget provides for the largest research spending increase in more than a decade. According to the bill, the National Institutes of Health (NIH) receives a \$3 billion, 8.3% increase to \$37 billion. A report on Sciencemag.org notes that this is "well

Physicians support 12.6 million jobs, \$2.3 trillion in economic activity

Physicians add opportunity, growth and prosperity to the US national economy by creating 12.6 million jobs and generating \$2.3 trillion in economic activity, according to a new report, *The National Economic Impact of Physicians*, released in January by the American Medical Association (AMA).

"The positive impact of physicians extends beyond safeguarding the health and welfare of their patients," said AMA President David O. Barbe, MD, M.H.A. "The AMA's economic impact study illustrates that physicians are strong economic drivers that are woven into their local communities by the commerce and jobs they create. These quality jobs generate taxes to support schools, housing, transportation and other public services in local communities."

The new study quantifies the economic boost that 736,873 patient care physicians nationwide provide to the economy. The study measures physicians' impact using four key economic indicators:

- **Jobs**: Physicians support 12.6 million jobs 17.1 for each physician on average.
- Economic activity: Physicians generate \$2.3 trillion in economic output, comprising 13% of the national economy.

Each physician generates \$3.2 million on average.

- Wages and benefits: Physicians contribute \$1 trillion in total wages and benefits paid to workers across the country, empowering a high-quality, sustainable workforce. Each physician contributes \$1.4 million to workers' wages and benefits on average.
- State and local tax revenue: Physicians' contribution to the national economy generates \$92.9 billion in state and local tax revenue for their communities-translating to \$126,129 for each physician on average enabling community investments to be made.

The report found that every dollar applied to physician services supports an additional \$2.84 in other business activity. An additional 11 jobs, above and beyond the clinical and administrative personnel that work inside a physician practice, are supported for each one-million dollars of revenue generated by a physician's practice. In addition, physicians generate more economic output, produce more jobs and pay more in wages and benefits than professionals working in higher education, nursing and community care facilities, legal services and home health.

Read the report here: www.PhysiciansEconomicImpact.org

above the increase proposed by either the House of Representatives or the Senate in their versions of the spending bills, and a blunt rejection of the 22% cut proposed by the White House".

The \$3bn increase in funding for the NIH was welcomed by several organisations.

American Heart Association CEO Nancy Brown said: "Congress delivered a great gift to Americans suffering from heart disease and stroke with passage of this legislation. The substantial budget increases provided for medical research and prevention are just what we need to take on the heavy burden cardiovascular disease will continue to place on our nation."

Research! America President and CEO Mary Woolley applauded the unprecedented boost in funding for the National Institutes of Health and significant increases for other federal health agencies in FY18 to accelerate medical progress, public health and scientific innovation. "The omnibus bill is a positive step forward in strengthening our global competitiveness and our nation's commitment to research and public health."

The Association of American Medical Colleges stated that the legislation will "allow for more life-changing research to be performed" and enable "major scientific breakthroughs".

American Psychiatric Association welcomed the budget. "We are pleased that to-

day's budget deal included \$6 billion to fight opioid abuse, one of the most critical public health issues facing our nation today. The opioid crisis has taken a heavy toll on millions of families in America. We applaud Congress for approaching these issues in a bipartisan way. Our members stand ready to provide our expertise in treating this epidemic."

National Institutes of Health

NIH's significant budget boost will be divided among its 27 institutes, centers and divisions, including the two which are responsible for heart disease and stroke research. The National Heart, Lung, and Blood Institute will receive \$848 million in additional funds, increasing its budget to \$3.3 billion, and the National Institute of Neurological Disorders and Stroke will receive \$832 million, enlarging its budget to \$2.1 billion.

"We strongly encourage the NHLBI and the NINDS to invest this funding in heart and stroke research," Brown declared. "Cardiovascular disease, if left unchecked, is projected to affect 45 percent of Americans by 2035. Research is our best hope to wipe out the serious health and economic crisis we will be facing if this prediction becomes a reality."

Also included in the budget is \$1.8 billion for Alzheimer's disease research, an increase of \$414, and \$543 million for clinical and translational science funding, an increase of \$27 million.

Other research areas to receive funding include:

- \$400 million (+ \$140 million) for the Brain Research through Application of Innovative Neurotechnologies (BRAIN) initiative
- \$290 million (+ \$60 million) for the All of Us research initiative a study to track the health of one million Americans over 10 years (formerly called the Precision Medicine Initiative)
- \$10 million (+ \$8 million) for regenerative medicine research
- \$100 million (+ \$40 million) for research to develop a universal flu vaccine
- \$351 million (+ \$17 million) for research on combating antibiotic-resistant bacteria, and
- \$351 million (+ \$17 million) for Institutional Development Awards (IDeA).

Within the total, the legislation includes \$300 million for the Cancer Moonshot and \$12.6 million for the Gabriella Miller "Kids First" pediatric cancer research initiative.

The bill supports a new multi-year Down syndrome research initiative that will expand NIH support for research on Trisomy 21 and related diseases and disorders.

The bill also includes a provision requiring NIH to continue reimbursing grantee research institutions for facilities and administrative costs.

According to a report in *Nature*, the White House had sought to cut the NIH



budget by 18% in 2018, in part by eliminating one of the agency's 27 institutes – the Fogarty International Center in Bethesda, Maryland, which helps to train researchers and healthcare providers overseas. The spending plan released by Congress includes nearly \$76 million for the centre.

The NIH states that more than 80% of its 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 state and around the world.

About 10% of the NIH's budget supports projects conducted by nearly 6,000 scientists in its own laboratories.

Centers for Disease Control and Prevention

The NIH was not the only agency to see more federal support in the omnibus bill. The Centers for Disease Control and Prevention's (CDC) received \$8.3 billion – an

increase of \$1.1 billion above the fiscal year 2017 level.

The American Heart Association pointed out that specific CDC programs which help Americans manage risk factors before they result in heart attacks and strokes also obtained increases or their funding remained the same as last year's, including:

- CDC's Heart Disease and Stroke Prevention, which will receive \$140 million, a 7.7% increase over 2017
- CDC's Million Hearts, which is slated for \$4 million (same as 2017), despite being zeroed out in the administration's budget
- CDC's WISEWOMAN, will get \$21.120 million, the same amount as last year.

The American Heart Association noted that it as extremely pleased to see that this legislation did not contain any tobacco policy riders that were under consideration in the past, such as ones that would exempt premium cigars from FDA regulation or alter the grandfather date,

so e-cigarettes and other tobacco products would be exempt from FDA product reviews. Fortunately, none of those riders were in the omnibus, and to top it off the legislation funded the CDC's Office on Smoking and Health at \$210 million, \$5 million more than 2017.

Importance of government funding

A recent study published in the Proceedings of the National Academy of Sciences (doi: 10.1073/pnas.1715368115) makes a strong case for the importance of government funding for basic research. According to STAT it is the first to capture the full scope of public funding behind FDA-approved drugs. In essence, the study points out that federally funded studies contributed to the science that underlies every one of the 210 new drugs approved between 2010 and 2016. The STAT report notes that of those 210 drugs, 84 were first-in-class drugs, meaning they treat disease through novel mechanisms or molecular targets.

More than \$800,000 invested in congenital heart defect research

The Children's Heart Foundation and the American Heart Association today announced their latest collaborative investment in research to better understand and treat congenital heart defects (CHDs), the number one birth defect in the United States. This is the fourth round of their co-funded Congenital Heart Defect Research Awards program and represents a \$826,600 investment in seven research programs from around the country. The program will ultimately fund more than \$22 million in CHD-specific research through 2021.

At least 40,000 infants are estimated to be affected by congenital heart defects each year in the United States. About 25% of babies born in the US with a CHD require invasive treatment in their first year of life. Research that helps understand, identify and treat CHDs is helping these children live longer healthier lives. It is estimated that more

than 800,000 American adults are living with a CHD.

"We are honored and excited to continue our research funding partnership with the American Heart Association," said Tamara Thomas, President of The Children's Heart Foundation. "Through this collaboration and our ongoing commitment to research focused on congenital heart defects, we strive to make a lasting impact in the lives of those with congenital heart defects. This \$826,600 of new research will help bring innovative solutions to survival rates and care."

The seven new grants are:

• Craig Broberg of Oregon Health & Science University, Portland – Using existing clinical records from multiple hospitals across the country on patients born with a systemic right ventricle due to transposition of the great arteries who are now adults, this study will study fac-

tors that determine which patients do well and which have severe heart failure, such as need for heart transplant. The study will be the largest collection of data on such patients thus far. It will provide a greater understanding of what leads to heart deterioration, and therefore what treatment options may have the most potential benefit.

• Srinivas Manideep Chavali of University of California, San Francisco – While poor neurodevelopmental outcomes in the survivors of congenital heart disease (CHD) remain a serious concern, the underlying pathology is not yet clearly understood. This research will focus on the role of blood flow in building myelin, which protects and coast brain cells, allowing for health brain development. A better understanding of the relationship between CHDs and brain health will aid in developing treatment.





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- ▶ (continued...)
- Ibrahim Domian of Massachusetts General Hospital Understanding how the heart forms is important to treat congenital heart defects and this study will look at a specific gene which controls how proteins are broken down to form the heart. This will help isolate specific targets that need to be controlled to produce a healthy heart.
- Nicole Fleming of University of North Carolina, Chapel Hill Using zebrafish, which are fast-growing and easy to manipulate, and whose heart cells are easy to see, this study aims to understand defective ventricular growth in embryos and better understand pharmacological treatments that may improve heart function.
- Chulan Kwon of Johns Hopkins University School of Medicine – Examining the biology of cardiac progeni-
- tor cells (CPCs), which act as building blocks for a developing heart will provide fundamental insights into how improper regulation of factors affecting CPC multiplication can lead to congenital heart disease, which may provide a new direction for preventive or therapeutic approaches. In addition, the knowledge gained from this work might be directly applied to control CPCs in a dish, which will accelerate CPC-mediated heart regenerative research to repair heart disease.
- Yuntao Song of Cincinnati Children's Hospital Medical Center Many congenital heart defects relate to a issue in the cardiac outflow tract. This study will examine the roles specific genes play in developing the cardiac outflow tract which ones lead to a healthy development and which lead to defects.
- Kathryn Vannatta of Nationwide Children's Hospital – As more children survive congenital heart defects, society needs a better understanding of how to support them as they grow. This study will identify details about social difficulties experienced by children with severe forms of CHD, including levels of social withdrawal, disruptive behavior, and whether survivors are victimized by peers. It will examine whether CHD survivors have more of those interactions or have fewer friends than healthy classmates. The study will test whether these difficulties are explained by cognitive and social-affective abilities or less engagement in physical activity and extracurricular activities, as well as the benefits of different parenting practices and types of school environments in promoting social competence.

Nebraska Medicine is one of the first to offer the newly, FDA-approved Chimeric Antigen Receptor (CAR T-cell) therapy.



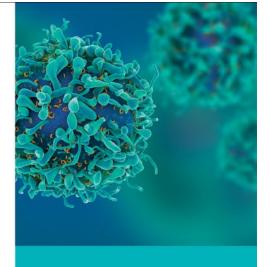
"This type of treatment can't be done at just any hospital or center in the United States. It's limited with respect to what's needed to process the cells and the specialized patient care," explains Julie Vose, MD, hematologist and medical oncologist at Nebraska Medicine

and chief of hematology/oncology at the University of Nebraska Medical Center (UNMC).



Contact the International Healthcare Services

Website: unmc.edu/international Phone: +1 402.559.3090 Email: oihs@nebraskamed.com



Refer a patient for CAR T-cell

The CAR T-cell therapy is open to adult patients (19 years and older) with relapsed b-cell lymphomas, which is a subtype of non-Hodgkin lymphoma.

Nebraska Medicine is one of the first to offer the newly FDA-approved Chimeric Antigen Receptor (CAR) T-cell Therapy

Thoughtful, respected and consistent are words used to describe the nearly four decades of research within the lymphoma study group the University of Nebraska Medical Center (UNMC), and it's clinical partner Nebraska Medicine, have in the United States. These qualities are a result of leadership and teamwork that are unparalleled in the pursuit of excellence for lymphoma care.

"For the next four decades and beyond, we have a goal of maintaining the excellence and international recognition brought forth by my colleagues," says Matthew Lunning, DO, hematologist and medical oncologist at Nebraska Medicine and assistant professor in the division of hematology/oncology at UNMC. "I have championed as a clinical investigator, the continuation of cuttingedge medical research at the new Fred & Pamela Buffett Cancer Center at Nebraska Medicine/UNMC."

Significant advances have been made in cancer care, including the exciting change in patient care involving a technology called chimeric antigen receptor (CAR) T-cell therapy. While initially only available on clinical trials for people with refractory or relapsed diffuse large B-cell lymphoma, it is now approved by the United States Food and Drug Administration (FDA) for commercial use.

CAR T-cell therapies continue to be a rapidly evolving field with the goal to continue to improve on the paradigm shifting results that led to a major unmet medical need for effective therapies. Across the United States, patients with diffuse large B-cell lymphoma who have received this therapy have had continued complete remission rates of nearly 40 percent. Patients who relapse after a stem cell transplant or are not candidates for a transplant may be potential candidates for CAR T-cell therapy.



The University of Nebraska Medical Center team involved in the development of the chimeric antigen receptor (CAR) T-cell therapy. From left to right: Philip Bierman, MD, Matthew Lunning, DO, James O. Armitage, MD, Gregory Bociek, MD, Julie Vose, MD and Katherine Byar, APRN-NP

During the first phase of CAR T-cell therapy, the patient's T cells are collected as an outpatient procedure at Nebraska Medicine. The cells are then sent to a pharmaceutical company lab where they are genetically modified and grown until there are millions of them. The process in the lab takes about two to six weeks. When the cells are returned to Nebraska Medicine, they are placed in a specialized processing center to complete the procedure. In the meantime, the patient receives several days of chemotherapy to make room for the CAR T-cells. The CAR T-cells are then infused into the patient, where they multiply and attack and kill the cancerous lymphoma cells.

All Nebraska Medicine staff involved in the CAR T-cell therapy have undergone and passed a rigorous training program before Nebraska Medicine could be approved to administer the treatment. Nebraska Medicine is one of a few centers in the United States to offer CAR T-cell therapy.

Nizar Mamdani, Executive Director of Nebraska Medicine's International Health-care says: "Our CAR T-Cell expert team is a remarkable example of the caliber of specialists and researchers working tirelessly to help provide better treatment options. Through collaborative strategic partnerships with 133 institutions in 45 countries, we continue to offer innovative treatment options, as well as tele-pathology and second opinion consultation services for cancer care, neurology, transplantation and other specialties to patients around the world".

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An artist's impression of the King Abdullah Bin Abdulaziz Medical City in Bahrain

Interview

The beauty of modular hospitals



Modular hospitals save time and money in design and construction and result in healthcare facilities that are attractive, innovative, efficient and well built. *Middle East Health* speaks to **Aladin Niazmand**, the Director of TAHPI, Director of Health Projects International (HPI) and CEO, KEF-TAHPI Design Studio about their modular hospital developments in the Middle East.

Middle East Health: Can you give a bit of background about TAHPI, where the company is based and what it does?

Aladin Niazmand: TAHPI was established in Australia more than 25 years ago, we have since become a multi-award-winning group that is recognized by the global medical industry for our

exceptional healthcare planning and design as well as standards, guidelines and specialist software development.

Today we have an international branch network that spans continents, from Sydney, Kuala Lumpur, Coimbatore (India), Dubai, Abu Dhabi, Muscat, Doha and London. We have our largest branch in the UAE and maintain JV offices in Hong Kong, Saudi Arabia and Lebanon.

We are a specialist firm of health planners. Health planning is defined as "Planning for the Health of People". This discipline includes Health Service Planning, Healthcare Architecture, Interior Design, Medical Planning, Equipment

Planning, Biomedical Engineering and Healthcare MEP Engineering. Our firm's tagline is A to Z of Health Planning and that is exactly what our services encompass – we are there from conception of the project all the way through feasibility studies, briefing, design and construction supervision. We offer all the services in this field in-house. On a wider spectrum we also create Health Facility Standards and Guidelines for 10 countries and regions. We create specialist Health Planning software which is used by more than 8000 hospitals and more than 3000 consultants.

MEH: What sets the company apart from its competitors when providing these services?

AN: We offer smart, rapid procurement and economically sustainable solutions. These two approaches and concepts have garnered tremendous recognition over the last few years, especially in the Middle East. Our company is the go-to choice for facilities which require state-of-the-art infrastructure, designed and delivered quickly using a combination of modular design and massively parallel processes for off-site prefabrication.

TAHPI is seen as a library of knowledge in the field of Healthcare Briefing and Design, partially through the CPD-approved educational courses conducted by us 3-4 times a year at Dubai Healthcare City.

We speak the language of healthcare professionals and managers. We listen carefully, adapt and respond. However, when necessary, we also educate and lead. We help the clients with difficult questions and give them the tools for decision making within the complex ecosystem of healthcare.

MEH: Cost is a key factor in hospital construction. What does TAHPI bring to the table that can help keep these costs down?

AN: TAHPI's mission is to pursue Rapid and Affordable procurement of Modular and Prefabricated Healthcare Facilities world-wide. We aim to design and construct healthcare facilities ranging from small rural clinics to multispeciality teaching hospitals and medical cities by pioneering modular design hospitals, built and assembled in the factory, ready to operate. The estimated cost reduction (by QS analysists) is 30% less than conventional construction. This requires decades-long investment in all aspects of the profession from rapid briefing based on ready-to-use but customisable components. These are assembled in perfectly formed, neat and modular plans with optimum flows and adjacencies. The plans remain highly adaptive where any functional unit can be changed to any other unit when necessary in the future. All plans remain expandable in multiple ways without being land-locked within finite shapes or odd one-off configurations. TAHPI's modular designs are factory friendly and designed for 50-plus year life span, easy maintenance and economical operation.

MEH: Does the company focus exclusively on new build hospitals or does it also do building conversions?

AN: We cover every permutation of facility procurement from new Greenfield projects to refurbishments and expansions. Internationally, more than 70% of all healthcare projects are refurbishments and expansions. The trick is to make every step in the refurbishment and expansion to bring the facility closer to perfection rather than accept a build-up of compromises. Conversions, from one use to another is also a TAHPI speciality. We have often converted office buildings and residential buildings into successful hospitals using a variety of smart techniques. We know how to overcome the typical restrictions of such projects from low floor-to-floor heights to restrictive building configuration, inadequate patient sized lifts and wrong MEP provisions.

MEH: TAHPI has completed several hospital construction projects in Australia and Asia. How long has the com-

pany been operating in the Middle East and what projects has it completed in this region?

AN: TAHPI has designed over 250 hospital projects in a wide range of disciplines, both public and private.

The first project that initially brought us into the UAE was winning the masterplanning and needs analysis tender for Al Wasl Hospital, now known as Latifa Hospital [in Dubai]. That was in 2008 and we have made UAE home for 10 years now. Using Dubai as the main regional hub with close to 80 specialist staff, TAHPI has been responsible for the design of two Medical Cities in the Kingdom of Saudi Arabia and one in Bahrain. Through this office TAHPI has designed 12 private hospitals in the UAE and the University Cancer Care Hospital in Muscat – a major new healthcare facility in that city. TAHPI has prepared healthcare capacity planning for the governments of Dubai and Abu Dhabi twice and developed the new Health Facility Guidelines for Abu Dhabi. TAHPI has prepared more than 20 feasibility studies for a variety of projects in the region. The company is currently completing the new Health Facility Guidelines for Dubai.

MEH: Hospital design has evolved substantially over the past decade. Where does TAHPI look to ensure that its hospital designs are innovative and forward-looking?

AN: One of TAHPI's biggest innovative achievements was the development of our web-based Health Facility Briefing System (HFBS) used for the rapid procurement of standards-based health facility briefs, room data sheets, room layouts, equipment schedules, budgeting, etc.

This tool revolutionises the accessibility of ready-to-use information, improves accuracy and reduces time in which healthcare facilities are designed. The time saving can be used for true innovation rather than re-discovering common elements of good practice every single time by every design team.

The second and even more revolutionary innovation, which I have men-

tioned earlier in terms of cost cutting, are the 'modular' hospitals or 'catalogue' hospitals.

It became clear to me that there was a lot of repetition in the design and building of hospitals. Discussions with clients were taking place on every aspect of every room in every department in a similar manner. But after a lot of timewasting, many facilities were roughly arriving at the same conclusions.

As investors or developers may only commission two hospitals in their careers – they were not realising how much time and effort was being wasted going over the same ground. The same questions – the same answers, the same mistakes and the same solutions in constant repetition. They did not question the fact that they were paying for solutions which were already discovered and used by others around the world because the consultants gave the impression that everything was "bespoke", "purpose designed" and that "innovation" demanded it.

To me, the entire process was shocking in its waste of human knowledge, energy, time and money. Because of self-interest in doing "new" work and earning fees, no-one else was challenging the status quo. It is no surprise that every element of healthcare facility design and procurement is more expensive than is reasonable. This does not happen in other industries, where the products get better and more innovative every year whilst the price drops. That is the magic of the Industrial Revolution. Design to perfection once, then build as many of them as there is a market will buy.

Operational models for such products also tend to converge around just a few aspects. Just look at the number of large plans available and the operational models of the airlines. They are very similar and competitors and users don't mind.

As a separate line of business, we decided to bring that model into health-care facilities. As a start, we made modular pre-designed hospitals, less than 12 models available in a catalogue form. They range from as small as 18-bed remote regional hospitals to 500-bed teaching hospitals. The clients can buy them at a fraction of the normal design

fee to suit a variety of land sizes, height limits and specialties. Alternatively, they can pay nothing for the design, but get it delivered off our factory and assembled (dry) on the site. The result is a conventional, strong, modern and long-lasting hospital.

So, what is the catch? Under this scheme, the client will not "own" the design. The same design may be built by another client in another city with minor customisations. By accepting that, they are effectively sharing the cost of design with hundreds of other clients around the world. That is no different to driving the same car as a million others who have chosen that brand of car and pay nothing for its design.

This also has the benefit of considerable time saving (around 30%) and cost saving (around 30%). The first of the TAHPI Modular Catalogue Hospitals, called Meitra, with more than 220 beds over 6 storeys was completed and handed over in 2017. It was over 80% built at the KEF factory, delivered and dry-assembled on its site in Calicut, Kerala, India. The same year, it won the best hospital design award.

MEH: Are there specific challenges to building hospitals in the Middle East that you don't see in other regions? How do you overcome these?

AN: TAHPI initially faced challenges in get¬ting our regional clients to understand the difference between Healthcare Facility, Healthcare Service and simple Real Investment. A lot of clients were comparing healthcare facilities with what they were familiar with, such as hotels. They over-emphasised multi-storey lobbies with polished granite and tended to see that as a sign of quality. Presentation is important in healthcare facilities, but reputations are gained or lost based on outcomes. Furthermore, many decisions were being taken based on intuition or by limited opinion polling. Business cases were also based on techniques often used for "marketing and market research" rather than the science of healthcare service planning.

I am happy to see real evidence that our efforts have made a big impact in the region and the results are much better. Compared to 10 years ago, I now see a real appreciation for the role of specialist heath planners, focussing on correct planning, efficiency, flows and flexibility.

Similarly, doing a proper service plan and full financial feasibility study is no longer a rarity, as through the Capacity Planning work, a lot of the base information is now given away by the health authorities for free.

Furthermore, a focus on building hospitals alone is not sufficient. We have seen a shift in the emphasis towards increasing throughput, shortening the length of stay and increasing the occupancy levels. These have almost the same impact as building more facilities. However, achieving such efficiencies sometimes requires a surgical operation on the facility itself.

MEH: What are the main countries in the Middle East where you are doing business and what is the outlook for the market over the next 10-15 years?

AN: Our work within the UAE itself is actually small compared to the work we do from the UAE for the whole region. The UAE has been a fantastic regional hub for us to serve clients in the wider region from a strategically central location that is easy to reach, stable and very pleasant. For example, we are working on the Sultan Qaboos Cancer Centre in Muscat, Oman and are completing our project on the King Abdullah Medical City in Bahrain from our UAE base.

We will continue our work here in the GCC where we have become well known. In terms of the Middle East we aim to work in all countries as soon as the opportunity arises, but I think the UAE will always be our main regional hub. From this base we have also been venturing into the emerging African market, we just finished designing a major university hospital in Kampala, Uganda. We have done Health Facility design guidelines and clinical service planning for certain regions in Africa on behalf of UNICEF.

Another focus of our work is in the northern emirates of the UAE where we see a lot of upgrades and some new facilities being developed.



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The factory in Zakroczym is one of the assets the company is most proud of. It is extremely modern and equipped not only with the most up to date technology and newest generation of machinery for drug production, but also with pro-ecological solutions and systems aiming to increase the quality and safety of work. The factory gained the European GMP (Good Manufacturing Practice) Certification, GLP (Good Laboratory Practice) Certification, and the Quality Management Systems ISO 9001:2008 Certification. These practices allow successful completion of contract manufacturing projects and individual development activities of clients' private labels. LEK-AM – your trusted and honest partner in the Polish pharmaceutical industry!

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Epidemiological findings of major chemical attacks in the Syrian war are consistent with civilian targeting: a short report

By Jose M. Rodriguez-Llanes, Debarati Guha-Sapir, Benjamin-Samuel Schlüter and Madelyn Hsiao-Rei Hicks

Abstract

Evidence of use of toxic gas chemical weapons in the Syrian war has been reported by governmental and nongovernmental international organizations since the war started in March 2011. To date, the profiles of victims of the largest chemical attacks in Syria remain unknown. In this study, we used descriptive epidemiological analysis to describe demographic characteristics of victims of the largest chemical weapons attacks in the Syrian war. We analysed conflict-related, direct deaths from chemical weapons recorded in non-government-controlled areas by the Violation Documentation Center, occurring from March 18, 2011 to April 10, 2017, with complete information on the victim's date and place of death, cause and demographic group. 'Major' chemical weapons events were defined as events causing ten or more direct deaths.

As of April 10, 2017, a total of 1206 direct deaths meeting inclusion criteria were recorded in the dataset from all chemical weapons attacks regardless of size. Five major chemical weapons attacks caused 1084 of these

documented deaths. Civilians comprised the majority (n = 1058, 97.6%) of direct deaths from major chemical weapons attacks in Syria and combatants comprised a minority of 2.4% (n = 26). In the first three major chemical weapons attacks, which occurred in 2013, children comprised 13%-14% of direct deaths, ranging in numbers from 2 deaths among 14 to 117 deaths among 923. Children comprised higher proportions of direct deaths in later major chemical weapons attacks, forming 21% (n = 7) of 33 deaths in the 2016 major attack and 34.8% (n = 32) of 92 deaths in the 2017 major attack. Our finding of an extreme disparity in direct deaths from major chemical weapons attacks in Syria, with 97.6% of victims being civilians and only 2.4% being combatants provides evidence that major chemical weapons attacks were indiscriminate or targeted civilians directly; both violations of International Humanitarian Law (IHL). Identifying and quantifying chemical weapons violations requires inter-disciplinary collaboration to inform international policy, humanitarian intervention and legal action.

Background

The use in war of chemical weapons was condemned by the general opinion of the civilized world and prohibited with the signing of the 1925 Geneva Protocol^[1]. Further prohibition includes the Conven-

tion on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction (CWC), which became binding international law in 1997^[2]. In violation of these prohibitions, some parties to war

have used chemical weapons in conflicts^[3], including in Syria. Evidence of use of chemical weapons in Syria in the form of numerous toxic gas attacks has been reported by governmental and non-governmental international organizations since



A screenshot from Al Jazeera news video of the chemical weapons attack in Khan Sheikhoun, Syria in April 2017.

the Syrian war started in March 2011. Joint investigations by the Organization for the Prohibition of Chemical Weapons (OPCW) with the United Nations (UN) between April and November 2013 confirmed the use of chemical weapons in the Ghouta area of Damascus on 21 August 2013 and on a smaller scale, in Jobar on 24 August 2013, Saraqueb on 29 April 2013, Ashrafiah Sahnaya on 25 August 2013 and Khan Al Asal on 19 March 2013[4]. Later reports provided evidence with a high degree of certainty that chlorine gas was used as a weapon in the villages of Talmenes, Al Tamanah, and Kafr Zita from April to August 2014^[5]. On 21 August 2015, the OPCW fact-finding mission (FFM) reported on the investigation of several incidents in the Idlib governorate between 16 March 2015 and 20 May 2015 and concluded that these gas attacks likely

involved the use of sulphur mustard and in occasions combined with chlorine^[6]. The Syrian American Medical Society (SAMS) carried out parallel investigations involving the collection by medical staff of biological samples taken from the many patients treated after gas attacks and environmental samples collected from the area of attacks. SAMS identified the use of three toxic gases - Sarin, chlorine and mustard agents - and confirmed the findings of OPCW-UN inves-tigations^[7]. In April 4, 2017 missiles launched from air allegedly loaded with toxic chemical gases attacked the town of Khan Sheikhoun in Idlib, Syria. The Violations Documentation Center (VDC) reported at least 92 identi- fiable deaths by the time of this study^[8] and others, even more^[9]. The medical humanitarian NGO, Médecins Sans Frontières (MSF) concluded that at least

two toxic gases, Sarin and chlorine, may have been used in these attacks, based on evidence from MSF medical teams supporting the emergency department of Bab Al Hawa hospital and other hospitals^[10]. A joint FFM by the OPCW-UN reported the presence of Sarin or a Sarin-like substance in laboratory samples taken by the FFM team during the autopsies of three victims by this attack^[11]. To the date of this study, the Joint Investigative Mechanism (JIM) of the OPCW/UN, based on the FFM reports, concluded that the Syrian Air Force was the perpetrator of at least three attacks with chlorine (Kafr Zita - 18 April 2014, Omenas - 16 March 2015 and Binnish, 24 March 2015). It also concluded that the Islamic State of Iraq and the Levant (ISIS/ ISIL) perpetrated at least one attack with mustard agent (Mare'e, 21 August 2015[12]. Investigations and evidence of the use

of chemical weapons in Syria reported by governmental and non-governmental international organizations are essential components of civilian protection.

The research community has so far contributed relatively little to civilian protection or to understanding the public health consequences of chemical weapons attacks in Syria^[13–16]. In earlier studies we described patterns of direct deaths and victim characteristics caused by the range of weapons used in the Syrian war from the beginning of the war in March of 2011 through December 2016^[15, 16]. Here we use descriptive epidemiological analysis to address in detail the fundamental question of who have been the victims of the largest chemical weapons attacks in the Syrian war from March 18, 2011 to April 10, 2017.

Methods

Data were obtained with permission from the VDC^[8], a non-profit, non-governmental independent organisation that tracks and documents in the public domain warrelated deaths from the beginning of the Syrian war. Direct deaths documented by the VDC are arguably a verifiable minimum; most other sources report higher numbers but are without a comparable verification protocol^[17, 18]. Only the VDC systematically reports sex, age category (children versus adult), and victim's status (civilian versus combatant) of each recorded direct death from the Syrian war, thereby making these data particularly useful for epidemiological analysis of the impact of weapons on the Syrian civilian population[15-18].

The VDC applies international standards for documentation of human rights violations by a ground network consisting of a minimum 30 internationally-trained field reporters^[15, 16]. Field reporters collect data in three steps. First, initial information on one or more victims is gathered, mainly from hospitals, morgues, relatives of the victims, and media sources. Second, the initial report is further confirmed, where possible, by supporting information on victims such as videos or photographs. Third, key information missing on victims is actively investigated until completion of record. VDC registries are verified daily, updated with new information and records for each death: demographics, date, loca-

tion, cause of death and civilian versus combatant status. The VDC identifies combatant deaths by an iterative process including multiple sources of information and validation. All those identified as combat- ants by VDC in our analyses had information on military rank or armed group (n = 26). Given that ascertaining information on victims in governmentcontrolled areas is often challenging, as stated by others conducting studies on the Syrian war^[16, 19], we analysed data from non- government-controlled areas. Our inclusion criteria were: conflict-related, direct deaths from chemical weapons attacks, occurring from March 18, 2011 to April 10, 2017, with complete information on the victim's date and place of death, cause and demographic group (adult male, adult female, child). Chemical weapons were defined as toxic substances delivered in any form. This study focused on 'major' chemical weapons events, defined as those causing ten or more direct deaths thereby meeting the inclusion criteria set out by the authors of this study. For the purposes of this study, we defined children as individuals younger than 18 years of age, consistent with the Convention on the Rights of the Child^[20]. Further details on the VDC dataset and data collection are described elsewhere^[8, 15, 16].

Deaths from major chemical weapons attacks

A total of 1206 direct deaths meeting inclusion criteria were identified in the dataset from all chemical weapons attacks regardless of size during the study period. Five major chemical weapons attacks were identified that caused direct deaths of ten or more individuals. The five major chemical weapons attacks resulted in a total of 1084 documented direct deaths recorded as of 10 April 2017 and meeting study criteria. As is apparent from Table 1, VDC data indicate that nearly all of those who died from the five largest chemical attacks in Syria were civilians. Civilians composed 97.6% (n = 1058) of direct deaths from major chemical weapon attacks and combatants only 2.4% (n = 26). This extreme disparity in effect on victims suggests that chemical weapons attacks in Syria were indiscriminate or targeted against civilians, both being violations of The research community has so far contributed relatively little to civilian protection or to understanding the public health consequences of chemical weapons attacks in Syria.

International Humanitarian Law (IHL). The extreme disparity is also consistent with arguments that chemical weapon attacks were not as much a war tactic against opponents as a terror and displacement strategy against Syrian civilians.

Among the 1058 civilian direct deaths from major chemical attacks, civilian men carried the largest burden of death comprising over half of direct civilian deaths in the five major chemical attacks (n = 579, 54.7%), women 30.0% (n = 318) and children 15.2% (n = 161). Of the earliest four major chemical attacks, in 2013, two occurred in Aleppo (19 March 2013 and 13 April 2013) and one in Ghouta, Damascus suburbs (21 August 2013). In the 21 August 2013 attack in Damascus suburbs, which caused the largest number of 897 civilian deaths among the five major attacks, 30 % of the victims killed were women (Table 1). In the case of the Ghouta attack, independent investigations by OPCW/UN found positive for Sarin and Sarin signatures biological samples from various victims. The other two former attacks were field-investigated but were inconclusive on chemical used^[4]. After 3 years, on 12 December 2016, Jrouh village in Hama was bombed by two shells filled with Sarin gas which is a lethal toxic gas.

Table 1 Direct deaths of civilians and combatants attributed to major chemical weapons attacks in the Syrian war (March 18th, 2011 to April 10th, 2017)

| Location (city/village, province) | Date | Adult Males n (%) | Adult Females n (%) | Children n (%) | Civilian deaths per attack n (%) | Deaths per attack, % of total deaths an (%) |
|-----------------------------------|----------|-------------------------|---------------------|-------------------|----------------------------------|---|
| Khan Al Asal, Aleppo | 19-03-13 | 12 (54.5) | 7 (31.8) | 3 (13.6) | 22 (100.0) | 22 (1.8) |
| Sheikh Magsoud, Aleppo | 13-04-13 | 9 (64.3) | 3 (21.4) | 2 (14.3) | 14 (100.0) | 14 (1.2) |
| Ghouta, Damascus Suburbs | 21-08-13 | 524 ^b (56.8) | 282 (30.5) | 117 (12.7) | 897 (97.2) | 923 ^b (76.5) |
| Jrouh, Hama | 12-12-16 | 21 (63.6) | 5 (15.2) | 7 (21.2) | 33 (100.0) | 33 (2.7) |
| Khan Sheikhoun, Idlib | 04-04-17 | 39 (42.4) | 21 (22.8) | 32 (34.8) | 92° (100.0) | 92 (7.6) |
| Total | | 605 ^b (55.8) | 318 (29.3) | 161 (14.9) | 1058 (97.6) | 1084 ^b (89.9) |

All chemical weapons attacks caused a total of 1206 documented direct deaths. 'Major' chemical weapons attacks were defined as those causing ten or more direct deaths. Of which 26 deaths were of adult male combatants from the Free Syrian Army (FSA). Cocumented as of 10 April 2017. Source: VDC

Over a fifth of the immediate deaths from this attack were of children (n = 7). As can be seen in Table 1, children comprised higher proportions of direct civilian deaths in the last two of the five major chemical attacks during the study period. In particular, the most recent major chemical attack, on 4 April 2017 in Khan Sheikhoun, Idlib, where Sarin or Sarin-like substances were used[11], caused the highest proportion of deaths of children, who composed onethird of direct deaths from this attack (n = 32, 34.8%). As was the case in four of the five major chemical weapons at- tacks during the study period, no combatants were documented dead from the attack (Table 1), a finding that supports arguments that IHL was violated with respect to the protection of civilians.

Consequences of chemical attacks

Sarin and other nerve agents are organophosphorus compounds that attack the nervous system by interfering with degradation of the neurotransmitter acetylcholine at neuromuscular junctions. Death occurs from asphyxia due to loss of control and paralysis of muscles involved in breathing^[3, 21]. Exposure to Sarin can be fatal through dermal contact, by breathing air containing Sarin or by consuming contaminated food or water^[3, 21-23]. However, this intoxication risk is short-lasted as Sarin does not persist more than a 4-8 days in the environment^[22]. Chlorine gas is the elemental form of Chlorine and is a severe pulmonary, dermal as well as digestive irritant. Inhalation causes life-threatening respiratory distress and fluid accumulation in the lungs potentially leading to death by

suffocation^[7]. Sulfur mustard, commonly known as mustard gas, is a class of cytotoxic compounds. Sulfur mustard compounds can be severe dermal, conjunctival and pulmonary irritants, can cause severe burns and are carcinogenic as well as blistering agents^[3, 6, 7].

All of these toxic gases are heavier than air, causing the chemical agents to sink to low-lying areas to create a greater exposure hazard_[7, 23]. Because of this, civilians who shelter in basements, which typically offer greater protection from explosive attacks such as barrel bombs, are at a heightened risk of death from chemical attacks, such as from barrel bombs containing chlorine used in Syria^[7]. Being closer to the ground, children are more exposed to chemical agents. In addition, small children are at especially high risk from chemical agents as they have a higher body-surface-areato-mass ratio; skin that is more permeable, and high metabolic and respiratory rates^[24-26]. The first reaction to bombing is to take shelter, but people are often unaware that they must also close doors, windows and air vents to prevent gas entering^[7]. Populations subject to chemical attacks are usually uninformed on precautionary behaviors to reduce exposure and health consequences, pointing to the importance of public awareness campaigns such as those initiated in some areas of Syria^[7]. Barriers that need to be overcome for effective public awareness campaigns in conflict areas can include disrupted infrastructure, population displacement, lack of educational resources, and limited communication and movement in an insecure environment.

Recommendations: a call to advocacy and action

The UN Security Council (UNSC) and the world have condemned chemical attacks in Syria to little effect. In 2013, under President Bashar al-Assad, Syria became a State Party to the Treaty on the Chemical Weapons Convention as part of an agreement to acknowledge and relinquish its stocks of Sarin, Venomous Agent X, and mustard gas. Subsequently, use of nerve agents de- creased, but was replaced by increased use of chlorine gas^[7]. The UNSC Resolution 2209 condemned the use of chlorine gas as a weapon in Syria in 2015, yet chlorine attacks continued to be documented^[7]. Regarding the destruction of the chemical weapons production facilities under the 2013 agreement, one hangar remains undestroyed and the condition of two other stationary aboveground facilities is unknown due to the security situation. In May 2016 the UNSC passed Resolution 2286 condemning attacks on medical facilities and personnel. In November 2016 Syrian pro-government forces carried out a chemical attack against $medical\ personnel^{[27]}.$

It is essential that impartial and credible investigations of these chemical weapon attacks continue by the OPCW-UN and NGOs and that a structure of IHL standards and prohibitions exists. However, as suggested by this course of events, if violations of IHL against using chemical weapons are allowed to continue with impunity, then offenders have no incentive to end the use of chemical weapons until their goals are achieved, as can be argued is occurring in Syria. For

actors in conflict who find chemical attacks acceptable, moral condemnation by international bodies is ineffectual unless backed up by active prevention or consequences. Prevention by decreasing access to resources and components that are necessary to produce chemical weapons could potentially decrease the use of chemical weapons, but this can be difficult. For example, chlorine gas is relatively cheap to produce, is an agent commonly used in the chemical industry and is thus difficult to control^[28]. We suggest urgent attention to the strict control of commercial sales of chlorine, for example by a regulatory authority, given that its use has become normative in the Syrian war as a weapon^[7].

Increasing preparation, education and resources to deal with chemical attacks can decrease mortality and decrease the severity of injuries. Training of first response and medical personnel for appropriate responses to chemical attacks is an important measure to reduce casualties^[3, 7, 29]. Despite great effort by medical and support personnel in Syria, training in Syria has been limited by the insecure environment, lack of supplies and severe overwork of the medical personnel caring for casualties of war^[7, 29, 30].

Decontamination and protective equipment to minimize continued exposure to chemical agents is essential during rescue and treatment of chemical attack victims in order to reduce injuries and deaths^[3, 7, 29]. Sarin is highly toxic even in very small amounts, and when absorbed through skin or respiratory channels can cause death within a few minutes to 2 h^[3, 23]. Mustard agents produce the first symptoms in 2-24 h after exposure, have no antidote, cause long-term injuries and have a lower lethal capacity than Sarin-like substances^[3, 6]. Due to lack of adequate protective equipment, especially in besieged areas, first responders and medical staff in Syria have sickened and died from chemical contamination while treating victims of attacks, and cross-contamination of patients occurs^[7]. Personal Protection Equipment (PPE) kits for first responders and medical staff are an acute need[7, 29]. Severe shortages of antidotes such as atropine, ventilation equipment, protective equipment and means to clean or store contaminated clothing have increased chemical attack casualties in the Syrian war and continue to be critical unmet needs^[7, 29, 30]. We urge increasing supplies of these basic, critical resources to medical personnel working in Syria in order to improve survival and in order to decrease the immediate and long-term impacts of chemical weapon attacks

Long-term health effects of chemical exposure are not only generally unknown to local populations but can also last for years[3, 31]. The physical, neurological and mental health effects from chemical weapons exposure are both acute and long-term, requiring adequate resources for immediate treatment and for longterm effects. Some of the attacked areas are farming hamlets and are especially vulnerable to the potential contamination of food and the food chain by persistent agents such as mustard and nerve agents^[28, 32]. Even if people are aware of the risks, frequently there are no alternative sources to meet their basic needs. Hence, attacks on rural regions with Sarin may have additional effects^[31]. Having these facts in mind, risk communication, public awareness programs and monitoring for long-term effects are important public health measures to reduce the immediate and long-term burden of chemical attacks. The development of communications systems using social media and cell phone technology could provide wide-spread, rapid, public safety instructions, education and alerts for chemical weapons attacks[33, 34].

Epidemiological research on the public health impact of chemical weapons can increase awareness and information on the scope of effects on the population and can identify particularly vulnerable groups^[13]. Such information can inform policy and interventions. Increased interdisciplinary communication and collaboration between researchers, personnel in the field and NGOs gathering data and experience may be especially important in addressing the impact of armed conflict on populations.

Conclusions

We found that civilians comprised the vast majority of direct deaths from major chemical weapon attacks compared to combatants, to a degree that suggests that chemical weapon attacks in Syria were indiscriminate or targeted against civilians in violation of IHL. Children comprised higher proportions of direct deaths in the two most recent major chemical attacks of the study period, including in Khan Sheikhoun where they comprised one-third of all immediate deaths. The UNSC and other international bodies should not only investigate perpetrators of chemical attacks but also hold them accountable for their actions. Simultaneously, the international community needs to respond quickly with greater practical support to Syrian medical and emergency facilities so that they can meet the acute medical needs of a population targeted by chemical attacks.

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The datasets generated and analysed during the current study are available in the VDC database, http://www.vdc-sy.info/index.php/en/martyrs.

Ethics approval and consent to participate

The Ethical Board of the Université catholique de Louvain advised that informed consent was not required for analysis of these mortality data collected for purposes other than this study and in the public domain.

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KIMES 2018 hosts its biggest expo with more than 1300 exhibitors

The 34th annual KIMES (Korea International Medical & Hospital Equipment Show) was the largest in the event's history. Held from 15-18 March 2018 at the COEX exhibition centre in Seoul, South Korea, the exhibition hosted 1313 companies from 34 countries, more than in any other previous year.

Achieving this milestone in the event's history is a clear indication of the increasing significance of the show. It is also a clear sign that the world's leading medical device manufacturers and service providers recognise the importance of KIMES as a major platform for showing off their products to the Korean and East Asian markets.

As well as the many foreign companies exhibiting their products – 117 from the United States, 165 from China, 90 from Germany, among others – many of the of the exhibitors comprised Korean companies, including several leading global players such as Samsung and DK Medical Solutions.

According to KIMES organisers Korea E&EX Inc., more than 3500 foreign buyers attended this year's event. This points to the growing significance of Korean medical devices in foreign markets. This is, of course, a key reason for the event itself – that is the promotion Korean medical device exports.

Having spoken to several Korean companies at the event it is apparent that they are raising the bar with regard to quality and sophistication of their devices and by keeping their price point low they now provide strong competition to more well-known and established companies in the West.



Hyun Chul Oh, the marketing and sales director of Exoatlet stands next to the exoskeleton they had on show at KIMES 2018.

A case in point is the Korean company Exoatlet which has developed a robotic exoskeleton for rehabilitative walking assistance. Hyun Chul Oh, marketing and sales director of Exoatlet, explained that the exoskeleton's specifications are on a par or even better than its competitors in the United States, yet they can offer the product a substantially lower price point.

Oh talked a bit about the device, and explained that it has 24 modes to suit a variety of patient gaits – long step, short step, etc.

"The exoskeleton is currently being used in 40 Korean hospitals as a test bed," Oh said. It is being retailed in South Korea and will be commercialised this year in several other countries. "We have contracts with hospitals in Singapore, Malaysia and Thailand," he added.

"We will open subsidiaries in China, Japan, Europe and the US later this year," he said, adding: "We expect to complete our CE registration by the end of this year."

He explained that on a single charge the exoskeleton can run for eight hours — "the whole day, which is important for commercialisation purposes".

"Our competitor's products only run for three hours," he noted.

"In a single day, one system can be used for many patients ranging between 150-190 cm in height and up to a maximum of 100kg in weight."

Discussing the price for the device, he said: "In Korea it retails for US\$70,000. To third-party retailers we will sell it for \$45,000. Our competitors in the United States are selling a similar product for \$130,000."

"We believe our competitive price is important as we want to increase patient access to this innovative rehabilitative device," Oh explained.

Robots take over

The director of the Korea E&EX Inc remarked in his speech at the opening ceremony that he noticed when looking over the estimated 30,000+ products on show that, compared to previous years, there has been a definite swing in the focus of innovation from imaging devices to robotic devices. Exoatlet's exoskeleton is an example of this.

However, as well as the advanced robotic and imaging devices on show there were also a number of quite simple, but ingenious novel medical devices being exhibited.

EZpole

An example of one of these products is the EZpole developed by a small Korean company called mobiU. The EZpole is a clev-



Hyung Seok Kim, CEO mobiU, demonstrates the use of the EZpole - a wearable IV pole

erly designed, simple pole that attaches to a patient's shoulder to hold up an IV drip. The patient wears the device while walking around, giving them independent mobility while still having an IV drip attached and working.

Hyung Seok Kim, CEO mobiU, remarked that by enabling greater patient mobility, this speeds up recovery.

Auto needle removal instrument

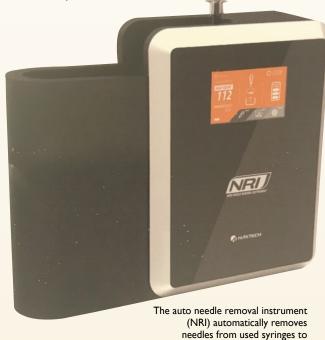
Another useful device launched at KIMES 2018 was the portable auto needle removal instrument (NRI-15M) developed by Korean company Hastechnology. The device was developed to prevent needle stick injuries, a common hazard in healthcare facilities. The NRI is simple to use. A healthcare worker places the used syringe with needle into the device. The device cleanly snaps off the needle from the syringe

and collects the used needles in a con-



A patient wears the simple, yet innovative EZ-pole – a wearable IV pole

tainer which can then be easily and safely discarded. The NRI has an LCD screen with indicators to keep track of the current state of separation of the needle from the syringe and will let the healthcare worker know when the needle container is full and ready for disposal.



prevent needle stick injuries.

Researchers find proteins that may govern memories that last a life time

In the tiny brain space where two nerve cells meet, chemical and electric signals shuttle back and forth, a messaging system that ebbs and flows in those synaptic spaces, sometimes in ways that scientists believe aid and abet learning and memory. But because most of the proteins found in those synapses die and renew themselves so rapidly, scientists have had a hard time pinning down how synapses are stable enough to explain the kind of learning and memory that lasts a lifetime.

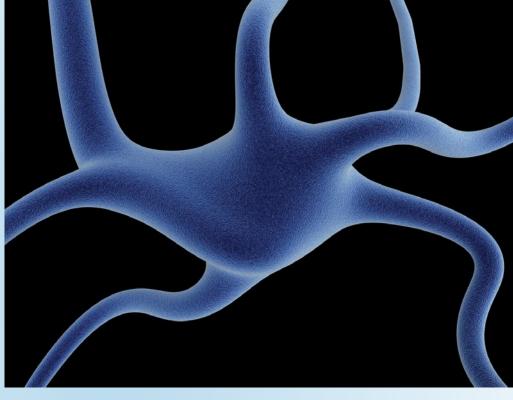
Now, Johns Hopkins neuroscientists report success in using large-scale studies of proteins and high-tech chemical analysis to discover 164 proteins within synapses in mice that outlast neighbouring proteins by weeks and months. These stable proteins, they say, may be part of the molecular machinery that governs long-term memory and learning — as well as loss of memory — in all mammals, including humans. A summary of their experiments is published in the 2 April 2018 issue of *Proceedings of the National Academy of Sciences*.

"We knew that the overall structure of synapses tends to be very stable, lasting at least a year in the brains of rats," says Richard Huganir, Ph.D., professor and director of the Solomon H. Snyder Department of Neuroscience and director of the Kavli Neuroscience Discovery Institute at the Johns Hopkins University School of Medicine.

"So, we reasoned, there must be proteins in those synapses that are long-lasting, too, and we believe we have found a lot of them."

To do so, Prof Huganir and his colleagues focused on a group of eight mice bred in the laboratory and fed with chow that contained a molecular tracer able to glom onto the animals' proteins.

The tracer was an organic compound called an amino acid, the building blocks of proteins. But these amino acids contained extra neutrons, which would make the protein "heavier" when analysed by a mass spectrometer.



The mice ate the food with "heavy" amino acids for seven weeks. During this period, long-lasting proteins tended to incorporate the heavy tracer at a slower rate than more short-lived proteins.

Then the mice received another seven weeks of food that contained "light" amino acids lacking the extra proton. Long-lived proteins turnover less frequently, and thus hang on to the heavy tracer.

The scientists then analysed brain tissue from two of the mice after the first seven weeks and two more mice after another seven weeks. They also put four of the mice into larger cages with tubes, beads and other objects to stimulate their brain activity and analysed brain tissue from two of them after each seven-week period.

Using a mass spectrometer, the scientists recorded the ratio of heavy to normal amino acids on 2,272 proteins located within synapses. Long-lived proteins retained more than half of the

heavy amino acids during the first sevenweek period.

Most of the proteins were short-lived, lasting a day or two, says Prof Huganir. But, the scientists found 164 proteins that lasted much longer – up to several weeks or months. Some are estimated to last for years.

Working with Akhilesh Pandey, M.D., Ph.D., at the Johns Hopkins McKusick/ Nathans Institute of Genetic Medicine, the research team next isolated and identified the long-lasting proteins. One of them belongs to the RAS signalling pathway, and others are linked with cellular scaffolding.

Prof Huganir and his team are continuing to study 50 of the most long-lived proteins among the group, some of which are estimated to last for years. As these "old" proteins can accumulate damage over time, he says his team will also be looking for any connections between the proteins and human age-related cognitive decline.

• doi: 10.1073/pnas.1720956115

Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

| Event | Date / City | Contact |
|--|--|---|
| ■ June 2018 | | |
| Middle East Obesity, Bariatric Surgery and Endocrinology Congress | 25-26 June 2018 Dubai, UAE | https://obesity-middleeast. conferenceseries.com/ |
| 24th World Nurse Practitioners & Healthcare Congress | 25-27 June 2018 Dubai, UAE | https://nursepractitioner.nursing- conference.com/middleeast |
| ■ July 2018 | | |
| 29th International Conference on Public Mental Health & Neurosciences | 16-18 July 2018 Dubai, UAE | https://mental-health. neurologyconference.com |
| 22nd World Nutrition and Pediatrics Healthcare Conference | 16-18 July 2018 Dubai, UAE | https://nutrition. pediatricsconferences.com |
| August 2018 | | |
| Middle East Obesity, Bariatric Surgery and Endocrinology Congress | 6-7 August 2017 Abu Dhabi, UAE | https://obesity-middleeast. conferenceseries.com |
| 28th International Conference on Cardiology and Healthcare | 9-11 August 2017 Abu Dhabi, UAE | https://healthcare.cardiology meeting.com |
| 9th International Conference on Food Safety and Health | 30-31 August 2018 Dubai, UAE | https://foodsafety.nutritional conference.com |
| September 2018 | | |
| 20th World Conference on Pharmaceutical Chemistry and Drug Design | 3-5 September 2018 Dubai, UAE | https://drug-chemistry. pharmaceuticalconferences.com |
| Egy Health Expo | 9-12 September, Cairo, Egypt | www.egyhealthexpo.com |
| 2nd International Conference on Prevention and Control of Infection | 13-15 September 2018, Dubai, UAE | https://go.evvnt.com/221370-0 |
| 4th International Anesthesia and Pain Medicine Conference | 17-18 September 2018 Dubai, UAE | https://anesthesiology. conferenceseries.com |
| 3rd Conference on Breast and Cervical Cancer | 27-28 September 2018 Abu Dhabi, UAE | https://breast-cervical. cancersummit.org |
| Fourth Annual MENA Internationa Orthopaedic Congress | 27-29 September 2018, Dubai, UAE | http://www.ptmg.com/ meeting-details/-358277 |
| October 2018 | | |
| 3rd Middle East International Dermatology & Aesthetic Medicine Conference & Exhibition | 4-6 October 2018, Dubai, UAE | www.meidamconf.com |









Agenda

Selected schedule of regional medical meetings, conferences and exhibitions

| Event | Date / City | Contact |
|--|--|---|
| 14th Conference on Infectious Diseases, Prevention a nd Control | 14-15 October 2018, Abu Dhabi, UAE | https://infectious-diseases. conferenceseries.com |
| 5th International Conference on Hypertension and Healthcare | 18-19 October 2018, Abu Dhabi, UAE | https://hypertension. cardiologymeeting.com |
| Abu Dhabi International Mental Health Conference | 19-20 October 2018, Abu Dhabi, UAE | https://go.evvnt.com/219604-2 |
| AHIMA World Congress (AWC) Healthcare Information Summit | 25-26 October 2018, Abu Dhabi, UAE | https://go.evvnt.com/221370-0 |
| November 2018 | | |
| 5th World Holistic Nursing Conference | 5-7 November 2018, Abu Dhabi, UAE | https://holistic. nursingconference.com |
| International Patient Experience Symposium | 12-14 November 2018, Abu Dhabi, UAE | https://pxsymposium.com |
| 7th International Conference on Chronic Obstructive Pulmonary Disease (COPD) | 15-16 November 2018, Dubai, UAE | https://copd. healthconferences.org |
| December 2018 | | |
| 12th International Conference on Orthopedics and Sports Medicine | 10-11 December 2018, Dubai, UAE | https://orthopaedics. healthconferences.org |
| 19th Annual Conference on Inhalation Toxicology | 13-14 December 2018, Dubai, UAE | https://inhalationtoxicology. conferenceseries.com |
| 13th Annual Conference on Dementia and Alzheimer's | 13-15 December 2018, Abu Dhabi, UAE | https://dementia. neuroconferences.com |



List your conference:

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

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

As one of the top ten pediatric hospitals in the United States, as ranked by *U.S. News & World Report*, Children's Hospital of Pittsburgh of UPMC is a pioneer in the field of liver transplantation, which has proven to be a life-changing solution for patients with metabolic disease.

Liver transplantation can dramatically reduce symptoms, and in cases like maple syrup urine disease (MSUD), can provide a cure.

Liver transplantation is more than a lifesaving procedure; it's also an attractive approach for improving quality of life for many patients with metabolic disease. In 2004, we developed the protocol for liver transplantation for MSUD. Today, we've performed more transplants on patients with MSUD than any other center in the world. That's more than 65 patients with a 100-percent survival rate. All of these patients show normal liver function, have avoided the risk of neurological complications, and enjoy an unrestricted diet.

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

Since the inception of our program in 1981, our world-renowned experts have performed more than 1,700 liver transplants — that's more than any other center in the United States — with survival rates that exceed national averages. Additionally, we've performed more than 320 liver transplants for patients with metabolic disease, which is more than any other center, including adult facilities. Also, we're leaders in living-donor liver transplants, which eliminate wait times for a deceased donor and can provide excellent outcomes.

Find out more about our excellent outcomes and extraordinary care.

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

